Spasticity in children and young people with non-progressive brain disorders: management of spasticity and co-existing motor disorders and their early musculoskeletal complications

National Collaborating Centre for Women's and Children's Health

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This guideline has been fully funded by NICE. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Implementation of this guidance is the responsibility of local commissioners and/or providers

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1 Guideline summary

1.1 Guideline development group membership, NCC-WCH staff and acknowledgements

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1.2 Foreword

This guideline covers the management of spasticity and co-existing motor disorders and their early musculoskeletal complications in children and young people (from birth up to their 19th birthday) with non-progressive brain disorders.

Cerebral palsy is the most common condition associated with spasticity in children and young people. The incidence of cerebral palsy is not known, but its prevalence in the UK is 186 per 100,000 population, with a total of 110,000 people affected. The guideline covers the management of spasticity associated with cerebral palsy, but not all aspects of the management of cerebral palsy.

The impact of spasticity and co-existing motor disorders and their early musculoskeletal complications on the child or young person varies. Common problems include impaired motor function affecting the person's ability to participate in society, pain from muscle spasms, motor developmental delay and difficulties with daily care due to the onset of secondary complications of spasticity. Management should be tailored to meet the problems faced by the individual child or young person and their individual goals.

Some of the guideline recommendations refer to the Gross Motor Functional Classification System (GMFCS). This is a five-point scale that describes gross motor function: level I, walks without restrictions; level II, walks without assistive devices; level III, walks with assistive devices; level IV, has limited self-mobility; level V, has severely limited self-mobility even with assistive devices.

There is considerable variation in practice in managing spasticity, including variation in the availability of treatments and the intensity of their use. This guideline will help healthcare professionals to select and use appropriate treatments for individual children and young people.

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.

1.3 Care pathway

The care pathways are presented in separate files

1.4 Key priorities for implementation

Number	Recommendation	See section
	Principles of care	**4**
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.	4
3	If a child or young person receives treatment for spasticity from healthcare professionals outside the network team, this should be	4

Number	Recommendation	See section
	planned and undertaken in discussion with the network team to ensure integrated care and effective subsequent management.	
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.	4
8	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.	4
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.	4
	Physical therapy (physiotherapy and/or occupational therapy)	**4**
20	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.	4
34	Following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen or orthopaedic surgery, provide an adapted physical therapy programme as an essential component of management.	4
	Intrathecal baclofen	**8**
82	Consider treatment with continuous pump-administered intrathecal baclofen[*] 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).	8
	Orthopaedic surgery	**9**
107	An assessment should be performed by an orthopaedic surgeon within the network team if: • based on clinical findings (see recommendation 16) or radiological monitoring, there is concern that the hip may be	9

[*] At the time of publication (June 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.

Number	Recommendation	See section
	displaced • based on clinical or radiological findings there is concern about spinal deformity.	

1.5 Recommendations

Number	Recommendation	See section
	Principles of care	**4**
	Delivering care	4
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.	4
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 paediatric neurology, may be provided locally or regionally.	4
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.	4
	Management programmes	4
4	Following diagnosis, ensure that all children and young people with spasticity are referred without delay to an appropriate member of the network team.	4
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.	4
6	When formulating a management programme take into account its possible impact on the individual child or young person and their family.	4
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.	4
8	Identify and agree with children and young people and their parents or carers assessments and goals that: • are age and developmentally appropriate	4

Number	Recommendation	See section

	• focus on the following domains of the World Health Organization's International Classification of Functioning, Disability and Health:
	  ○ body function and structure
	  ○ activity and participation.	

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.	4
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.	4
	Supporting the child or young person and their family	
11	Offer contact details of patient organisations that can provide support, befriending, counselling, information and advocacy.	4
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).	4
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.	4
	Monitoring	
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.	4
15	The network of care should have a pathway for monitoring children and young people at increased risk of hip displacement.	4
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.	4
17	Perform a hip X-ray to assess for hip displacement: • if there are concerns about possible hip displacement • at 24 months in children with bilateral cerebral palsy.	4

Number	Recommendation	See section
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.	4
19	Consider repeating the hip X-ray every 6 months in children and young people with a hip migration: • greater than 15% **or** • increasing by more than 10 percentage points per year.	4
	Physical therapy (physiotherapy and/or occupational therapy)	**4**
	General principles	4
20	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.	4
21	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.	4
22	Give children and young people and their parents or carers verbal and written 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.	4
23	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.	4
24	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.	4
25	Ensure that any equipment or techniques used in the physical therapy programme are safe and appropriate, in particular in children or young people with any of the following: • poorly controlled epilepsy • respiratory compromise	4

Number	Recommendation	See section
	• increased risk of pulmonary aspiration • increased risk of bone fracture due to osteoporosis (for example, those who are non-ambulatory, malnourished or taking anticonvulsant therapy).	
26	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).	4
	Specific strategies	4
27	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.	4
28	When using 24-hour postural management strategies consider, on an individual basis, the following techniques: • low-load active stretching — the child or young person actively stretches their muscles with the aim of increasing range of movement • low-load passive stretching — sustained stretching using positioning with equipment, orthoses or serial casting.	4
29	Offer training to parents and carers involved in delivering postural management strategies.	4
30	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.	4
31	When undertaking task-focused active-use therapy consider an intensive programme over a short time period (for example, 4–8 weeks).	4
32	Consider muscle-strengthening therapy where the assessment indicates that muscle weakness is contributing to loss of function or postural difficulties.	4
33	Direct muscle-strengthening therapy towards specific goals using progressive repetitive exercises performed against resistance.	4
34	Following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen or orthopaedic surgery, provide an adapted physical therapy programme as an essential component of management.	4
35	Ensure that children and young people and their parents or carers understand that following treatment with botulinum toxin type A treatment, continuous pump-administered intrathecal baclofen treatment or orthopaedic surgery an adapted physical therapy programme will be an essential component of management.	4

Number	Recommendation	See section
	Continuing assessment	4
36	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.	4
	Orthoses	**5**
	General principles	5
37	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.	5
38	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.	5
39	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.	5
40	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.	5
41	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.	5
42	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.	5
43	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	5

Number	Recommendation	See section
	◦ 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.	
44	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.	5
	Specific uses	5
45	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).	5
46	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.	5
47	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.	5
48	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.	5
49	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.	5
50	Consider body trunk orthoses for children and young people with co-existing scoliosis or kyphosis if this will help with sitting.	5
51	Consider the overnight use of orthoses to: • improve posture • prevent or delay hip migration • prevent or delay contractures.	5
52	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.	5
53	If an orthosis is used overnight, check that it: • is acceptable to the child or young person and does not cause injury	5

Number	Recommendation	See section
	• does not disturb sleep.	
	Continuing assessment	5
54	Review the use of orthoses at every contact with the network team. 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.	5
	Oral drugs	**6**
55	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).	6
56	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).	6
57	If oral diazepam is initially used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.	6
58	Give oral diazepam treatment as a bedtime dose. If the response is unsatisfactory consider: • increasing the dose **or** • adding a daytime dose.	6
59	Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect.	6
60	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.	6
61	If adverse effects (such as drowsiness) occur with oral diazepam or oral baclofen, think about reducing the dose or stopping treatment.	6
62	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.	6

Number	Recommendation	See section
63	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.	6
64	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[†], levodopa[‡] or baclofen[§].	6
	Botulinum toxin type A	**7**
	General principles	7
65	Consider botulinum toxin type 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.	7
66	Consider botulinum toxin type 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.	7
67	Consider botulinum toxin type A[**] treatment after an acquired non-progressive brain injury if rapid-onset spasticity is causing postural or functional difficulties.	7
68	Consider a trial of botulinum toxin type A[††] treatment in children and young people with spasticity in whom focal dystonia is causing serious problems, such as postural or functional difficulties or pain.	7
69	Do not offer botulinum toxin type A treatment if the child or young person:	7

[†] At the time of publication (June 2012), trihexiphenidyl 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

[‡] At the time of publication (June 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

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

[**] At the time of publication (June 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. Where appropriate, informed consent should be obtained and documented.

[††] At the time of publication (June 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

Number	Recommendation	See section
	• has severe muscle weakness • had a previous adverse reaction or allergy to botulinum toxin type A • is receiving aminoglycoside treatment.	

70	Be cautious when considering botulinum toxin type A treatment if:
	
	• the child or young person has any of the following
	    o a bleeding disorder, for example due to anti-coagulant therapy
	    o generalised spasticity
	    o fixed muscle contractures
	    o 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 34).
		7

71	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.	7

72	When considering botulinum toxin type A treatment, provide the child or young person and their parents or carers with information about:
	
	• the possible benefits and the likelihood of achieving the treatment goals
	• what the treatment entails, including:
	    o the need for assessments before and after the treatment
	    o the need to inject the drug into the affected muscles
	    o the possible need for repeat injections
	    o 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
	• important adverse effects (see recommendation 74).
		7

73	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.	7
	Delivering treatment	7

74	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:
	    o swallowing difficulties
	    o breathing difficulties
	• how to recognise signs suggesting these complications are
		7

Number	Recommendation	See section
	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.	
75	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).	7
76	Consider ultrasound or electrical muscle stimulation to guide the injection of botulinum toxin type A.	7
77	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.	7
78	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.	7
79	If the use of 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.	7
80	Ensure that children and young people who receive treatment with botulinum toxin type A are offered timely access to orthotic services.	
	Continuing assessment	7
81	Perform a careful 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.	7
82	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.	7

Number	Recommendation	See section
	Intrathecal baclofen	**8**
	General principles	8
83	Consider treatment with continuous pump-administered intrathecal baclofen[‡‡] 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).	8
84	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.	8
85	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.	8
86	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.	8
87	If continuous pump-administered intrathecal baclofen is indicated in a child or young person with scoliosis in whom a spinal fusion procedure is likely to be necessary, implant the infusion pump before performing the spinal fusion.	8
88	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.	8
89	When considering continuous pump-administered intrathecal baclofen, inform children and young people and their parents or carers verbally and in writing about continuous pump-administered intrathecal baclofen. Give information about the following: • the surgical procedure used to implant the pump • the need for regular hospital follow-up visits • the requirements for pump maintenance	8

[‡‡] At the time of publication (June 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.

Number	Recommendation	See section
	• the risks associated with pump implantation, pump-related complications and adverse effects that might be associated with intrathecal baclofen infusion.	
	Intrathecal baclofen testing	8
90	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.	8

91	Before intrathecal baclofen testing, inform children and young people and their parents or carers verbally and in writing 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.
		8

92	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.	8
93	The test dose or doses of intrathecal baclofen should be administered using a catheter inserted under general anaesthesia.	8
94	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.	8
95	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).	8
96	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.	8

Number	Recommendation	See section
97	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.	8
98	Initial and post-test assessments should be performed by the same healthcare professionals in the specialist neurosurgical centre.	
	Continuous pump-administered intrathecal baclofen	8
99	Before implanting the intrathecal baclofen pump, inform children and young people and their parents or carers, verbally and in writing, 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.	8
100	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 96).	8
101	Support children and young people receiving treatment with continuous pump-administered intrathecal baclofen and their parents or carers by offering regular follow-up and a consistent point of contact with the specialist neurosurgical centre.	8
102	Monitor the response to continuous pump-administered intrathecal baclofen. This monitoring should preferably be performed by the healthcare professionals in the regional specialist centre who performed the pre-implantation assessments.	8
103	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).	8
104	Titrate the dose of intrathecal baclofen after pump implantation, if necessary, to optimise effectiveness.	8

Number	Recommendation	See section
105	If treatment with continuous pump-administered intrathecal baclofen does not result in a satisfactory response (see recommendation 104), 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.	
106	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.	8
107	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.	8
	Orthopaedic surgery	**9**
108	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.	9
109	An assessment should be performed by an orthopaedic surgeon within the network team if: • based on clinical findings (see recommendation 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.	9
110	Consider an assessment by an orthopaedic surgeon in the network team for children and young people with: • hip migration greater than 15% **or** • hip migration percentage increasing by more than 10 percentage points per year.	9
111	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.	9
112	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	9

Number	Recommendation	See section
	• 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.	
113	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.	9
114	The decision to perform orthopaedic surgery to improve gait should be informed by a thorough pre-operative functional assessment, preferably including gait analysis.	9
115	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.	9
116	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.	
	Selective dorsal rhizotomy	**10**
117	Offer selective dorsal rhizotomy to improve walking ability in children and young people with spasticity only as part of a national research programme designed to collect data on standardised long-term outcomes.	10

1.6 Key research recommendations

Number	Research recommendation	See section
	Inhibitors of functional ability	**4**
1	What are the greatest inhibitors of functional ability in children and young people with upper motor neuron lesions? Why this is important Children and young people with upper motor neuron lesions may experience: • reduced muscle strength • selective muscle control • spasticity. The relationships between these factors, and the extent to which the child or young person can develop or maintain functional ability, remain unclear. Prospective cohort studies, or large cross-sectional studies, are needed to explore the relationships between positive and negative effects of upper motor neuron lesions and to determine	4

Number	Research recommendation	See section
	which factor is the greatest inhibitor of functional ability. The studies should incorporate classification of functional ability based on validated scales, such as the GMFCS.	
	Postural management	**4**
2	What is the optimal postural management programme using a standing frame in children aged 1–3 years? Why this is important Children who are at GMFCS level IV or V may benefit from using a standing frame as part of a postural management programme. Clinical benefits might include improved weight bearing and walking and, as a result, reduced hip migration. Postural management programmes involving the use of standing frames are part of established clinical practice. However, the individual elements that optimise the effectiveness of such programmes merit further research. The research should compare the effectiveness of postural management programmes that incorporate different durations and timings of standing frame use. For example, what is the effectiveness of 1 hour per day in a single session compared with two sessions of 30 minutes per day? The research should be conducted in children aged 1–3 years. These children are likely to benefit the most from using standing frames (in terms of developing well-formed femoral heads and acetabulums) and they should find the use of standing frames acceptable (because they are lighter than older children and they do not have severe contractures).	4
	Botulinum toxin	**7**
15	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? Why this is important The Guideline Development Group's (GDG's) recommendation to consider offering botulinum toxin type A to children and young people with focal spasticity of an upper or lower limb reflected available evidence relating to the safety and effectiveness of botulinum toxin type A. In making their recommendations, the GDG emphasised the importance of establishing individualised goals that justify the use of this potentially harmful toxin to treat spasticity. The cost of the procedure combined with the risk of side effects means that clear treatment goals that will positively influence the child or young person's life should be identified before offering this treatment. The evidence reviewed for the guideline provided limited support for botulinum toxin type A in terms of achieving clinically important goals (including those related to function), and this discouraged the GDG from making a strong recommendation to offer treatment with botulinum toxin type A to all children and young people who are at GMFCS level I, II or III. Further research is needed to evaluate the effectiveness of botulinum toxin type A in comparison with other treatment options, particularly when used over long time periods (for	7

Number	Research recommendation	See section
	example, 10 years) and involving repeat injections, in this population of children and young people. Outcomes relating to improvements in gross motor function and participation in activities, and the psychological impacts of these factors, should be evaluated as part of the research.	
	Intrathecal baclofen	**8**
21	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? Why this is important The GDG's recommendation to consider offering continuous pump-administered intrathecal baclofen focused on children and young people in whom the use of appropriate non-invasive treatments did not relieve difficulties associated with spasticity (specifically pain or muscle spasms, posture or function, or ease of care). Such children and young people will typically be at GMFCS level IV or V. Further research is needed to evaluate the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared with usual care in these children and young people. Relevant research designs include randomised controlled trials, prospective cohort studies and qualitative studies. The outcomes to be investigated as part of the research include: quality of life; reduction of pain; reduction of tone; acceptability and tolerability; participation or inclusion; and adverse effects and their association with any potential predisposing factors.	8
	Selective dorsal rhizotomy	**10**
25	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? Why this is important The available evidence relating to selective dorsal rhizotomy suggests that the procedure results in some short- and medium-term improvements in motor function. The effects reported were not consistent across all studies nor sustained across all durations of follow-up investigated (6-24 months). The GDG considered that if the observed improvements could be maintained through to adult life then the outcomes of selective dorsal rhizotomy would be clinically important and this would be a cost effective treatment option. Further research is urgently needed to evaluate long-term outcomes (including adverse effects) of selective dorsal rhizotomy followed by an intensive rehabilitation programme involving physical therapy (and prioritising targeted strength training) compared with physical therapy alone. The research could be conducted using a range of designs, including randomised controlled trials and audits of outcomes from procedures already performed. The research should focus on selective dorsal rhizotomy performed: between the ages of 3 and 9	10

Number	Research recommendation	See section
	years in children with spasticity who are at GMFCS level II or III (because these children are likely to benefit most from selective dorsal rhizotomy) and before the development of significant contractures at the ankles, knees and hips. The following criteria should help to identify children who could be included in the research: abnormal tone (pure spasticity), good leg muscle strength, straight legs and minimal muscle shortening, good selective motor control in the legs, good cognitive skills, and not being overweight. Abnormal tone that is predominantly dystonia, and severe scoliosis or hip dislocation, should form part of the exclusion criteria. The research should be coordinated through a multicentre research programme; use nationally agreed outcome measures (such as incidence of neurological impairment and spinal deformity, the need for additional operations, and assessment of disability, social inclusion, and quality of life) and follow-up periods to facilitate national audit; and include assessment of the child's clinical condition before and after selective dorsal rhizotomy using the same formally validated assessment techniques; consider the timing of selective dorsal rhizotomy in relation to orthopaedic surgery if the child has muscle shortening or torsional abnormalities; consider the involvement of the child, their parents, carers or other family members, and members of the local multidisciplinary child development team in the rehabilitation programme after discharge from hospital; monitor the child's clinical condition regularly until they are fully grown (to detect and manage weight gain and orthopaedic and spinal complications). The following information should be given to children and their parents or carers to facilitate informed decision making about participation in research: selective dorsal rhizotomy is irreversible; there is a risk of serious temporary or permanent postoperative complications (such as deterioration in walking ability or bladder function) and later complications such as spinal deformity; prolonged physiotherapy and aftercare will be needed; additional surgery may be needed; subsequent to selective dorsal rhizotomy epidural anaesthesia will not be possible (for example, during additional surgery or childbirth); the evidence already available in relation to selective dorsal rhizotomy is based on studies involving small numbers of children, and there is currently no evidence from which to assess long-term outcomes (those experienced more than 24 months after performing selective dorsal rhizotomy, and preferably into adult life); confounding factors for long-term outcomes could include the natural history of the condition (for example, the child's condition might deteriorate over time regardless of whether or not selective dorsal rhizotomy is performed).	

1.7 Research recommendations

Number	Research recommendation	See section
	Physical therapy (physiotherapy and/or occupational therapy)	**4**

Number	Research recommendation	See section
1	What are the greatest inhibitors of functional ability in children and young people with upper motor neuron lesions?	4
2	What is the optimal postural management programme using a standing frame in children aged 1–3 years?	4
3	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?	4
4	What is the optimal duration for the passive stretch component of physical therapy?	4
5	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?	4
6	What is the clinical and cost effectiveness and optimal age for modified constraint-induced movement therapy?	4
	Orthoses	**5**
7	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?	5
8	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?	5
9	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?	5
10	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?	5
11	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?	5
	Oral drugs	**6**
12	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?	6
13	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?	6
14	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	6

Number	Research recommendation	See section
	as a symptom of their non-progressive brain disorder?	
	Botulinum toxin	**7**
15	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?	7
16	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?	7
17	What is the clinical and cost effectiveness of botulinum toxin type A for reducing muscle pain?	7
18	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?	7
	Intrathecal baclofen	**8**
19	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?	8
20	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?	8
21	What is the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared to usual care in children and young people who are at GMFCS level IV or V?	8
22	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?	8
	Orthopaedic surgery	**9**
23	What is the clinical and cost effectiveness of soft tissue surgery in terms of preventing hip dislocation?	9
24	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?	9
	Selective dorsal rhizotomy	**10**
25	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?	10
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?	10

1.8 Other versions of the guideline

The final published guideline will include access details of other versions of the guideline (the NICE guideline, the understanding NICE Guidance, and the NICE pathway)

1.9 Schedule for updating the guideline

Clinical guidelines commissioned by the National Institute for Health and Clinical Excellence (NICE) are published with a review date 3 years from the date of publication. Reviewing may begin before 3 years have elapsed if significant evidence that affects guideline recommendations is identified sooner.

2 Introduction

2.1 Spasticity and co-existing motor disorders

This guideline covers the management of spasticity and co-existing motor disorders and their early musculoskeletal complications in children and young people (from birth up to their 19th birthday) with non-progressive brain disorders.

What are spasticity and co-existing motor disorders?

Muscle hypertonia is defined as abnormally increased resistance to externally imposed movement about a joint (Sanger 2003). The term spasticity refers to a specific form of hypertonia in which one or both of the following are present (Sanger 2003):

- the resistance to externally imposed movement increases with increasing speed of stretch and varies with the direction of joint movement
- the resistance to externally imposed movement increases rapidly beyond a threshold speed or joint angle.

Spasticity is a component of the upper motor neurone lesion (UMNL) classically presumed to be caused by a lesion of the pyramidal tract between the motor cortex and the anterior horn cell in the spinal cord. Weakness, poor selective motor control, exaggerated deep tendon reflexes, and difficulties with motor planning are the other components of the UMNL.

Dystonia, chorea and athetosis are motor symptoms caused by lesions to the extra-pyramidal and other motor tracts. However, they can also be symptoms of progressive brain pathologies. In children with cerebral palsy, a broad diagnostic category of dyskinesia is used, and this is subdivided into children with dystonic cerebral palsy and choreo-athetoid cerebral palsy. Ataxia may be part of cerebral palsy; it is more common in children with hydrocephalus and can also be caused by progressive brain disorders.

It is now apparent that a single lesion in a motor tract can cause a mixed pattern of motor symptoms and that many children and young people have a mixed pattern. Although the primary lesion may be in one tract, it will have secondary effects on the function of other parts of the motor pathways. Therefore, the guideline considers all motor symptoms found in non-progressive brain disorders in children and young people as part of an extended UMNL. Children and young people with central disorders of motor function may present with different components of the extended UMNL, and this pattern may change over time.

Aetiology of cerebral palsy

Cerebral palsy is the most common condition responsible for an UMNL in children and young people. The incidence of cerebral palsy is not known, but its prevalence in the UK is 186 per 100,000 population, with a total of 110,000 people affected (Department of Health 2005). The guideline covers the management of spasticity associated with cerebral palsy, but not all aspects of the management of cerebral palsy.

In the definition of cerebral palsy, the accompanying disturbances of sensation, perception, cognition, communication, and behaviour, and the risks of epilepsy, and secondary musculoskeletal problems are added to highlight that the condition is caused by a brain injury or maldevelopment. The disorder of motor function may be a relatively mild part of the child or young person’s presenting problems. The presence of these other disorders may affect the child or young person’s ability to respond to therapy for the motor disorder, and may alter how that therapy is delivered. The accompanying problems may also be the predominant sign or symptom for the child or young person with a UMNL where the working diagnosis is not cerebral palsy.

Prematurity is a strong risk factor for development of an UMNL and cerebral palsy (Surman 2009). Forty percent of antenatal or perinatal acquired cerebral palsy occurs in children who are born prematurely and who may have additional non-neurological complications of prematurity (for example, chronic gastrointestinal disorders). Such complications may increase the negative impact of spasticity and co-existing dystonia on the child or young person (due to pain from gastro-oesophageal reflux or constipation) and so it is important that the child or young person is assessed in a holistic manner to detect and manage these exacerbating factors. The causes of preterm labour and the complications of prematurity contribute to the brain damage experienced by children and young people with cerebral palsy. The common pathology in prematurity-related cerebral palsy is abnormality on the white matter around the lateral ventricles in the brain (known as periventricular leukomalacia).

Difficulties during labour that affect oxygen and blood supply to the fetal brain are a common cause of brain damage leading to cerebral palsy. The strongest risk factor is the development of severe neonatal encephalopathy in the first few hours after birth. Different patterns of brain damage are recognised and these can help determine the type and severity of motor disorder and comorbidities that the child will subsequently develop.

Spasticity, dystonia, chorea and athetosis are not present at birth. A child is not diagnosed with cerebral palsy until it is apparent that they have a disorder of motor development and are not meeting motor milestones. A child who has a mild impairment of walking or hand function due to cerebral palsy may not be given a definite diagnosis until they are aged 2 years.

Between 20% and 30% of children with cerebral palsy have a postnatal acquired brain injury as the cause of their cerebral palsy (the remaining 70-80% of cases having an antenatal cause; Jacobsson 2004).

What is acquired brain injury?

Acquired brain injury, which refers to brain injury that occurs after the neonatal period (more than 28 days after birth), includes traumatic brain injury (such as head injury from road traffic accidents) and non-accidental brain injury, as well as brain injury from illnesses such as meningitis, encephalitis and cerebrovascular accidents (arterial and venous stroke). As a child or young person begins to recover from a traumatic brain injury, there may be an initial difficult period of severe spasticity and dystonia requiring intensive management and the emotional impact of the skills they have lost will need careful management.

The management of spasticity and associated motor disorders acquired after birth or after head injury follows the same principles as in children and young people with antenatal or perinatal causes of their motor disorders.

Issues not covered by this guideline

The management of spasticity and associated motor disorders caused by intracranial tumours, inborn errors of metabolism, and progressive degenerative diseases affecting the nervous system may have features of the UMNL, as will those associated with spinal cord injury, diseases and malformations. Each of these conditions is rare individually and management of the UMNL in these children and young people is excluded from this guideline. People aged over 19 years are also excluded from the guideline.

The management of pure dystonia, chorea, and athetosis in children and young people is excluded from the guideline. The GDG is aware that a child or young person with cerebral palsy may have a pure dystonic syndrome, but the majority of children and young people with a pure dystonia have a genetic syndrome or progressive disorder.

What are the approaches to characterising motor disorders?

Motor disorders caused by non-progressive pathology in children and young people are classified by the parts of the body that are affected predominantly (topography), by the predominant abnormality of tone or movement, by the severity of the functional impairment, and by aetiology.

Classification by topography has been used for many decades to describe motor impairment in cerebral palsy. There is no strong reason for not using the same system in children and young people who have a motor impairment following acquired brain injury. The traditional system used the terms monoplegia, diplegia, hemiplegia, and quadriplegia. Recently cerebral palsy experts have proposed a simplification to symmetrical or asymmetrical involvement with a description of the limbs most severely affected to distinguish between diplegia and quadriplegia (see the Surveillance of Cerebral Palsy in Europe (SCPE) network's classification tree for subtypes of cerebral palsy at http://www-rheop.ujf-grenoble.fr/scpe2/site_scpe/decisiontree.php). The GDG has used the newer terminology to classify motor disorders in the guideline recommendations. In the reviews of the evidence, however, the research studies identified for inclusion typically used the older terminology and did not report the characteristics of study participants in sufficient detail to allow the newer terminology to be applied. Thus, the descriptions of the evidence reflect the terminology used by the authors of the included studies.

Motor impairment can also be described in terms of the severity of functional motor impairment, which can be graded with the GMFCS. This is a five-point scale derived from a child or young person's gross motor abilities and measured by the Gross Motor Function Measure (GMFM). The GMFM is available in 88- and 66-item versions (GMFM-88 and GMFM-66, respectively) both of which measure of skills in lying and rolling (dimension A; GMFM-A), sitting (dimension B; GMFM-B), crawling (dimension C; GMFM-C), standing (dimension D; GMFM-D), and walking, running and jumping (dimension E; GMFM-E). The child or young person is scored on their ability to perform a particular type of movement; the total score across all items is matched against the predicted score based on age and placed in one of five categories (level I, II, III, IV or V). As the GMFCS is not yet widely used and understood by non-healthcare professionals, it may be appropriate to use a simpler grading system when communicating with schools, for example.

It has been proposed that upper limb function be graded using the Manual Ability Classification System (MACS), although this has not yet been validated to the same degree as the GMFM or GMFCS.

Current concepts of disability

In 2001, the World Health Organization (WHO) introduced the International Classification of Functioning, Disability and Health (ICF Framework; http://www.who.int/classifications/icf/en/). This complements the tenth revision of the International Classification of Diseases (ICD-10). The ICF Framework provides a common language to describe how a person with a health condition functions in their daily life, rather than focusing on a disease process. The framework takes into account the interaction between a person's state of health, their environment and personal factors. The terms 'body function and structure' and 'activity and participation' have replaced the terms 'impairment', 'disability' and 'handicap'. As part of the evaluation of effectiveness of interventions, newer outcome measures are based on this framework, allowing assessments over a broader area of the child or young person's life and assessment of positive experiences as well as problem areas.

Variability in condition in terms of the child or young person

Children and young people with non-progressive brain disorders may present with different symptoms depending on severity of motor impairment, developmental age, and the effects of therapy. There may be a profound impairment of motor function, severely affecting ability to participate in society, or there may be a mild impairment affecting sporting skills, for example. For some children and young people, pain from muscle spasms may be a major difficulty, while for others motor developmental delay may be the main concern. For the older or more severely affected child or young person there may be difficulties with daily care due to the onset of secondary complications of spasticity. Management should be tailored to meet the problems faced by the individual child or young person, and their individual goals, and this requires a multidisciplinary approach.

In children and young people with non-progressive brain disorders, the insult to the brain and motor pathways often occurs before the brain has grown fully and matured. Young children still have skills to learn, and management needs to be adapted to the child's stage of development.

Variability in available treatments

No treatment will cure the underlying brain disorder, although with time less severely affected children and young people may adapt and learn motor skills sufficient to participate fully in everyday life. For the more severely affected child or young person, treatment is an ongoing process that should be designed to meet the individual's needs as they grow and mature.

There is considerable variation in practice in managing spasticity, including variation in availability of treatments and the intensity of their use.

Physical therapy (physiotherapy and/or occupational therapy) is considered to be the mainstay of treatment for children and young people with motor disorders. Many techniques, including the use of orthoses, have been developed to manage spasticity and its complications and other co-existing motor disorders. Oral drugs have been available for a number of years, although there have been no clear guidelines on the use of the drugs. Newer drugs, licensed for use in adults, are used off-licence in children and young people in many areas.

Botulinum toxin (BoNT) treatment, particularly BoNT type A (BoNT-A), has been used in the management of spasticity for many years, and it is licensed for use in 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. It is frequently used off-license with regard to the muscle groups injected, the dose of toxin administered, and the frequency of administration. Techniques to improve the accuracy of injection localisation such as ultrasound and the use of muscle stimulators are under development, and BoNT-A is not currently available throughout England and Wales.

Intrathecal baclofen therapy, which is available in regional paediatric centres in England and Wales, is a complex therapy with ongoing costs, requiring a commitment from the child or young person or their parents to ensure regular follow-up and significant possible complications. Timing of referral for consideration of intrathecal baclofen (ITB) is important to prevent or delay the onset of secondary complications.

Selective dorsal rhizotomy (SDR) is a complex neurosurgical procedure frequently employed in the United States of America (USA) for management of spasticity. SDR has been the subject of a NICE interventional procedure guidance (IPG; 'Selective dorsal rhizotomy for spasticity in cerebral palsy', NICE IPG 373), is currently available in only one centre in England and Wales. The procedure requires prolonged post-operative rehabilitation, and there are risks of late-onset degenerative disorders of the spine as a complication.

For many years, orthopaedic surgeons led services for the management of motor disorders, particularly in cerebral palsy. The role of surgery has changed, however. Soft-tissue surgery is performed less frequently in children, perhaps because of the use of BoNT-A alone or in combination with orthoses. Surgery to correct bony deformity in ambulant and non-ambulant children and young people is performed more frequently, often in the form of multi-level surgery rather than as staged (sequential) surgery as happened in previous decades. Surgical treatments (orthopaedic and neurosurgical surgery) are expensive and are associated with post-operative morbidity. Recovery and rehabilitation following surgery may take up to 18 months.

ITB, BoNT-A, SDR, orthopaedic surgery, and physical therapies involving a high input from healthcare professionals potentially incur high costs to the National Health Service (NHS). The cost of treatments considered in this guideline would have to be added to the cost of equipment, house adaptations, and loss of parental earnings to represent the true cost to the NHS and other Government departments.

The ultimate goal of treatment is to maximise the child or young person's potential and promote independence and quality of life through to adult life. This may be achieved by improving motor function, relief of pain, and prevention of secondary musculoskeletal complications. Current clinical practice may take up a considerable amount of time from the child or young person, their family, and healthcare professionals delivering treatment. Monitoring the effect of an intervention over the course of several years is not easy, and for some approaches there is a limited theoretical framework. It may be difficult, therefore, to plan a management programme for an individual child or young person. Parents and carers will need guidance on making appropriate therapeutic decisions, and information about the time commitment needed.

Not all children with non-progressive motor disorders who can stand and walk in the first decade of life retain these abilities into adult life. It is important to give children and young people, and their parents, clear advice on prognosis and what the likely effects of a particular treatment options will be.

Planning treatment has become more complex following the increase in the range of treatments available for managing motor disorders during the past two decades. There is now a choice of treatment (for example, pain from muscle spasticity can be treated with oral drugs, BoNT-A, ITB, or postural management programmes). There is more to life than treatment and the child or young person should have a programme tailored for their current symptoms and their current and future needs.

This guideline will help healthcare professionals to select and use appropriate treatments for individual children and young people. Parents and carers also need guidance on choosing the most appropriate treatment, and to ensure that the time, effort and their personal resources are used to the best to enhance quality of life for the child or young person and their family.

2.2 For whom is this guideline intended?

This guideline is of relevance to those who work in or use the NHS in England and Wales:

- primary, community and secondary care healthcare professionals involved in the care of children and young people who have spasticity, co-existing motor disorders and their early musculoskeletal complications as a result of a non-progressive brain disorder
- those with responsibilities for commissioning and planning health services such as Primary Care Trust commissioners (UK), Welsh Assembly Government officers, public health and trust managers
- professionals working with children and young people or their families and carers in education or social services
- children and young people who have spasticity, co-existing motor disorders and their early musculoskeletal complications as a result of a non-progressive brain disorder and their families and other carers who are involved in making decisions about the most appropriate management choices.

2.3 Related NICE guidance

- 'Sedation in children and young people' (NICE clinical guideline 112)
- 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373).

3 Guideline development methodology

3.1 Methodology

This guidance was commissioned by NICE and developed in accordance with the guideline development process outlined in the 2009 edition of The Guidelines Manual (www.nice.org.uk/guidelinesmanual).

Information about the clinical areas covered by the guideline (and those that are excluded) is available in the scope of the guideline (reproduced in Appendix A).

All GDG members' potential and actual conflicts of interest were recorded on declaration forms provided by NICE (summarised in Appendix B). None of the interests declared by GDG members constituted a material conflict of interest that would influence recommendations developed by the GDG.

Organisations with interests in the management of spasticity, co-existing motor disorders and their early musculoskeletal complications in children and young people with non-progressive brain disorders were encouraged to register as stakeholders for the guideline. Registered stakeholders were consulted throughout the guideline development process. A list of registered stakeholder organisations for the guideline is presented in Appendix C.

In accordance with NICE's Equality Scheme, ethnic and cultural considerations and factors relating to disabilities have been considered by the GDG throughout the development process and specifically addressed in individual recommendations where relevant. Further information is available from www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp.

Developing review questions and protocols and identifying evidence

The GDG formulated review questions based on the scope (see Appendix A) and prepared a protocol for each review question (see Appendix D). These formed the starting point for systematic reviews of relevant evidence. Specific outcomes considered during the evaluation of published evidence are outlined in Appendix E. Published evidence was identified by applying systematic search strategies (see Appendix F) to the following databases: Medline, Medline In-Process, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and three Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and the Database of Abstracts of Reviews of Effects). Searches to identify economic studies were undertaken using Medline, Embase, the Cochrane Central Register of Controlled Trials, the NHS Economic Evaluation Database (NHS EED), and the Health Technology Assessment (HTA) database.

Dates of searching and database coverage are given with the details of the search strategies in Appendix F. Where appropriate, review questions were grouped together for searching. The search strategies from 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) were used for the SDR review. The search for the physical therapy review was limited by date (the search was limited to articles published after 1970), but the remaining searches were not. Animal studies were excluded from Medline and both Medline and Embase were limited to English-language studies only. Studies conducted in adult populations were not excluded using search filters. Scottish Intercollegiate Guidelines Network (SIGN) search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no systematic attempt to search grey literature (conference abstracts, theses or unpublished trials), nor was hand searching of journals not indexed on the databases undertaken.

Towards the end of the guideline development process, the searches were updated and re-executed to include evidence published and indexed in the databases before 8 August 2011.

Reviewing and synthesising evidence

Evidence relating to clinical effectiveness was reviewed and synthesised according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (see http://www.gradeworkinggroup.org/index.htm). In this approach, the quality of the evidence identified for each outcome listed in the review protocol is assessed according to the factors listed below, and an overall quality rating (very low, low, moderate or high) is assigned by combining ratings for the individual factors.

- Study design (as an indicator of intrinsic bias; this determines the initial quality rating).
- Limitations in the design or execution of the study (including concealment of allocation, blinding, loss to follow up; these and other sources of bias can reduce the quality rating).
- Inconsistency of effects across studies (this can reduce the quality rating where more than one study is considered).
- Indirectness (the extent to which the available evidence fails to address the specific review question; this can reduce the quality rating).
- Imprecision (the extent to which the point estimate or its confidence interval (CI) reflects a clinically important difference; this can reduce the quality rating).
- Other considerations (including large magnitude of effect, evidence of a dose-response relationship, or confounding variables likely to have reduced the magnitude of an effect; these can increase the quality rating in observational studies, provided no downgrading for other features has occurred).

The GDG considered that reduction of spasticity alone without concomitant clinically meaningful improvement in other patient-centred outcomes would be insufficient to recommend an intervention. At the start of the guideline development period, the GDG discussed, specified and prioritised units of measurement for each main outcome detailed in the scope. As far as possible the GDG selected similar units derived from validated and clinically used assessment techniques to be applied across each review for consistency (see Appendix E). Where outcomes from validated assessment techniques were not available in the literature, outcomes from non-validated tools were discussed with GDG members and included only on their advice.

The type of review question determines the highest level of evidence that may be sought. For issues of treatment, the highest possible evidence level is a well conducted systematic review or meta-analysis of RCTs, or an individual RCT. In the GRADE approach, a body of evidence based entirely on such studies has an initial quality rating of high, and this may be downgraded to moderate, low, or very low if factors listed above are not addressed adequately.

Various approaches may be used to assess imprecision in the GRADE framework. One such approach is to downgrade for imprecision on the basis of inadequate event rates (fewer than 300 for dichotomous outcomes) or inadequate study population size (less than 400 participants for continuous outcomes). No outcomes in this guideline met these criteria; therefore whilst footnotes were made to this effect, the outcomes were not downgraded based on these criteria. For dichotomous outcomes, where a 95% CI for a relative risk (RR) or odds ratio (OR) crossed the line of no effect and either one or both of the GRADE default lower or upper thresholds for downgrading (0.75 or 1.25), imprecision was rated as serious. Where the 95% CI was entirely below 0.75 or entirely above 1.25, or entirely between 0.75 and 1.25, the outcome was not downgraded for imprecision and the result could be interpreted as being clinically important. The results of many different assessment tools were examined as continuous outcomes in this guideline. The GDG sought to identify clinically important differences for the outcomes of each assessment tool. Where possible, the GDG's definitions were applied to data extracted from published articles to inform decisions about whether or not the quality of the evidence should be downgraded for imprecision. Where the GDG was unable to specify a clinically important difference, or the data were insufficient to permit extrapolation, the outcome was downgraded. Further details of the GDG's considerations in relation to defining clinically important differences for continuous outcome measures prioritised for inclusion in the guideline (such as scores from various assessment tools) are summarised in Appendix E.

For each review question the highest available level of evidence was sought. Where appropriate, for example, if a systematic review, meta-analysis or RCT was identified to answer a question directly, studies of a weaker design were not considered. Where systematic reviews, meta-analyses and RCTs were not identified other appropriate experimental or observational studies were included following discussion with the GDG.

The numbers of studies identified for each review question are summarised in Appendix G. Some studies were excluded from the guideline reviews after obtaining copies of the corresponding publications because they did not meet inclusion criteria specified by the GDG and recorded in the review protocols (see Appendix H). The characteristics of each included study were summarised in evidence tables for each review question (see Appendix I). Where possible, dichotomous outcomes were presented as RRs or ORs with 95% CIs, and continuous outcomes were presented as mean differences (MDs) with 95% CIs or standard deviations (SDs).

The body of evidence identified for each review question (or part of a review question) was presented in the form of a GRADE evidence profile summarising the quality of the evidence and the findings (pooled relative and absolute effect sizes and associated CIs). Where possible, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled RRs, pooled ORs, or weighted mean differences (WMDs). By default, meta-analyses conducted specifically for the guideline (see Tables 7.5 and 10.2) used a fixed effect model, and where statistically significant heterogeneity was identified a random effects model was used. Forest plots for all meta-analyses conducted specifically for the guideline are presented in Appendix J. The meta-analyses presented in Tables 7.1, 7.3 and 7.6 were reported in a Cochrane systematic review (Hoare 2010). Some of these meta-analyses were conducted using a fixed effect model and others were conducted using a random effects model. Where statistically significant heterogeneity was identified, the guideline evidence statements (see below) report findings from the individual studies that contributed to the meta-analysis. GRADE findings are presented in full in Appendix K and abbreviated versions (summary of findings without the individual components of the quality assessment) are presented in this document.

Incorporating health economics

The aims of the health economic input to the guideline were to inform the GDG of potential economic issues relating to spasticity, and to ensure that recommendations represented cost effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years (QALYs)), harms and costs of different care options.

The GDG prioritised a number of review questions where it was thought that economic considerations would be particularly important in formulating recommendations. Systematic searches for published economic evidence were undertaken for these questions. For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation. Reviews of the (very limited) relevant published health economic literature are presented alongside the corresponding clinical effectiveness reviews.

Health economic considerations were aided by original economic analysis undertaken as part of the development process. For this guideline the areas prioritised for economic analysis were as follows:

- physical therapy (physiotherapy and/or occupational therapy)
- orthoses
- BoNT
- continuous pump-administered ITB (CITB)
- orthopaedic surgery
- SDR.

Details of the health economic analyses conducted for the guideline are presented in Chapter 11.

The GDG considered using the EuroQol Group's EQ-5D instrument to evaluate quality of life, but had reservations about its application in children and young people. None of the studies identified for inclusion in the guideline reviews used the EQ-5D for children, and there was insufficient clinical evidence available for translation into the EQ-5D for children, or for subsequent health economic interpretation or analysis.

Evidence to recommendations

For each review question recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, short clinical and, where appropriate, cost effectiveness evidence statements were drafted by the technical team which were presented alongside the evidence profiles and agreed by the GDG. Statements summarising the GDG's interpretation of the evidence and any extrapolation from the evidence used to form recommendations were also prepared to ensure transparency in the decision-making process. The criteria used in moving from evidence to recommendations are summarised in Table 3.3.

In areas where no substantial clinical evidence was identified, the GDG considered other evidence-based guidelines and consensus statements or used their collective experience to identify good practice. The health economics justification in areas of the guideline where the use of NHS resources (interventions) was considered was based on GDG consensus in relation to the likely cost effectiveness implications of the recommendations. The GDG also identified areas where evidence to answer their review questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process formal consensus methods incorporating anonymous voting were used to consider all the clinical care recommendations and research recommendations that had been drafted previously. The GDG identified nine key priorities for implementation (key recommendations) and five high-priority (key) research recommendations. The key priorities for implementation were those recommendations thought likely to have the biggest impact on clinical care and outcomes in the NHS as a whole. The key research recommendations were selected in a similar way.

Table 3.3 Criteria considered in moving from evidence to recommendations

Criterion
Relative value placed on the outcomes considered
Consideration of clinical benefits and harms
Consideration of net health benefits and resource use
Quality of the evidence
Other considerations (including equalities issues)

Stakeholder involvement

Registered stakeholder organisations were invited to comment on the draft scope and the draft guideline. Stakeholder organisations were also invited to undertake a prepublication check of the final guideline to identify factual inaccuracies. The GDG carefully considered and responded to all comments received from stakeholder organisations. The comments and responses, which were reviewed independently for NICE by a Guidelines Review Panel, are published on the NICE website. [These details will apply to the final published guideline]

Specific considerations for this guideline

Physiotherapy and occupational therapy are core treatments for children and young people with spasticity although their primary aim is not to reduce spasticity (this is also true of orthoses). The GDG acknowledged that most children and young people included in clinical research studies would have received physiotherapy and/or occupational therapy. In the publications reviewed for the guideline it was not always clear exactly what form of therapy had been delivered, what sort of healthcare professional had prescribed or administered the therapy, how frequently or intensively the therapy had been administered, or whether the intervention and comparison groups had received the same forms of therapy. Nevertheless, those details of physiotherapy and/or occupational therapy interventions that were reported in each included study were recorded in the corresponding evidence tables (see Appendix I). The GDG agreed to use the term ‘physical therapy’ to encompass all interventions that would normally be prescribed or performed by a physiotherapist or an occupational therapist. When direct reference was made to a particular study, however, the terms used by the authors of the study publications were used. Physiotherapists and occupational therapists are referred to collectively as physical therapists in this guideline.

With regard to the age of participants in the research studies reviewed for the guideline, the term child is used to refer to people under the age of 11 years, and young person is used to refer to those aged 11-19 years.

4 Physical therapy (physiotherapy and/or occupational therapy)

Introduction

Children with developmental and physical problems due to a UMNL usually receive physical therapy (that is, physiotherapy and/or occupational therapy). Physical therapy usually starts when developmental concerns first arise, or at the time of injury, and it continues throughout childhood and into adult life. Physical therapists use a proactive and preventative approach centred on understanding the causes of the child or young person's current functional problems and how these impact upon their ability to develop and maintain skills and participate in home and school life, and in the wider community. As well as managing functional problems, physical therapists have a large educational and advisory role helping children and young people and their families understand their conditions and prognoses.

Spasticity usually forms one physical feature in a complex movement disorder caused as a result of a UMNL. Advances in the understanding of motor learning, neurodevelopment and how the child or young person responds to different situations and environmental changes support a functional approach to therapy, giving greater priority to maximising activity and participation in line with the domains of the WHO's ICF Framework (see http://www.who.int/classifications/icf/en/). The link between these domains is not clearly defined but it is recognised that negative and compensatory phenomena resulting from the UMNL (for example, neurological weakness, poor movement control, abnormal sensation, health issues, and reduced fitness and body condition) may have a more significant impact on a child or young person's ability to participate in everyday life than spasticity alone.

A child or young person's physical therapy needs, which are usually assessed on an individual basis, may be complex and multifaceted, changing throughout their lifetime as they develop physically and cognitively. The severity of the neurological damage, age demands and resulting functional problems determine physical therapy goals and interventions. Physical therapists recognise that a child or young person's cognitive ability, personality, health and fitness, family situation, comorbidities, environment and social context have a significant impact on activity and participation. Many physical therapy interventions have a wider impact and require shared responsibility between different types of healthcare professionals, the child or young person's family, and social care and education services.

Physical therapists recognise that movement difficulties in children and young people are complicated by growth and the effects of gravity, which can cause increasing secondary compensation effects of muscle and bony deformity. These can result in pain and limitation of activity causing reduced quality of life and increased family stress, emotional difficulties and care needs. Physical therapists are vital in recognising and managing these limitations, referring on to professional colleagues for advice and further management where necessary. Physical therapy is used in conjunction with other interventions such as oral drugs, BoNT-A, and orthopaedic surgery to improve effectiveness and aid rehabilitation.

Physical therapists have a wide range of skills and treatment options, and while there are similarities between approaches, clinical practice varies depending on the therapist's personal knowledge and skills, the model of service delivery favoured locally, and the child or young person's needs assessment. The amount and type of physical therapy received can vary widely.

Evidence for the effectiveness of physical therapy interventions and their benefits in terms of treating movement problems are considered in this chapter. Physical therapy (and the use of orthoses) is not undertaken primarily to reduce spasticity. Rather, the specific interventions that comprise physical therapy aim to maintain function, body alignment, etc and to prevent or delay secondary consequences of spasticity. The scope of the guideline is limited in that it specifically excludes holistic management of cerebral palsy and other non-progressive brain disorders, and thus it was necessary to prioritise issues to be considered as part of the guideline review in relation to physical therapy. The GDG's view was that most children and young people with spasticity would receive physical therapy as a baseline intervention, and they might or might not receive other interventions to manage muscle tone. The GDG prioritised consideration of physical therapy interventions that were most likely to be used in children and young people with spasticity. The group concluded that active-use therapy and other techniques that contribute to the objectives of strengthening, stretching and postural management should be considered in the guideline review. Thus the review conducted for the guideline focused specifically on the following physical therapy interventions.

- Task-focused active-use therapy (active-use therapy or constraint-induced movement therapy (CIMT; temporary restraint of an unaffected arm to encourage use of the other arm), and bimanual therapy (unrestrained use of both arms). Active-use therapy focuses on movement achieved by the child or young person themselves, in contrast to passive movements achieved by a third party (such as a healthcare professional or a parent or carer). The term task-focused is used to imply that the activity undertaken is goal-oriented.
- Strengthening interventions (progressive resistive exercise, rebound therapy, and treadmill training).
- Stretching (casting, including serial casting, and passive stretching).
- Postural management (24-hour postural management, functional sitting position, seating solutions including moulded seats, knee blocks, sleep systems, and standing frames).

The GDG sought evidence from studies that reported clearly defined techniques relevant to the prioritised interventions and were conducted using reasonably large samples of children and young people. Where the interventions evaluated in a particular study were not reported clearly or the number of children and young people who participated was less than 10 the study was excluded.

No related NICE guidance was identified for this review question.

Review question

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?

Description of included studies

Twelve studies reported in 14 publications were identified for inclusion for this review question (Aarts 2010; Aarts 2011; Dodd 2003; Dodd 2004; Fowler 2010; Katz-Leurer 2009; Law 2011; Lee 2008; Liao 2007; McNee 2007; Newman 2007; Novak 2009; Sakzewski 2011; Unger 2006). The studies addressed the following five comparisons.

- Active use therapy versus no active use therapy in children and young people with unilateral or bilateral spasticity was evaluated in three parallel RCTs reported in four publications (Aarts 2010; Aarts 2011; Katz-Leurer 2009; Novak 2009). In the first study (Aarts 2010; Aarts 2011), the participants were aged 2.5-8 years and all of them had unilateral spasticity; the intervention was described as CIMT in which each child was encouraged to actively use their affected arm during treatment while use of their unaffected arm was limited by use of a sling. In the second study (Katz-Leurer 2009) the participants were aged 7-13 years; these children and young people had unilateral or bilateral spasticity and physical therapy was based on repetition of exercises to facilitate performance of goals or daily activities. In the third study (Novak 2009) the participants were aged 3.5-7 years; these children had unilateral or bilateral spasticity and physical therapy was based on repetition of exercises to facilitate performance of goals or daily activities in an intervention termed an Occupational Therapy Home Programme (OTHP).

- Comparisons between different forms of active use therapy in children and young people with cerebral palsy were evaluated in one matched-pairs RCT (Sakzewski 2011) and one cluster RCT (Law 2011). In the first study (Sakzewski 2011) the participants were aged 5-16 years and they all had hemiplegia. The study compared the effectiveness of CIMT and bimanual therapy. The CIMT intervention involved the use of the child or young person's affected arm while use of the unaffected arm was limited by wearing a tailor-made glove designed to prevent grasp but allow the hand to be used for support. In the second study (Law 2011) the participants were children aged 12 months to 5 years 11 months with cerebral palsy who were at GMFCS level 1, 2, 3, 4 or 5. Physical therapy was based on either a child- or context-focused intervention to improve performance of functional tasks and mobility. The duration of each intervention was 6 months, and both treatment groups received 18-24 sessions of physical therapy. Assessments were conducted at baseline, 6 months and 9 months, and the children returned to their prestudy approaches to physical therapy between the 6- and 9-month assessments. The child-focused intervention identified impairments underlying functional limitations, and physical therapy was provided to remediate those impairments. The context-focused intervention did not include remediation of impairments; instead, it involved identification of barriers in the child's environment (for example, their home or preschool) or strategies used to achieve individualised tasks or goals, and modification of the environment and/or strategies to overcome those barriers. Additionally, the two interventions differed in terms of who delivered the treatment: in the child-focused approach the intervention was delivered collectively by a group of physiotherapists and occupational therapists, whereas in the context-focused approach each child was assigned a particular physiotherapist or occupational therapist who delivered the intervention. In both interventions, the five most frequently used approaches to physical therapy included practice of functional mobility activities. In the child-focused intervention the remaining four most frequently used approaches to physical therapy were: practice of upper extremity motor activities; training in components of movement; practice of stationary gross motor skills; and stretching. In the context-focused intervention the remaining four most frequently used approaches were: modifying the physical characteristics of the child's environment, materials or tools; changing a task instruction; adding adaptive equipment; and providing education or instruction to the child's family.
- Strengthening versus usual care not including strengthening in children and young people with unilateral or bilateral spasticity was evaluated in five parallel RCTs reported in six publications (Dodd 2003; Dodd 2004; Fowler 2010; Lee 2008; Liao 2007; Unger 2006). In all five studies the intervention was a strengthening programme consisting of progressive resistive exercises. No evidence was identified for inclusion in relation to other strengthening interventions, such as treadmill training or rebound therapy. The participants in the two publications that related to the first study (Dodd 2003; Dodd 2004) were aged 8-18 years and 8-16 years, respectively; those in the second study (Fowler 2010) were aged 7-18 years; those in the third study (Lee 2008) were aged 4-12 years; those in the fourth study (Liao 2007) were aged 5-12 years; and those in the fifth study (Unger 2006) were aged 13-18 years).
- Serial casting versus usual care not including serial casting in children aged 6 years 1 month to 10 years 3 months with unilateral or bilateral spasticity was evaluated in one cross-over RCT (McNee 2007).
- Early casting after BoNT versus delayed casting after BoNT in children aged 3.5-7.5 years with unilateral or bilateral spasticity was evaluated in one parallel RCT (Newman 2007).

Evidence profiles

Active use therapy versus no active use therapy

None of the studies identified for inclusion reported reduction of spasticity.

One study (Aarts 2011) reported range of movement in the upper limb. The outcomes reported included active range of movement (AROM), in which movement is achieved by the child or young person themselves, and passive range of movement (PROM), in which movement is achieved by the actions of a third party.

Table 4.1 Evidence profile for active use therapy compared with no active use therapy in children with unilateral spasticity; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Active use therapy	No active use therapy	Relative (95% CI)	Absolute (95% CI)	
AROM wrist extension at week 9 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 4.5 higher (4.29 lower to 13.29 higher)*	MODERATE
AROM wrist extension at week 17 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 3.1 higher (10.68 lower to 16.88 higher)*	MODERATE
PROM wrist extension at week 9 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 3.6 higher (0.46 lower to 7.66 higher)*	MODERATE
PROM wrist extension at week 17 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 3.9 higher (0.57 lower to 8.37 higher)*	MODERATE
AROM elbow extension at week 9 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 2.9 higher (2.72 lower to 8.52 higher)*	MODERATE
AROM elbow extension at week 17 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 5.2 higher (0.52 lower to 10.92 higher)*	MODERATE
PROM elbow extension at week 9 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 1.4 higher (1.76 lower to 4.56 higher)*	MODERATE
PROM elbow extension at week 17 (better indicated by higher values)					
1 study (Aarts 2011)	28	22	-	MD 3.6 higher (0.76 to 6.44	HIGH

				higher)	

AROM active range of movement, CI confidence interval, MD mean difference, PROM, passive range of movement
* Calculated by the NCC-WCH

Three studies reported outcomes relevant to optimisation of function and movement (Aarts 2010; Katz-Leurer 2009; Novak 2009). The outcomes reported included Assisting Hand Assessment (AHA), Goal Attainment Scaling (GAS; including GAS T-scores), Canadian Occupational Performance Measure (COPM; including domains relating to performance (COPM-P) and satisfaction (COPM-S).

Table 4.2 Evidence profile for active use therapy compared with no active use therapy in children with unilateral or bilateral spasticity; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Active use therapy	**No active use therapy**	**Relative (95% CI)**	**Absolute (95% CI)**	
AHA score at week 9 (range 0 to 100, change from baseline, better indicated by higher values)					
1 study (Aarts 2010)	28[a]	22[b]	-	MD 4.3 higher (0.28 to 8.32 higher)*	MODERATE
AHA score at week 17 (range 0 to 100, change from baseline, better indicated by higher values)					
1 study (Aarts 2010)	28[c]	22[d]	-	MD 4.70 higher (1.58 to 7.82 higher)*	MODERATE
GAS score at week 9 (% children who showed an increase of 2 points or more compared to baseline)					
1 study (Aarts 2010)	23/28* (82%)	5/22* (23%)	RR 3.61 (1.64 to 7.96)*	59 more per 100 (from 15 more to 100 more)*	HIGH
GAS score at week 17 (% children who showed an increase of 2 points or more compared to baseline)					
1 study (Aarts 2010)	24/28* (86%)	8/22* (36%)	RR 2.36 (1.33 to 4.18)*	49 more per 100 (from 12 more to 100 more)*	HIGH
GAS T-score at week 8 in 4-week OTHP group (better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-[e]	HIGH
GAS T-score at week 8 in 8-week OTHP group (better indicated by higher values)					
1 study (Novak 2009)	12	12[a]	-	-[f]	HIGH
GAS T-score at week 8 in 4-week versus 8-week OTHP groups (better indicated by higher values)					
1 study (Novak 2009)	11	12[g]	-	-[h]	MODERATE
COPM-P score at week 8 in 4-week OTHP group (better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-[i]	HIGH
COPM-P score at week 8 in 8-week OTHP group (better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-[j]	HIGH

COPM-P score at week 8 in 4-week versus 8-week OTHP groups (better indicated by higher values)					
1 study (Novak 2009)	11	12[g]	-	-[k]	MODERATE
COPM-P score at week 9 (range 0 to 10, better indicated by higher values)					
1 study (Aarts 2010)	28[l]	22[m]	-	-[n]	HIGH
COPM-P score at week 17 (range 0 to 10, change from baseline, better indicated by higher values)					
1 study (Aarts 2010)	28[o]	22[p]	-	MD 2.00 higher (1.20 to 2.80 higher)*	HIGH
Walking speed at 6 weeks (change from baseline, m/second, 10-minute walk test, better indicated by higher values)					
1 study (Katz-Leurer 2009)	10[q]	10[r]	-	MD 0.03 higher (0.06 lower to 0.12 higher)	LOW

AHA assisting hand assessment, CI confidence interval, COPM-P Canadian Occupational Performance Measure – Performance, COPM-S Canadian Occupational Performance Measure – Satisfaction, Goal Attainment Scaling, MD mean difference, OTHP Occupational Therapy Home Programme, RR relative risk, SD standard deviation

* Calculated by the NCC-WCH

a Change from baseline at week 9 mean (SD) = 6.8 (8.2)

b Change from baseline at week 9 mean (SD) = 2.5 (6.3)

c Change from baseline at week 17 mean (SD) = 6.4 (5.7)

d Change from baseline at week 17 mean (SD) = 1.7 (5.5)

e Results for comparison of 4-week OTHP versus no programme reported as an effect size of 37.8 (95% CI 26.9 to 48.8) p=0.01

f Results for comparison of 8-week OTHP versus no programme reported as an effect size of 17.9 (95% CI12.4 to 23.4) p=0.01

g Comparison is 4-week OTHP group versus 8-week OTHP group, not to no programme group

h Results for comparison of 4-week OTHP versus 8-week OTHP reported as an effect size of 0.5 (95% CI -13.4 to 14.4) p=0.94

i Results for comparison of 4-week OTHP versus no programme reported as an effect size of 2.4 (95% CI 0.7 to 4.2) p=0.01

j Results for comparison of 8-week OTHP versus no programme reported as an effect size of 1.4 (95% CI 0.6 to 2.2) p=0.01

k Results for comparison of 4-week OTHP versus 8-week OTHP reported as an effect size of 0.7 (95% CI -1.2 to 2.6) p=0.45

l Change from baseline at week 9 mean (SD) = 3.5 (1.3)

m Change from baseline at week 9 mean (SD) = 1.2 (1.1)

n Mean difference reported as 2.1 (95% CI 1.43 to 2.72) effect size reported as 1.31

o Change from baseline at week 17 mean (SD) = 3.6 (1.6)

p Change from baseline at week 17 mean (SD) = 1.6 (1.3)

q Change scores after 6 weeks mean (SD) = 0.04 (0.1)

r Change scores after 6 weeks Mean (SD) = 0.01 (0.1)

Two studies reported outcomes relevant to acceptability and tolerability (Aarts 2010; Novak 2009).

Table 4.3 Evidence profile for active use therapy compared with no active use therapy in children with unilateral or bilateral spasticity; treatment acceptability assessment

Number of studies	Number of participants		Effect		Quality
	Active use therapy	No active use therapy	Relative (95% CI)	Absolute (95% CI)	
COPM-S score at week 8 in 4-week OTHP group (range 0 to 10, change from baseline, better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-[a]	HIGH

COPM-S score at week 8 in 8-week OTHP group (range 0 to 10, change from baseline, better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-[b]	HIGH
COPM-S score at week 8 in 4-week OTHP versus 8-week OTHP groups (better indicated by higher values)					
1 study (Novak 2009)	12	12[c]	-	-[d]	MODERATE
COPM-S score at week 9 (range 0 to 10, change from baseline, better indicated by higher values)					
1 study (Aarts 2010)	28[e]	22[f]	-	-[g]	HIGH
COPM-S score at week 17 (range 0 to 10, change from baseline, better indicated by higher values)					
1 study (Aarts 2010)	28[h]	22[i]	-	MD 2.00 higher (1.20 to 2.80 higher)*	HIGH

CI confidence interval, COPM-P Canadian Occupational Performance Measure – Performance, COPM-S Canadian Occupational Performance Measure – Satisfaction, MD mean difference, OTHP Occupational Therapy Home Programme, RR relative risk, SD standard deviation
* Calculated by the NCC-WCH
a Results for comparison of 4-week OTHP versus no programme reported as an effect size of 2.5 (95% CI 0.8 to 4.3) p=0.01
b Results for comparison of 8-week OTHP versus no programme reported as an effect size of 1.5 (95% CI 0.3 to 2.6) p=0.01
c Comparison is 4-week OTHP group versus 8-week OTHP group, not to no-programme group
d Results for comparison of 4-week OTHP versus 8-week OTHP reported as an effect size of 0.8 (95% CI -1.1 to 2.8) p=0.40
e Change from baseline at week 9 mean (SD) = 3.7 (1.6)
f Change from baseline at week 9 mean (SD) = 1.4 (1.1)
g Mean difference reported as 2.2 (95% CI 1.51 to 2.86) effect size reported as 1.32
h Change from baseline at week 17 mean (SD) = 3.6 (1.6)
i Change from baseline at week 17 mean (SD) = 1.6 (1.3)

None of the studies reported outcomes relevant to pain (reduction of pain) or quality of life.

One study investigated adverse effects (Novak 2009). Parents were asked to report adverse events to the physical therapist by telephone or face-to-face contact.

Table 4.4 Evidence profile for occupational therapy home programme for 4 or 8 weeks compared with no occupational therapy home programme in children with unilateral or bilateral spasticity; adverse events

Number of studies	Number of participants		Effect		Quality
	4- or 8-week occupational therapy home programme	No occupational therapy home programme	Relative (95% CI)	Absolute (95% CI)	
Adverse events					
1 study (Novak 2009)	0/24 (0%)	0/12 (0%)	-	-[a]	LOW

CI confidence interval
a No adverse events reported in either group

Comparison between different forms of active use therapy

Neither of the studies identified for inclusion reported reduction of spasticity.

Both studies reported outcomes relevant to optimisation of function and movement (Law 2011; Sakzewski 2011). The outcomes reported included the Melbourne Assessment of Unilateral Upper Limb Function (MAUULF) and the Pediatric Evaluation of Disability Inventory (PEDI).

Table 4.5 Evidence profile for constraint-induced movement therapy versus bimanual therapy in children and young people with spasticity; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Constraint-induced movement therapy	**Bimanual training**	**Relative (95% CI)**	**Absolute (95% CI)**	
AHA at 3 weeks (change from baseline; better indicated by higher values)					
1 study (Sakzewski 2011)	31	31	-	MD 1.2 higher (1.2 lower to 3.5 higher)	MODERATE
AHA at 26 weeks (change from baseline; better indicated by higher values)					
1 study (Sakzewski 2011)	28	30	-	MD 0.7 lower (3.1 lower to 10.3 higher)	MODERATE
MAUULF at 3 weeks (change from baseline; better indicated by higher values)					
1 study (Sakzewski 2011)	31	31	-	MD 1.8 higher (0.3 lower to 4.0 higher)	MODERATE
MAUULF at 26 weeks (change from baseline; better indicated by higher values)					
1 study (Sakzewski 2011)	28	30	-	MD 4.4 higher (2.2 to 6.7 higher)	MODERATE

AHA Assisting Hand Assessment, CI confidence interval, MAUULF Melbourne Assessment of Unilateral Upper Limb Function

Table 4.6 Evidence profile for child-focused intervention compared with context-focused intervention in children with spasticity; joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Child-focused intervention	**Context-focused intervention**	**Relative (95% CI)**	**Absolute (95% CI)**	
Range of movement right hip abduction at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.98 lower (5.56 lower to 3.6 higher)*	LOW
Range of movement right hip abduction at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.3 higher (3.07 lower to 5.67 higher)*	LOW
Range of movement left hip abduction at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.65 lower (6.08 lower to	LOW

				2.78 higher)*	
Range of movement left hip abduction at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.42 higher (2.95 lower to 5.79 higher)*	LOW
Range of movement right hip extension at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.39 higher (0.3 lower to 1.08 higher)*	LOW
Range of movement right hip extension at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.16 higher (0.16 lower to 0.48 higher)*	LOW
Range of movement left hip extension at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.62 higher (0.18 lower to 1.42 higher)*	LOW
Range of movement left hip extension at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.03 lower (0.31 lower to 0.25 higher)*	LOW
Range of movement right popliteal angle at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.48 higher (4.43 lower to 7.39 higher)*	LOW
Range of movement right popliteal angle at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.29 lower (7.06 lower to 6.48 higher)*	LOW
Range of movement left popliteal angle at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 3.54 higher (2.65 lower to 9.73 higher)*	LOW
Range of movement left popliteal angle at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 2.67 higher (3.87 lower to 9.21 higher)*	LOW
Range of movement right ankle dorsiflexion at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.58 lower (5.86 lower to 4.7 higher)*	LOW
Range of movement right ankle dorsiflexion at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.78 higher (4.98 lower to 6.54 higher)*	LOW

Range of movement left ankle dorsiflexion at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.32 lower (5.8 lower to 5.16 higher)*	LOW
Range of movement left ankle dorsiflexion at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.6 higher (4.83 lower to 6.03 higher)*	LOW

CI confidence interval, MD mean difference
* Calculated by the NCC-WCH

Table 4.7 Evidence profile for child-focused intervention compared with context-focused intervention in children with spasticity; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Child-focused intervention	Context-focused intervention	Relative (95% CI)	Absolute (95% CI)	
PEDI self-care functional skills at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 2.49 higher (3.25 lower to 8.23 higher)*	LOW
PEDI self-care functional skills at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.11 higher (6.22 lower to 6.44 higher)*	LOW
PEDI mobility functional skills at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.17 higher (7.27 lower to 9.61 higher)*	LOW
PEDI mobility functional skills at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.52 higher (7.26 lower to 10.3 higher)*	LOW
PEDI self-care caregiver assistance at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.58 lower (9.2 lower to 8.04 higher)*	LOW
PEDI self-care caregiver assistance at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.28 higher (7.78 lower to 10.34 higher)*	LOW
PEDI mobility caregiver assistance at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 0.42 higher (9.64 lower to 10.48 higher)*	LOW

PEDI mobility caregiver assistance at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 3.18 higher (7.25 lower to 13.61 higher)*[a]	LOW
GMFM-66 total score at 6 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 1.17 higher (3.64 lower to 5.98 higher)*	LOW
GMFM-66 total score at 9 months (final score; better indicated by higher values)					
1 study (Law 2011)	71	57	-	MD 2.73 higher (2.33 lower to 7.79 higher)*	LOW

CI confidence interval, GMFM-66 Gross Motor Function Measure 66-item score, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory
* Calculated by the NCC-WCH
a The study authors reported a small but unquantified statistically significant change from baseline to 9 months, reflecting an increase in the child-focused group and a decrease in the context-focused group at 9-months' follow-up

Neither study reported outcomes relevant to acceptability and tolerability, pain (reduction of pain), quality of life, or adverse effects.

Strengthening versus usual care not including strengthening

None of the studies identified for inclusion reported reduction of spasticity.

All five RCTs reported outcomes relevant to optimisation of function and movement (Dodd 2003; Fowler 2010; Lee 2008; Liao 2007; Unger 2006).

Table 4.8 Evidence profile for strengthening programmes (progressive resistive exercises) compared with usual care in children with unilateral or bilateral spasticity; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Strengthening	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-88, goal dimension score at 6 weeks (change from baseline, better indicated by higher values)					
1 study (Liao 2007)	10[a]	10[b]	-	MD 8.6 higher*[c]	LOW
GMFM-D (standing) score (GMFM version not reported) at 6 weeks (change from baseline, better indicated by higher values)					
1 study (Lee 2008)	9[d]	8[e]	-	MD 0.6 lower*[f]	MODERATE
1 study (Dodd 2003)	11[g]	10[h]	-	MD 1 lower*	MODERATE
GMFM-D (standing) score (GMFM version not reported) at 18 weeks (change from baseline, better indicated by higher values)					
1 study (Dodd 2003)	11[i]	9[j]	-	MD 0.9 lower*[k]	MODERATE
GMFM-E (walking, running and jumping) score (GMFM version not reported) at 6 weeks (change from baseline, better indicated by higher values)					

1 study (Lee 2008)	9[l]	8[m]	-	MD 1 higher*	MODERATE
1 study (Dodd 2003)	11[n]	10[o]	-	MD 3.2 higher*	MODERATE
GMFM-E (walking, running and jumping) score (GMFM version not reported) at 18 weeks (change from baseline, better indicated by higher values)					
1 study (Dodd 2003)	11[p]	9[q]	-	MD 5.9 higher*[r]	MODERATE
GMFM-66 total score (change from baseline at 12 weeks, better indicated by higher values)					
1 study (Fowler 2010)	29[s]	29[t]	-	MD 0.7 higher*[u]	MODERATE
GMFM (version not reported) total score at 6 weeks (change from baseline, better indicated by higher values)					
1 study (Lee 2008)	9[v]	8[w]	-	MD 0 higher*	MODERATE
1 study (Dodd 2003)	11[x]	10[y]	-	MD 1.2 higher*	MODERATE
GMFM (version not reported) total score at 18 weeks (change from baseline, better indicated by higher values)					
1 study (Dodd 2003)	11[z]	9[A]	-	MD 2 higher*	MODERATE
Walking speed (m/minute) at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Liao 2007)	10[B]	10[C]	-	MD 9.2 higher*[D]	LOW
Walking speed (centimetres/second) at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Lee 2008)	9[E]	8[F]	-	MD 25.5 higher[G]	MODERATE
Walking speed (metres/minute) at 6 weeks (10m walk test) (change from baseline) (Better indicated by higher values)					
1 study (Dodd 2003)	11[H]	10[I]	-	MD 0.4 lower*	MODERATE
Walking speed (millimetres/second) at 8 weeks (change from baseline) (Better indicated by higher values)					
1 study (Unger 2006)	24[J]	13[K]	-	MD 0.3 higher	LOW
Walking speed (30-second walk test) Change from baseline at 12 weeks (Better indicated by higher values)					
1 study (Fowler 2010)	27[L]	28[M]	-	MD 2.2 higher*[N]	MODERATE
Walking speed (metres/minute) at 18 weeks (10-minute walk test, change from baseline, better indicated by higher values)					
1 study (Dodd 2003)	11[O]	9[P]	-	MD 0.7 lower*	MODERATE

Timed stair(s) at 6 weeks (change from baseline, better indicated by lower values)					
1 study (Dodd 2003)	11[Q]	9[R]	-	MD 5.6 lower*[S]	MODERATE
Timed stair(s) at 18 weeks (change from baseline, better indicated by lower values)					
1 study (Dodd 2003)	11[T]	9[U]	-	MD 0.4 lower*	MODERATE

ANCOVA analysis of covariance, CI confidence interval, GMFM Gross Motor Function Measure, GMFM-66 Gross Motor Function Measure 66-item score, GMFM-88 Gross Motor Function Measure 88-item score, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, NS, not (statistically) significant, SE standard error;

* Calculated by the NCC-WCH

a Pre-training score = 76.6 (SE 4.4), Adjusted post-training = 82.7 (SE 0.7)

b Pre-training score = 83.1 (SE 3.2), Adjusted post-training = 80.6 (SE 0.7)

c ANCOVA of post strengthening training scores: P (1 tailed) = 0.02 reported

d Pre-training: 73.5±25.7, at 6 weeks = 73.8±26.6

e Pre-training: 74.5±23.7, at 6 weeks = 75.4±22.7

f p=NS reported

g Baseline score = 75.2 (14.4), at 6 weeks = 80.1 (13.7)

h Baseline score = 74.6 (20.9), at 6 weeks = 80.5 (12.6)

i Baseline score = 75.2 (14.4), at 18 weeks = 80.4 (13.2)

j Baseline score = 74.6 (20.9), at 18 weeks = 80.7 (15.0)

k NS (p value not reported)

l Pre-training score: 61.6±34.1, at 6 weeks = 63.0±34.4

m Pre-training score: 61.4±33.9, at 6 weeks = 61.8±34

n Baseline score = 52.8 (31.3, at 6 weeks = 57.2 (29.7)

o Baseline score = 68.3 (30.1), at 6 weeks = 69.5 (27.9)

p Baseline score = 52.8 (31.3), at 18 weeks = 58.2 (31.3)

q Baseline score = 68.3 (30.1), at 18 weeks = 67.8 (28.6)

r NS (p value not reported)

s Change from baseline (mean (95% CI)) Cycling group = 1.2 (0.5 to 1.8)

t Change from baseline (mean (95% CI)) Control group = 0.5 (-0.2 to 1.3)

u NS (p value not reported)

v Pre-training score = 86.5±13.3, Follow up at 6 weeks = 87±13.5

w Pre-training score = 85.2±13.4, Follow up at 6 weeks = 85.7±13.3

x Baseline score = 64.2 (27.8), at 6 weeks = 69.0 (21.4)

y Baseline score = 71.7 (24.9), at 6 weeks = 75.3 (21.3)

z Baseline score = 64.2 (27.8), at 18 weeks = 69.6 (21.4)

A Baseline score = 71.7 (24.9), at 18 weeks = 74.3 (21.4)

B Pre-training speed m/min = 56.9 (SE 5.1) Adjusted post-training speed 61.3 (1.7)

C Pre-training speed m/min = 63.8 (SE 3.0) Adjusted post-training speed 59.0 (1.7)

D ANCOVA of post strengthening training scores: P (1 tailed =: 0.18 (NS) reported

E Pre-training speed cm/s = 54.7±30.7, at 6 weeks: 78.2±39.3

F Post training speed cm/s = 74.6±38.7, at 6 weeks: 67.8±37.2

G p<0.05 when compared to control group

H Baseline speed (m/min) = 47.4 (23.3), at 6 weeks = 48.0 (21.2)

I Baseline speed (m/min) = 49.5 (24.5), at 6 weeks = 50.5 (20.8)

J Pre-training speed mm/s = 1075.6 (235.4) Post-training = 1119.3 (232.5)

K Pre-training speed mm/s = 1128 (132.0) Pre-training = 1171.4 (141.9)

L Change from baseline (mean (95% CI)) Cycling group: 1.2 (-3.9 to 6.2)

M Change from baseline (mean (95% CI)) Control group: 3.4 (-1.7 to 8.4)

N p = 0.52 reported

O Walking speed (m/min) at baseline = 47.4 (23.3), at 18 weeks = 48.6 (23.3)

P Walking speed (m/min) at baseline = 49.5 (24.5), at 18 weeks = 51.4 (16.5)

Q Timed stair, s, at baseline = 27.4 (34.7), at 6 weeks = 21.1 (25.6)

R Timed stair, s, at baseline = 22.4 (20.5), at 6 weeks = 21.7 (21.5)

S p=0.10 reported
T Timed stair (s) at baseline = 27.4 (34.7), at 18 weeks = 25.1 (33.6)
U Timed stair (s) at baseline = 22.4 (20.5), at 18 weeks = 19.7 (15.2)

None of the studies reported pain (reduction of pain).

Two of the studies reported outcomes relevant to quality of life (Dodd 2004; Unger 2006).

Table 4.9 Evidence profile for strengthening programmes (progressive resistive exercises) compared with usual care in children with unilateral or bilateral spasticity; quality of life

Number of studies	Number of participants		Effect		Quality
	Strengthening	Usual care	Relative (95% CI)	Absolute (95% CI)	
Self-perception of functional competence at 8 weeks (composite score/25, change from baseline, better indicated by higher values)					
1 study (Unger 2006)	24[a]	13[b]	-	MD 0.1 lower*[c]	LOW
Self-perception of body image at 8 weeks (composite score/25, change from baseline, better indicated by higher values)					
1 study (Unger 2006)	24[d]	13[e]	-	MD 2.9 higher*[f]	LOW
Self-perception (global self-worth) at 18 weeks (score 0 to 4, better indicated by lower values)					
1 study (Dodd 2004)	10[g]	6[h]	-	MD 0.02 higher*[i]	LOW

CI confidence interval, MD mean difference, NS not (statistically) significant
* Calculated by the NCC-WCH
a Pre-training score = 19.9 (3.4), Post-training score = 21.3 (3.3)
b Pre-training score = 19.0 (3.2), Post-training score = 20.5 (3.3)
c p = NS reported
d Pre-training score = 23.9 (4.1), Post-training score = 25.9 (3.4)
e Pre-training score = 23.2 (4.6), Post-training score = 22.3 (4.7)
f $p < 0.05$ reported
g Baseline score = 3.41 (0.38), Follow up at 18 weeks = 3.57 (0.45)
h Baseline score = 3.27 (0.52), Follow up at 18 weeks = 3.41 (0.49)
i p=NS reported

Two of the studies investigated adverse effects (Dodd 2003; Fowler 2010).

Table 4.10 Evidence profile for strengthening programmes (progressive resistive exercises) compared with usual care in children with unilateral or bilateral spasticity; adverse events

Number of studies	Number of participants		Effect		Quality
	Strengthening	Usual care	Relative (95% CI)	Absolute (95% CI)	
Adverse effects: pressure on shoulder, mild foot and ankle discomfort					
1 study (Dodd 2003)	3/11 (27.3%)[a]	0/9 (0%)	-	-	LOW
Adverse effects: mild pain, soreness or muscle cramping					

1 study (Fowler 2010)	17/29 (58.6%)	0/29 (0%)	-	-	LOW
Adverse effects: observed falls					
1 study (Fowler 2010)	6/29 (20.6%)	0/29 (0%)	-	-	LOW
Adverse effects: skin rash					
1 study (Fowler 2010)	1/29 (3.4%)[b]	0/29 (0%)	-	-	LOW

CI confidence interval
* Calculated by the NCC-WCH
a Three adverse events were reported in the strengthening group. One participant reported pressure on the shoulders from the backpack. As a result, weights were carried in a home-made vest to distribute the load more evenly. Two participants reported mild foot and ankle discomfort during the heel raise exercise. To alleviate this, the physiotherapy trainer modified the exercise so that ankle dorsiflexion did not exceed the plantargrade position. This modification enabled these participants to continue without incident.
b One child with a skin rash related to the HR sensor

None of the studies reported outcomes related to acceptability and tolerability.

Serial casting versus usual care not including serial casting

The only study identified for inclusion (McNee 2007) did not report reduction of spasticity, but did report optimisation of movement at the ankle joint.

Table 4.11 Evidence profile for serial casting compared with usual care in children with unilateral or bilateral spasticity; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Serial casting	Usual care	Relative (95% CI)	Absolute (95% CI)	
PROM ankle dorsiflexion (knee flexed, change from baseline at 12 weeks, better indicated by higher values)					
1 study (McNee 2007)	9	9	-	MD 11.66 higher (4.17 to 19.15 higher)	MODERATE
PROM ankle dorsiflexion (knee extended, change from baseline at 12 weeks), better indicated by higher values)					
1 study (McNee 2007)	9	9	-	MD 1.450 higher (2.84 lower to 5.75 higher)	LOW

CI confidence interval, MD mean difference, PROM, passive range of movement

The study also reported optimisation of function in terms of walking speed.

Table 4.12 Evidence profile for serial casting compared with usual care in children with unilateral or bilateral spasticity; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Serial casting	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**	
Walking speed (m/second, tridimensional gait analysis, change from baseline at 12 weeks, better indicated by higher values)					
1 study (McNee 2007)	9[a]	9[b]	-	MD 0.03 lower (0.18 lower to 0.13 higher)[c]	LOW

CI confidence interval, MD mean difference, NS not (statistically) significant, SD standard deviation
a Change from baseline at 12 weeks mean (SD) = -0.01 (0.1)
b Change from baseline at 12 weeks mean (SD) = 0.02 (0.2)
c p=NS reported

The study did not report pain (reduction of pain), quality of life, adverse effects, or acceptability and tolerability.

Early casting after botulinum toxin versus delayed casting

The only study identified for inclusion (Newman 2007) reported outcomes relevant to reduction of spasticity and optimisation of movement of the joint. The outcomes reported included Modified Tardieu Scale (MTS) scores.

Table 4.13 Evidence profile for early casting after botulinum toxin compared with delayed casting after botulinum toxin in children with unilateral or bilateral spasticity; tone and joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Early casting post botulinum toxin	**Delayed casting post botulinum toxin**	**Relative (95% CI)**	**Absolute (95% CI)**	
MTS score, gastrosoleus spasticity at 3 months after casting (better indicated by lower values)					
1 study (Newman 2007)	6[a]	6[b]	-	MD 9.20 higher (1.37 to 17.03 higher)[c]	LOW
PROM 3 months after casting (better indicated by higher values)					
1 study (Newman 2007)	6[d]	6[e]	-	MD 2.00 higher (6.76 lower to 10.76 higher)[f]	LOW
MTS score, gastrosoleus spasticity at 6 months after casting (better indicated by higher values)					
1 study (Newman 2007)	6[g]	6[h]	-	MD 15.00 higher (4.42 to 25.58 higher)[i]	LOW
PROM 6 months after casting (better indicated by higher values)					
1 study (Newman 2007)	6[j]	6[k]	-	MD 0.40 lower (10.39 lower to 9.59 higher)[l]	LOW

CI confidence interval, MD mean difference, MTS Modified Tardieu Scale, PROM, passive range of movement
a Change from baseline at 3 months = -7.0 (6.7)
b Change from baseline at 3 months = -16.2 (5.4)
c p = 0.007 reported
d Change from baseline at 3 months = 9.8(8.1) p = 0.012 from baseline
e Change from baseline at 3 months = 7.8 (5.2) p = 0.002 from baseline
f p = 0.556 reported
g Change from baseline at 6 months = 2.9 (9.9)
h Change from baseline at 6 months = -12.1 (6.1)
i p = 0.002 reported
j Change from baseline at 6 months = 6.0 (9.2) p = 0.108 from baseline
k Change from baseline at 6 months = 6.4 (6.0) p = 0.013 from baseline
l p = 0.907 reported

The study did not report optimisation of function, quality of life, or pain (reduction of pain).

The study reported adverse effects.

Table 4.14 Evidence profile for early casting after botulinum toxin compared with delayed casting after botulinum toxin in children with unilateral or bilateral spasticity; adverse events

Number of studies	**Number of participants**		**Effect**		**Quality**
	Early casting post botulinum toxin	**Delayed casting post botulinum toxin**	**Relative (95% CI)**	**Absolute (95% CI)**	
Pain in first 48 hours after cast application requiring recasting					
1 study (Newman 2007)	3/6 (50%)[a]	0/6 (0%)[b]	-	-	LOW

CI confidence interval
a Three children complained of pain that required recasting
b Chi-squared, p=0.08

The study did not report outcomes related to acceptability and tolerability.

Evidence statement

Active use therapy versus no active use therapy

No evidence was identified in relation to reduction of spasticity.

With regard to optimisation of range of movement, one RCT provided evidence of increases in AROM and PROM wrist extension at 9 and 17 weeks compared to baseline after children received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care, although these improvements were not statistically significant. (MODERATE) The same RCT reported evidence of increases in AROM elbow extension at 9 or 17 weeks compared to baseline in children who received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to those who received 8 weeks of usual care, although these improvements were not statistically significant. (MODERATE) Improvements in PROM elbow extension in children who received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care (MODERATE) were not statistically significantly different at 9 weeks compared to baseline (MODERATE), but were statistically significant at 17 weeks compared to baseline. (HIGH)

With regard to optimisation of function and movement, one RCT provided evidence of a statistically significant improvement in hand function (AHA scores) at 9 weeks and 17 weeks compared to baseline in children who received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care. (MODERATE) The same RCT provided evidence of a statistically significant improvement in GAS scores at 9 weeks and 17 weeks compared to baseline `after children received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care. (HIGH)

A further RCT provided evidence of statistically significant improvements in goal attainment (GAS T-scores) and performance (COPM-P scores) at 8 weeks in children who received a 4-week OTHP and children who received an 8-week OTHP as compared to children who did not receive the programme. (HIGH) However, there were no statistically significant differences in GAS T-scores or COPM-P scores between the children who received the 4-week programme and those who received the 8-week programme. (MODERATE)

One RCT provided evidence of statistically significant improvements in performance (COPM-P scores) at 9 weeks and 17 weeks compared to baseline after children received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care. (HIGH)

One RCT reported an improvement in walking speed (10-minute walk test) at 6 weeks compared to baseline after children and young people received a 6-week home-based task-oriented exercise programme (including sit to stand and step-up exercises) as compared to those who did not receive the programme, although this improvement was not statistically significant. (LOW)

With regard to acceptability and tolerability, one RCT provided evidence of statistically significant improvements in satisfaction (COPM-S scores) at 8 weeks in children who received a 4-week OTHP and those who received an 8-week OTHP as compared to children who did not receive the programme. (HIGH) However, no statistically significant differences in satisfaction (COPM-S scores) between the children who received the 4-week programme and those who received the 8-week programme were reported. (MODERATE)

A further RCT provided evidence of statistically significant improvements in satisfaction (COPM-S scores) at 9 weeks and 17 weeks after children received 6 weeks of modified CIMT and 2 weeks of bimanual training as compared to children who received 8 weeks of usual care. (HIGH)

No evidence was identified in relation to pain (reduction of pain) or quality of life.

With regard to adverse effects, one RCT provided evidence that no adverse effects were observed in children who received a 4-week or 8-week OTHP or in children who did not receive the programme. (LOW)

Comparison between different forms of active use therapy

No evidence was identified in relation to reduction of spasticity.

With regard to optimisation of function one RCT provided evidence of an improvement in AHA scores at 3 weeks compared to baseline, but a reduction at 26 weeks compared to baseline in children and young people with hemiplegia who received CIMT as compared to those who received bimanual training. These findings were not statistically significant. (MODERATE) The same RCT provided evidence of an improvement in MAUULF scores at 3 weeks compared to baseline in children with hemiplegia who received CIMT as compared to those who received bimanual training. This finding was not statistically significant. (MODERATE) At 26 weeks there was evidence of a statistically significant improvement in MAUULF scores compared to baseline in children and young people with hemiplegia who received CIMT as compared to those who received bimanual training. (MODERATE)

With regard to optimisation of range of movement, one cluster RCT provided evidence of a reduction in both right and left hip abduction at 6 months and an improvement at 9 months (final score analysis) in children who received child-focused physical therapy as compared to those who received context-focused physical therapy. These findings were not statistically significant. (LOW) The same cluster RCT reported that there was an improvement in both right and left hip extension at 6 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. At 9 months (final score analysis), there was improvement in hip extension in the right leg, but a reduction in the left leg in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW) The same cluster RCT reported that there was an improvement in both right and left popliteal angle at 6 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. At 9 months (final score analysis), there was a reduction in the right popliteal angle range of movement, but an improvement in the left leg in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW) The same cluster RCT provided evidence of a reduction in both right and left ankle dorsiflexion at 6 months and an improvement at 9 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW)

With regard to optimisation of function the same cluster RCT provided evidence of an improvement in PEDI self-care and mobility functional skills scale scores at both 6 and 9 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW)

The same cluster RCT provided evidence of a reduction in PEDI self-care caregiver assistance scale scores at 6 months but an improvement at 9 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW) PEDI mobility caregiver assistance scale scores were improved at both 6 and 9 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW) However, the study authors reported an unquantified statistically significant improvement in PEDI self-care functional skills scale scores at 9 months compared to baseline in children who received the child-focused intervention as compared to those who received the context-focused intervention.

The same cluster RCT provided evidence of an improvement in GMFM-66 scores at 6 and 9 months (final score analysis) in children who received the child-focused intervention as compared to those who received the context-focused intervention. These findings were not statistically significant. (LOW)

No evidence was identified in relation to acceptability and tolerability, pain (reduction of pain), quality of life, or adverse effects.

Strengthening versus usual care not including strengthening

No evidence was identified in relation to reduction of spasticity.

With regard to optimisation of function and movement, mean change scores from baseline were calculated by the NCC-WCH technical team from data reported in individual publications as baseline values between the groups were often different and so final score comparisons would not be representative estimates of actual treatment effects. Standard errors (SEs) or SDs were not reported in the included studies for these mean change estimates. Hence the following findings provide an estimate of the direction of the treatment effect but the statistical significance of the mean change scores comparisons could not be determined.

One RCT found an improvement in function (GMFM 88 goal dimension) at 6 weeks compared to baseline in children and young people who received a strengthening programme for 6 weeks compared to those who received their regular physical therapy instead of the programme. The statistical significance of this finding could not be determined. (LOW)

Two RCTs provided evidence of a reduction in function (GMFM-D, standing) at 6 weeks compared to baseline in children and young people who received a strengthening programme compared to those who received conventional therapy. The participants received a 5-week strengthening programme in one study and a 6-week strengthening programme in the other. The statistical significance of these findings could not be determined. (MODERATE) The second RCT also provided evidence of a reduction in function (GMFM-D) at 18 weeks compared to baseline in children and young people who received a 6-week strengthening programme as compared to those who received usual care instead of the programme. The statistical significance of this finding could not be determined. (MODERATE)

Two RCTs provided evidence of an improvement in function (GMFM-E, walking, running and jumping) at 6 weeks compared to baseline in children and young people who received a strengthening programme compared to those who received conventional physical therapy. (MODERATE) The participants received a 5-week strengthening programme in one study and a 6-week strengthening programme in the other. The statistical significance of the findings could not be determined. (MODERATE) The second RCT also provided evidence of an improvement in function (GMFM-E) at 18 weeks compared to baseline in children and young people who received a 6-week strengthening programme as compared to those who received usual care instead of the programme. The statistical significance of this finding could not be determined. (MODERATE)

A further RCT reported an improvement in function (GMFM-66 total score) at 12 weeks compared to baseline in children and young people who received a 12-week strengthening programme as compared to those who did not receive the programme, although this finding was reported as not being statistically significant. (MODERATE)

One RCT reported no difference in function (GMFM total score) at 6 weeks compared to baseline in children and young people who received a strengthening programme for 5 weeks as compared to those who received conventional physical therapy for 5 weeks. The statistical significance of this finding could not be determined. (MODERATE) Another RCT reported an improvement in function (GMFM total score) at 6 weeks and at 18 weeks compared to baseline in children and young people who received a strengthening programme for 6 weeks as compared to those who received conventional physical therapy for 6 weeks. The statistical significance of these findings could not be determined. (MODERATE)

One RCT reported an improvement in walking speed (three-dimensional gait analysis) at 8 weeks in children and young people who received a strengthening programme for 8 weeks as compared to those who did not receive the programme. (LOW)

Another RCT reported an improvement in walking speed (30-second walk test) at 12 weeks after children and young people received a 12-week strengthening programme as compared to those who did not receive the programme. (MODERATE)

One RCT reported a reduction in walking speed (10-minute walk test) at 18 weeks after children and young people received a 6-week strengthening programme as compared to those who received usual care instead of the programme. (MODERATE) The same RCT found children and young people who participated in a 6-week strengthening programme performed a timed stair test more quickly at 6 or 18 weeks compared to those who received usual care instead of the programme. (MODERATE)

Five RCTs reported estimates of walking speed. Two RCTs provided evidence of improvement in walking speed at 6 weeks compared to baseline in children and young people who received a strengthening programme for 5 weeks (LOW) and 6 weeks (MODERATE) compared to those who received their usual physical therapy only. The statistical significance of these findings could not be determined.

One further RCT provided evidence of a reduction in walking speed at 6 weeks compared to baseline in children and young people who received a strengthening programme for 6 weeks compared to those who received their usual physical therapy only. The statistical significance of this finding could not be determined. (MODERATE)

Another RCT provided evidence of an improvement in walking speed (three-dimensional gait analysis) at 8 weeks compared to baseline in children and young people who received a strengthening programme for 8 weeks as compared to those who did not receive the programme. The statistical significance of this finding could not be determined. (LOW)

Another RCT provided evidence of an improvement in walking speed (30-second walk test) at 12 weeks after children and young people received a 12-week strengthening programme as compared to those who did not receive the programme. (MODERATE)

One RCT provided evidence of an improvement in walking speed (10-minute walk test) at 18 weeks compared to baseline after children and young people received a 6-week strengthening programme as compared to those who received usual care instead of the programme. The statistical significance of this finding could not be determined. (MODERATE) The same RCT provided evidence of an improvement in a timed stair test at 6 and 18 weeks after children and young people started a 6-week strengthening programme as compared to those who received usual care instead of the programme. The statistical significance of this finding could not be determined. (MODERATE)

No evidence was identified in relation to pain (reduction of pain).

With regard to quality of life, one RCT provided evidence of a decrease in self-perception of functional competence at 8 weeks compared to baseline, but an improvement in self-perception of body image at 8 weeks compared to baseline in children and young people who received a strengthening programme for 8 weeks as compared to those who did not receive the programme. The statistical significance of these findings could not be determined. (LOW) One RCT provided evidence of an improvement in self-perception (global self-worth) at 18 weeks compared to baseline after children and young people received a 6-week strengthening programme as compared to those who received usual care instead of the programme. (LOW) With regard to adverse effects, one RCT reported that 27.3% of children who received a 6-week strengthening programme experienced pressure on the shoulder, mild foot discomfort or mild ankle discomfort. No episodes of these adverse events were reported in the group that did not receive the intervention. (LOW) A further RCT reported that 58.6% of children and young people who received a 12-week strengthening programme complained of mild pain, soreness, or muscle cramping 20.6% were observed falling, and 3.4% experienced a skin rash related to the equipment used. No episodes of these adverse events were reported in the group that did not receive the intervention. (LOW)

No evidence was identified in relation to acceptability and tolerability.

Serial casting versus usual care not including serial casting

No evidence was identified in relation to reduction of spasticity.

With regard to optimisation of movement, one RCT provided evidence of a statistically significant improvement in PROM ankle dorsiflexion (knee flexed) at 12 weeks compared to baseline after children received serial casting as compared to when the same children did not receive casting. (MODERATE) The RCT also provided evidence of an improvement in PROM ankle dorsiflexion (knee extended) at 12 weeks compared to baseline after the children received serial casting as compared to when they did not receive casting, although this improvement was not statistically significant. (LOW)

With regard to optimisation of function, the RCT reported an improvement in walking speed (tridimensional gait analysis) at 12 weeks compared to baseline after the children received serial casting as compared to when they did not receive casting, although this improvement was not statistically significant. (LOW)

No evidence was identified in relation to pain (reduction of pain), quality of life, adverse effects, or acceptability and tolerability.

Early casting after botulinum toxin versus delayed casting

With regard to reduction of spasticity, one RCT provided evidence of a statistically significant reduction in spasticity (MTS score) at 3 and 6 months compared to baseline in children who received casting 4 weeks after BoNT treatment as compared to those children who received casting immediately after BoNT treatment for the treatment of spastic equinus. (LOW) The same RCT reported an improvement in PROM at the ankle after 3 months compared to baseline, but a decrease compared to baseline at 6 months in children who received casting immediately after BoNT treatment compared to those who received casting 4 weeks after BoNT treatment. These findings were not statistically significant. (LOW)

No evidence was identified in relation to optimisation of function, pain (reduction of pain), or quality of life.

With regard to adverse effects, the RCT provided evidence that 50% of children who received casting immediately after BoNT treatment required a change of cast within 48 hours of having their first cast applied because of pain. None of the children who received casting 4 weeks after BoNT treatment required a change of cast for this reason. (LOW)

No evidence was identified in relation to acceptability and tolerability.

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion.

- casting plus BoNT versus BoNT only
- postural management versus usual care not including postural management
- passive stretching versus usual care not including passive stretching
- neurodevelopmental treatment (NDT).

Health economics

No economic evaluations of physical therapy were identified in the literature search conducted for the guideline. There is very limited good quality evidence of clinical effectiveness for physical therapy. After much discussion, the GDG came to the view that it would not be possible to quantify the mean benefits of physical therapy to inform a cost effectiveness analysis. A simple cost description showed 1 hour per week of physical therapy would cost approximately £2,000 per year (see Chapter 11). The costs would need to be considered alongside the benefits to determine value for money, and this would require comparative long-term data which are not currently available.

Evidence to recommendations

Relative value of outcomes

Although physical therapy might not alter spasticity the GDG considered that this should be assessed and that the Ashworth and Tardieu scales and the Modified Ashworth Scale (MAS) and the MTS were appropriate outcomes measures because they are widely used in research. Optimisation of movement was prioritised as this is a prime aim of physical therapy. AROM was considered a useful indicator of selective muscle control and hence a potentially important outcome. PROM was also considered important because muscle tightness may be improved by physical therapy. Walking speed and distance (endurance) were also considered to be clinically important outcome measures because improvement would increase the ability to participate in activities and join in with peers. Optimisation of function is often the cornerstone of physical therapy programmes and was, therefore, considered to be an important outcome. The GDG prioritised commonly employed measures of function including the AHA, the GAS, the PEDI and the GMFM (66- or 88-item versions). The GDG recognised, however, that some of these outcome measures may not be sensitive enough to detect clinically important improvements in function. Measurements of quality of life were also considered important as outcomes of physical therapy, and the GDG prioritised measures such as COPM-S and COPM-P scales (both subjective scales), the Child Health Questionnaire (CHQ), and the Pediatric quality of life inventory (PedsQL) as useful measures. Pain was regarded as an important outcome, in that the GDG consensus was that physical therapy might have a role in the management of painful muscle spasms and chronic pain more generally, and the GDG agreed that reported outcomes based on objective pain scales should be included. Certain adverse effects might be anticipated with physical therapy, including pain and discomfort. Injury might also be important, and such effects were included as important outcomes. Finally, acceptability and tolerability of physical therapy interventions was considered by the GDG to be a key outcome.

Quality of evidence and trade-off between clinical benefits and harms

The evidence sought for the guideline review related to four key areas of physical therapy: task-focused active-use therapy, muscle strengthening, passive stretching, and postural management.

Task-focused active-use therapy

Task-focused active-use therapy programmes have been used widely with the intention of improving functional activities and enhancing participation in normal activities to the best of the individual's ability. These approaches have been recommended in part based on 'motor learning' principles.

Programmes typically consist of functional activities carried out with instruction and demonstration followed by feedback. Repetition and practice are considered to be critically important. Functional activities include daily maintenance activities, such as standing to perform a task (for example, brushing one's teeth).

Moderate- to high-quality evidence from RCTs supported the effectiveness of active-use therapy consisting of CIMT followed by bimanual training in improving upper limb function. There was evidence suggesting improved hand function and GAS scores, and of improved performance scores and reported satisfaction scores up to 17 weeks after 4-8 week blocks of such therapy. The GDG made a specific recommendation based on these studies.

The GDG considered that active-use therapy was likely to be particularly effective in young children because before 8 years of age, children with spasticity are still developing their mobility and hand-skill strategies. However the group did not think it would be helpful to introduce specific age limits into the recommendations because development in this population is highly individualised. Instead the group considered that decision making should be determined by clinical judgement based on clinical indications and individual needs. The GDG considered that active-use therapy provided in the context of the child's normal activities, for instance at a nursery or at home, was more likely to prove effective than those developed in a more abstract setting because, in the group's experience, it would increase the likelihood of the child engaging with the treatment, and opportunities to use the treatment would arise more often as a result. The group did, however, acknowledge that the practicalities of providing therapy in the context of the child's normal activities would need to be considered at a local level. Seeing children at home or nursery rather than in a clinic may mean a physical therapist will see fewer children because they need to spend more time travelling. This trade-off is reflected in the wording of the recommendation.

One RCT provided moderate- to high-quality evidence for significant improvements in goal attainment using an individualised occupational therapy programme delivered at the child or young person's home (OTHP) over 4 or 8 weeks. The programme interventions varied greatly depending on individual goals, and they included specific goal-directed training, handwriting task training, recreation and sports therapy, play therapy and CIMT. In addition to these active-use interventions, other strategies employed included parent education and positive behavioural support, and the use of adaptive equipment, strength training and orthoses. Using these diverse interventions there were improvements for both the 4- and 8-week groups in relation to GAS, participation (COPM-P) and satisfaction (COPM-S). There was, however, no significant difference between the different durations of the programme (4 or 8 weeks). The GDG considered that this study highlighted the success that could be achieved with appropriately focused therapy strategies, and especially active-use therapy, in achieving specific treatment goals. The group also considered that this study highlighted the importance of individualised physical therapy and this was reflected in the recommendations.

Another RCT examined the effect of a 6-week home-based course of active-use therapy including a programme of motor and balance tasks for children and young people with spasticity due to cerebral palsy or a traumatic brain injury but there was only one relevant outcome reported and this was that there was no evidence that this approach improved walking speed.

A further RCT compared the effectiveness of child- versus context-focused approaches to physical therapy. The child- and context-focused interventions differed in terms of content and who provided the physical therapy, and the GDG recognised the need for further research in this area, particularly among children and young people who are at GMFCS level I, II or III.

Muscle strengthening

The studies of physical therapy aimed at muscle strengthening all focused on progressive resistive training. None of these found evidence of improved function. One reported evidence of improved self-perception (a measure of quality of life). The evidence was largely of poor quality for the outcomes examined, and the sample sizes were often small. The descriptions of the 'usual therapy' with which the strengthening programmes were compared were unclear. Despite this relative lack of evidence for clinically important outcomes, the GDG consensus, based on their recognition of the importance of muscle weakness in some individuals and their experience with such physical therapy, was that muscle strengthening could be a useful goal in appropriately selected children and young people. In those with spasticity muscle weakness can be an important contributor to motor difficulties and impaired function. It may be difficult to differentiate weakness of neurological origin from that due to under-use, and in a given individual it may not always be clear at the outset to what degree strengthening can be achieved through physical therapy. Nevertheless the GDG consensus was that improved strength and the possibility of an associated overall improvement in physical fitness may be important as goals for some children and young people. This might be especially true for those who otherwise have a limited opportunity to participate in exercise programmes.

The GDG therefore recommended that consideration be given to the use of muscle strengthening therapy where, based on the assessment, it is thought likely that muscle weakness is contributing to loss of function or postural difficulties. The GDG recommended that strengthening therapies be directed towards specific goals, and should incorporate progressive repetitive exercises against resistance.

Passive stretching

Passive stretching, whether manually through the use of casts, or otherwise, has been a part of physical therapy for many years. Current physical therapy programmes often include brief, manual passive stretching intended to help maintain soft tissue length and hence prevent deformity. The GDG noted that no evidence was found with regard to this approach to physical therapy. The group's consensus was that any effect derived from this approach might be expected to be short-lived, and so they did not recommend it.

Serial casting is often used with the intention of increasing the range of joint movement by lengthening soft tissues. Such therapy is often employed in conjunction with other interventions (for example, to improve a child or young person's ability to tolerate an orthosis). One study reported that serial casting improved PROM (ankle dorsiflexion). In terms of movement and function outcomes the evidence did not show that serial casting improved walking speed, or measures of function, or quality of life. The GDG nevertheless considered that sustained low-load stretching using positioning with equipment and/or orthoses or serial casting was more likely to be effective in maintaining soft tissue length and preventing or limiting deformity. This was directly relevant to the group's considerations in relation to postural management (see below).

Although there was a lack of comparative studies on serial casting employed after BoNT treatment (BoNT with or without subsequent serial casting), it is common practice to employ serial casting in this setting with the aim of enhancing range of movement following reduction in muscle tone. The GDG agreed, based on their experience and the underlying principles of this approach, that this was a worthwhile treatment strategy. There is variation in practice regarding the interval from BoNT treatment to the first cast application. The GDG considered this a significant issue, as injection and casting require the expertise of different services and hence there could be resource implications. The GDG noted the evidence that starting casting about 4 weeks after BoNT treatment did not alter the therapeutic effect, but it was much better tolerated that immediate casting. Problems of tolerance arose in 50% of those who began cast treatment immediately, and these problems required removal and replacement of casts. While the study population in this trial was small, the GDG was persuaded that delayed casting was preferable and made a recommendation accordingly.

Postural management

Postural management is a widely accepted aspect of physical therapy employed to improve certain functional abilities and to slow or prevent the development of musculoskeletal deformity. Despite this, the GDG noted that no studies were identified that examined the effectiveness of postural management programmes. Nevertheless, the GDG consensus was that postural management based on appropriate individual goals has an important role in the management of spasticity and associated motor disorders. It was considered likely to have an important role in children and young people with functional limitations and in those at risk of deformity or with actual deformity arising due to limitation of movement. The GDG consensus was that the movement and positional needs of the child or young person over a 24-hour period should be considered. In assessing the postural management programme, account should be taken of sleeping and resting positions, sitting and standing, of the individual's opportunities for movement, and their recreational, play and leisure activities. Consideration should be given to the full range of settings in which postural management might usefully apply. Postural management might entail positioning to take account of the child or young person's tone and to support them to facilitate participation in activities appropriate to their stage of development. The GDG's view, based on their clinical experience, was that 24-hour postural management programmes should incorporate periods of low-load active stretching (during which the child or young person engages in activities aimed at improving range of movement) and/or periods of sustained low-load passive stretching using positioning with equipment, serial casting or orthoses.

The GDG considered that training and support of family members or carers was key to successful postural management. It was also essential that a child or young person receiving this form of physical therapy was regularly reviewed to assess their needs and progress, and to consider the use of appropriate forms of equipment.

The GDG considered that benefits derived from physical therapy would need to be balanced against any significant disadvantage. The group agreed that adverse events associated with physical therapy were likely to be relatively uncommon and often minor (for example, minor injury, discomfort or pain) or manageable with modification of the physical therapy programme. The group acknowledged that intensive physical therapy could be associated with significant disruption to the lives of the child or young person and their parents or carers, but thought that this potential risk could be mitigated through recommendations to ensure that these individuals should be provided with adequate information to allow them to make informed choices about the nature of the physical therapy programme being undertaken. The strongest evidence identified in the guideline review related to the use of task-focused active-use therapy. In particular, there was evidence that this approach could improve function and quality of life. Although long-term benefit needs further evaluation, the available evidence suggests that intensive goal-directed active-use therapy results in functional improvement, at least in the short term. Even in children and young people with an existing fixed deformity, physical therapy can be very effective in helping accommodate the deformity so as to maintain function. The GDG also noted that the deformity and reduced participation evident in children and young people who lack access to physical therapy suggested long-term benefits are to be obtained. The group therefore concluded, based on the trial evidence and their clinical experience, that some specific physical therapy techniques, when considered in relation to specific goals such as enhancing skill development, function and ability to participate in everyday activities or preventing complications such as pain or contractures, could provide sufficient benefit to outweigh any risks.

The group also agreed that maintaining an effective physical therapy programme was contingent upon ongoing assessment of the child or young person's needs and those of their family, and the acceptability of the programme to the child or young person and their family or carers. Only through regular reassessment will it be possible to determine whether a physical therapy programme is achieving its intended goals. Over time, as the child or young person grows and develops, it would be likely that the physical therapy programme would need to be modified. The GDG made recommendations with regard to these aspects of physical therapy treatment.

Trade-off between net health benefits and resource use

Provision of physical therapy throughout childhood and into adult life has significant resource implications. The GDG acknowledged that the evidence for effectiveness for various commonly employed physical therapy interventions (including regimens aimed at muscle strengthening, stretching and postural management) was limited. Nevertheless, the group believed, based on the rational principles underlying these regimens and their experience of using these forms of physical therapy in practice, that when employed in suitably selected children and young people they were an essential component of management. Moreover, as mentioned previously, all of the physical therapy techniques detailed in the recommendations are currently in use in the management of spasticity and, therefore, the GDG agreed that it would be possible to implement the guidance without incurring an uplift in resources. In addition, resources may be recovered as a result of the GDG's decision not to recommend brief, manual passive stretching which is currently widely used. The resources associated with the GDG's emphasis on the need for appropriate concomitant physical therapy in relation to BoNT-A and ITB treatment and orthopaedic surgery would be balanced by the increased likelihood of success with those other treatments, leading to greater cost effectiveness overall.

Other considerations

As stated in Section 3.1, the GDG considered physical therapy to mean physiotherapy and/or occupational therapy, and the phrase 'physical therapy' has been used throughout the recommendations to incorporate both forms of therapy. The GDG consensus was that although children and young people may enter a network of care (see below) by a variety of different routes, physical therapy would always be the cornerstone of spasticity management regardless of the severity of the child or young person's condition, the underlying cause or other individual factors. The group therefore recommended that all children and young people with spasticity should be referred promptly for a physical therapy assessment by professionals within the network of care. The GDG acknowledged that in clinical practice the first physical therapy professional most children and young people would be referred to would be a physiotherapist (rather than an occupational therapist), but in some (albeit less frequent) circumstances an occupational therapist could be involved from the outset and this is reflected in the recommendation.

The GDG recognised that it is important to consider whether any equipment or techniques used in a physical therapy programme are safe and appropriate, especially with regard to comorbidities. The group was aware that some children and young people with epilepsy may be at risk of injury associated with sudden movement or falls. Proximity to certain equipment could pose a risk for them and their individual needs should be considered. The group was also aware that children and young people with serious respiratory disorders could be at risk of respiratory decompensation. Care should be taken in such cases when considering strategies for postural management to ensure that the child or young person's respiratory effort is not impaired, as this would increase the risk of respiratory failure. The group was aware that some children and young people with spasticity are at increased risk of pulmonary aspiration due to gastro-oesophageal reflux or impaired airway protective reflexes. The safe positioning of such children and young people should be considered, for example, with regard to postural management. The group was also aware that children and young people who are non-ambulatory, malnourished or taking anticonvulsant therapy are at increased risk of developing osteoporosis. Children and young people with severe spasticity in particular may have one or more of these risk factors and so the GDG agreed that in such cases consideration should be given to the risk of pathological fractures occurring with certain approaches to physical therapy or the use of certain equipment.

The GDG also emphasised in the recommendations the importance of taking account of the implications for the child or young person and their families in implementing a proposed physical therapy programme. Many forms of physical therapy require a sustained commitment and rely on participation of the child or young person and their family over long periods of time. The specific resources of the family and the environmental factors affecting the individual and family require careful consideration when considering the choice of physical therapy if a successful outcome is to be achieved. Certain approaches and the use of certain equipment may be impractical in individual home settings, or there may be a need to adapt the setting to enable the required physical therapy. Moreover, certain cultural practices might act as barriers to particular forms of physical therapy. For example, cultural norms might discourage activities such as swimming and hydrotherapy or group activities with members of opposite sex. In formulating physical therapy programmes healthcare professionals should, therefore, consider potential individual barriers to implementation and seek ways of overcoming such barriers to provide programmes that are acceptable to the individual child or young person and their family.

The GDG believed that appropriate information sharing and the use of written educational materials might facilitate physical therapy. In particular, when children and young people and their families have a proper understanding of their condition and its management, and of realistic goals of physical therapy and are partners in the agreed programme of physical therapy, a successful outcome is much more likely. The GDG concluded that healthcare professionals considering who should deliver physical therapy should take account of whether the child or young person and their parents or carers are able to deliver the specific therapeutic intervention, what training might be needed for the child or young person or their parents or carers, and the wishes of the child or young person and their parents or carers. The GDG emphasised that who delivers physical therapy should be an area of negotiation for the child or young person, their parents or carers, and healthcare professionals. Further, parents and carers who deliver physical therapy, and especially those involved in delivering postural management programmes, should be offered appropriate training and support. Moreover, the GDG considered that where physical therapy is being delivered as an adjunct to other more invasive treatments, it is necessary to ensure that children and young people and their parents and carers understand the need for an appropriately adapted physical therapy programme as an essential component of the overall treatment programme.

Physical therapy in association with other treatment options

While the GDG considered that physical therapy has a central role in the management of spasticity and associated motor disorders, there are many children and young people for whom it is insufficient. Other treatments, for example management with orthoses, BoNT treatment, ITB or orthopaedic surgery may be necessary to improve function and prevent or ameliorate disability and deformity. However, in children and young people undergoing such interventions the GDG recognised that physical therapy is essential to achieving a successful outcome. Also, for those children and young people who might undergo SDR (currently to be offered only in a research context – see Chapter 10), post-operative rehabilitation with an appropriately adapted physical therapy programme is essential.

Principles of care

The GDG's considerations in relation to the evidence identified for this review question and others identified several common themes, and the GDG concluded that these were best addressed through the development of recommendations defining overarching principles of care. These recommendations are underpinned by the concept of a network of care. Networks of care are established in various areas of NHS practice, therefore these recommendations are made with a view to reducing variations in access to care, but they are broad enough to account for local service arrangements. On balance it is expected that the guideline recommendations are sufficiently flexible to be implemented within existing resources. The specific issues and associated actions that the GDG identified as important principles of care were as follows.

Delivering care

The GDG consensus was that all children and young people with spasticity should have access to a network of care. The concept of a network of care was deemed appropriate by the GDG as the complexity of this condition means that the same specific healthcare professionals would not always be involved in the care of every child or young person. This framework can be adapted based on the services that would be most appropriate given the needs of the local community, and is recommended on the understanding that decisions in relation to the details of how care is delivered would be made by local trusts. The aim of the network is to ensure that the experience of all children and young people reflects current good practice with regard to continuity of care, multidisciplinary working and timely access to appropriate treatment. The GDG considered that the key aspects of ensuring these aims were the use of agreed care pathways, effective communication and integrated team working within the network. The group also concluded that, while it was not appropriate to recommend exact service formations, some distinction could be made between expertise that should be available locally versus that which could be provided at either a local or a regional level. Specifically, given the needs of the majority of children and young people with spasticity the GDG concluded that expertise in paediatrics, nursing, physiotherapy, and occupational therapy should be available locally, whereas access to other expertise including orthotics, orthopaedic surgery and paediatric neurology may be provided locally or regionally. The group also noted that all members of the network team should be experienced in the management of spasticity in children and young people. Although the principle of the network is based on it not having specific geographical boundaries, the GDG acknowledged that occasionally children and young people might receive treatment outside the network (for example, in a private health care setting or outside England and Wales). The group therefore made a recommendation that in such cases this treatment should be planned and undertaken in discussion with the network team to ensure integrated care and effective subsequent management.

Management programmes

Patient-important outcomes were central to the GDG's considerations. It was agreed that the ultimate goal of treatment is to maximise the child or young person's potential and quality of life through to adulthood. The group felt that the impact of treatment on clinical and social aspects of the child or young person's disability, and the child or young person's value judgements regarding their quality of life, needed to be considered throughout treatment. Attitudes among children and young people with regard to their disabilities may differ, as may the weight they place on benefits of available treatment options. For example, walking ability might be improved with an appropriate orthosis, enabling a child or young person to keep up with peers and participate more fully in life, whereas for another child or young person the benefit of walking derived from an orthosis might not outweigh harm from perceived social stigma of wearing the device. In all their discussions, the GDG emphasised the need to take into account the thoughts, wishes, levels of attainment etc of each child or young person, and their parents or other carers.

The GDG therefore considered provision of individualised management programmes to be essential, and they agreed that such programmes should be goal-focused and developed in partnership with the child or young person and their parents or other carers. The group considered that the success of the clinical aspects of management should focus on the WHO's ICF Framework (see http://www.who.int/classifications/icf/en/) with specific reference to the domains of body function and structure and activity and participation. Although the holistic management of spasticity was outside the scope of the guideline, the GDG took the view that management programmes should consider the possible impact of the programme on the child or young person and their family and this would take account of other aspects of care that were not covered by the guideline. In order to facilitate joint decision making between children and young people and their parents and carers and healthcare professionals, relevant, and age and developmentally appropriate, information and education materials, discussion opportunities and advice should be offered. Discussion of developmental potential, and how this might be influenced by different treatments, was also highlighted as an important element of care. Based on their clinical experience, the GDG was also concerned that children and young people with co-existing cognitive impairment should have access to appropriate treatments. The GDG acknowledged that assessing possible treatment benefits in such children and young people was likely to be more difficult, especially if the child or young person had limited communication. To mitigate this risk the GDG made a specific recommendation that careful consideration be given to the impact of spasticity on children and young people with cognitive impairments.

Supporting the child or young person and their family

The GDG noted that management of spasticity involves a long-term commitment for the child or young person and their family and that the network team has an important role to play in providing ongoing support throughout development. In particular, the group noted that the network team should ensure the timely provision of equipment associated with particular interventions, that they should play a central role during transition and should provide children and young people and their parents or carers contact details of patient organisations that can provide support, befriending, counselling, information and advocacy.

Monitoring

Monitoring for the response to treatments received, worsening of spasticity, developing secondary consequences of spasticity (for example pain or contractures) and the need to change individualised goals were also identified as important elements of care. In particular, the GDG 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 the group made specific recommendations to this effect (see Chapter 9 for further details of the rationale for these recommendations).

Recommendations

Number	Recommendation
	Principles of care
	Delivering care
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.
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

Number	Recommendation
	team should provide local expertise in paediatrics, nursing, physiotherapy and occupational therapy. Access to other expertise, including orthotics, orthopaedic surgery and paediatric neurology, may be provided locally or regionally.
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
4	Following diagnosis, ensure that all children and young people with spasticity are referred without delay to an appropriate member of the network team.
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.
6	When formulating a management programme take into account its possible impact on the individual child or young person and their family.
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.

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:
	  ○ body function and structure
	  ○ activity and participation.

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

Number	Recommendation
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
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.
15	The network of care should have a pathway for monitoring children and young people at increased risk of hip displacement.
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.
17	Perform a hip X-ray to assess for hip displacement: • if there are concerns about possible hip displacement • at 24 months in children with bilateral cerebral palsy.
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.
19	Consider repeating the hip X-ray every 6 months in children and young people with a hip migration: • greater than 15% **or** • increasing by more than 10 percentage points per year.
	Physical therapy (physiotherapy and/or occupational therapy)
	General principles
20	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.
21	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.
22	Give children and young people and their parents or carers verbal and written 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.
23	When formulating a physical therapy programme for children and young people

Number	Recommendation
	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.
24	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.
25	Ensure that any equipment or techniques used in the physical therapy programme are safe and appropriate, in particular in 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 non-ambulatory, malnourished or taking anticonvulsant therapy).
26	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
27	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.
28	When using 24-hour postural management strategies consider, on an individual basis, the following techniques: • low-load active stretching — the child or young person actively stretches their muscles with the aim of increasing range of movement • low-load passive stretching — sustained stretching using positioning with equipment, orthoses or serial casting.
29	Offer training to parents and carers involved in delivering postural management strategies.
30	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.
31	When undertaking task-focused active-use therapy consider an intensive programme over a short time period (for example, 4–8 weeks).
32	Consider muscle-strengthening therapy where the assessment indicates that muscle weakness is contributing to loss of function or postural difficulties.

Number	Recommendation
33	Direct muscle-strengthening therapy towards specific goals using progressive repetitive exercises performed against resistance.
34	Following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen or orthopaedic surgery, provide an adapted physical therapy programme as an essential component of management.
35	Ensure that children and young people and their parents or carers understand that following treatment with botulinum toxin type A treatment, continuous pump-administered intrathecal baclofen treatment or orthopaedic surgery an adapted physical therapy programme will be an essential component of management.
	Continuing assessment
36	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.

Number	Research recommendation
1	What are the greatest inhibitors of functional ability in children and young people with upper motor neuron lesions? **Why this is important** Children and young people with upper motor neuron lesions may experience: • reduced muscle strength • selective muscle control • spasticity. The relationships between these factors, and the extent to which the child or young person can develop or maintain functional ability, remain unclear. Prospective cohort studies, or large cross-sectional studies, are needed to explore the relationships between positive and negative effects of upper motor neuron lesions and to determine which factor is the greatest inhibitor of functional ability. The studies should incorporate classification of functional ability based on validated scales, such as the GMFCS.
2	What is the optimal postural management programme using a standing frame in children aged 1–3 years? **Why this is important** Children who are at GMFCS level IV or V may benefit from using a standing frame as part of a postural management programme. Clinical benefits might include improved weight bearing and walking and, as a result, reduced hip migration. Postural management programmes involving the use of standing frames are part of established clinical practice. However, the individual elements that optimise the effectiveness of such programmes merit further research. The research should compare the effectiveness of postural management programmes that incorporate different durations and timings of standing frame use. For example, what is the effectiveness of 1 hour per day in a single session compared with two sessions of 30 minutes per day? The research should be conducted in children and aged 1–3 years. These children are likely to benefit the most from using standing frames (in

	terms of developing well-formed femoral heads and acetabulums) and they should find the use of standing frames acceptable (because they are lighter than older children, and they do not have severe contractures).
3	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?
4	What is the optimal duration for the passive stretch component of physical therapy?
5	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?
6	What is the clinical and cost effectiveness and optimal age for modified constraint-induced movement therapy?

5 Orthoses

Introduction

The term orthosis refers to an externally applied device intended to modify the structural and functional characteristics of the neuromuscular and skeletal systems. An orthosis may be recommended as one of a range of measures to manage the effects of altered muscle tone and associated abnormal postures. The prevention of persistently abnormal postures reduces the risk of musculoskeletal adaptations that lead to fixed structural deformities. Orthoses are often used in conjunction with other interventions such as physical therapy (physiotherapy and/or occupational therapy) or BoNT treatment. They may also be used following orthopaedic surgery. They may be used to facilitate function (for example, improving hand use) or to prevent deformity (for example, by applying sustained muscle stretch during the night).

There are many types of orthosis. This chapter focuses on orthoses used in the management of limb and trunk spasticity. The technology and materials used to construct orthoses is evolving constantly. Orthoses may be manufactured as standard devices for a particular purpose or be custom-made for an individual by an orthotist or other trained professional. Orthoses may be beneficial in terms of enhancing function and posture, but they may have disadvantages too. They may be considered to be unsightly or cause discomfort and pressure injuries and, if used inappropriately, they may affect function adversely.

Orthoses may improve gait and facilitate walking. Key considerations when examining the use of orthoses in this setting are the degree of ankle dorsiflexion at initial foot contact (when the foot is first placed on the ground), during terminal stance (when the foot is pushing off the ground), and at floor clearance during the swing phase of the step. Each of these aspects impacts on the child or young person's gait. Spasticity often interferes with a child or young person's ability to achieve ankle dorsiflexion (resulting in an equinus foot posture) and this impedes walking. Spasticity can also cause excessive knee or hip flexion resulting in a crouched posture (crouch gait), and this makes walking inefficient and tiring. Children and young people often find that fatigue of this kind impairs their ability to participate in activities with peers. Speed of walking may be used as an indication of gait efficiency, including the ability to keep up with peers.

For this review question the following types of orthoses, including several types of ankle-foot orthosis (AFO), were considered.

- Solid (or rigid) ankle-foot orthosis (SAFO): this prevents dorsiflexion and plantarflexion. It is used to prevent excessive plantarflexion or knee hyperextension during standing or walking. Knee hyperextension is a common problem, and tends to induce foot plantarflexion automatically.
- Posterior leaf spring ankle-foot orthosis (PLSAFO): this supports the foot and ankle, preventing excessive plantarflexion. It also provides some flexibility in the foot plate. This enables some passive dorsiflexion and, therefore, aids in the toe-off phase of walking.
- Hinged ankle-foot orthosis (HAFO): this incorporates a block that can prevent dorsiflexion or plantarflexion, depending on individual need. For most children and young people the aim is prevention of plantarflexion, but those prone to a crouch gait may benefit from control of dorsiflexion.
- Anterior ground reaction force ankle-foot orthosis (GRAFO): this applies forces to the shin in the standing position, which helps to reduce knee flexion and the tendency to adopt a crouch position.
- Supramalleolar orthosis (SMO): this allows ankle movement in the sagittal plane and does not prevent equinus but has some potential to control foot inversion and eversion.

- Prescribed footwear: the review question also specified consideration of the use of footwear often prescribed for children and young people with mild spasticity because it is thought to be useful in supporting the ankle and providing a stable base for weight bearing and movement.
- Knee orthoses: these are designed to prevent knee movement (static orthoses) and are intended to control crouching or provide sustained leg muscle stretch. One form of knee orthosis is a leg gaiter, which consists of a brace with vertical support ribs that is wrapped around the knee to prevent bending.
- Hip orthoses: these are orthoses intended to limit movement to a more functional range throughout the gait cycle or when standing or sitting.
- Upper limb orthoses: these include prefabricated, custom-made, neoprene and thermoplastic upper limb orthoses. They can be static orthoses designed to prevent abnormal postures or dynamic orthoses used to support the upper limb in an efficient posture to improve function.
- Trunk orthoses: the trunk orthoses considered in this review question are classed as spinal braces or thoracic-lumbar-sacral orthoses (TLSOs). These are static orthoses used to prevent or reduce abnormal spinal postures, such as scoliosis or kyphosis.

No relevant NICE guidance was identified for this review question.

Review question

What is the effectiveness of orthotic interventions (for example, AFOs, 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?

Description of included studies

Seven RCTs were identified for inclusion for this review question (Buckon 2001; Buckon 2004a; Carlson 1997; Elliott 2011; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005).

Six cross-over RCTs (Buckon 2001; Buckon 2004a; Carlson 1997; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005) randomised participants to a particular sequence of AFO use. These studies addressed the following four comparisons.

- SAFOs versus no treatment in children and young people with diplegia and hemiplegia were evaluated in five cross-over RCTs (Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005). In three of the studies (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002) the participants were aged 4-18 years (Sienko-Thomas 2002 reported a subgroup analysis for those children and young people in Buckon 2001 who were able to go up and down stairs during a barefoot assessment with or without the use of a handrail). In the other studies (Rethlefsen 1999; Radtka 2005) the participants were aged 5-13.5 years and 4-16 years, respectively.
- HAFOs with plantarflexion stop versus SAFOs in children and young people with diplegia and hemiplegia were also evaluated in the same five cross-over RCTs (Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005).
- PLSOs versus SAFOs in children and young people with diplegia and hemiplegia were evaluated in three of the same cross-over RCTs (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002).
- SMOs versus SAFOs in children and young people aged 4-11 years with diplegia were evaluated in one cross-over RCT (Carlson 1997).

One parallel RCT evaluated the use of an elastomere arm splint versus no orthosis in children and young people aged 8-15 years with hemiplegia or quadriplegia (Elliott 2011). The arm splint extended from the wrist to the axilla and was worn to address pronation-flexion or supination-extension function.

Evidence profiles

Solid ankle foot orthosis versus no treatment (weight bearing or non-weight bearing)

All five studies identified for inclusion examined outcomes assessing optimisation of movement (Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005).

Table 5.1 Evidence profile for solid ankle orthosis compared with no treatment in children with diplegia; lower limb; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Solid ankle-foot orthosis	No solid ankle-foot orthosis	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[a]	42 limbs[b]	-	MD = 3.6 higher (1.42 higher to 5.78 higher)*	LOW
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 12.20 higher (5.46 higher to 18.94 higher)*	MODERATE
Ankle dorsi/plantarflexion at initial contact (post hoc analysis, better indicated by higher values)					
1 study (Radtka 2005)	12[e]	12[f]	-	MD = 15.23 higher (11.02 higher to 19.44)*	LOW
Ankle dorsiflexion terminal stance (better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[g]	42 limbs[h]	-	MD = 0.00 higher (2.71 lower to 2.71 higher)*	LOW
Ankle dorsiflexion terminal stance (post hoc analysis, better indicated by higher values)					
1 study (Radtka 2005)	12[i]	12[j]	-	MD = 12.80 higher (8.35 higher to 17.25 higher)*	LOW
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2004a)	16[k]	16[l]	-	MD = 6.80 higher (0.03 lower to 13.63 higher)*	LOW
Peak dorsiflexion time (%, better indicated by higher values)					
1 study (Buckon 2004a)	16[m]	16[n]	-	MD = 9.00 higher (0.36 lower to 18.36 higher)*	LOW

Peak dorsiflexion swing (better indicated by higher values)					
1 study (Buckon 2004a)	16[o]	16[p]	-	MD = 10.80 higher (3.46 higher to 18.14 higher)*	MODERATE
Range (better indicated by higher values)					
1 study (Buckon 2004a)	16[q]	16[r]	-	MD = 19.10 lower (26.59 lower to 11.61 lower)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2004a)	16[s]	16[t]	-	MD = 0.00 higher (3.46 lower to 3.46 higher)*	LOW
Dorsiflexion knee flexion (degrees, better indicated by higher values)					
1 study (Buckon 2004a)	16[u]	16[v]	-	MD = 2.00 higher (7.30 lower to 3.30 higher)*	LOW
Knee, initial contact (degrees, better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[w]	42 limbs[x]	-	MD = 1.00 lower (6.15 lower to 4.15 higher)*	LOW
Knee, terminal stance (degrees, better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[y]	42 limbs[z]		MD = 1.00 lower (5.28 lower to 3.28 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 3 ± 4
b Mean final score ± SD reported as -0.6 ± 6
c Mean final score ± SD reported as 5.0 ± 4.5
d Mean final score ± SD reported as -7.2 ± 13
e Mean final score ± SD reported as 7.09 ± 5.06
f Mean final score ± SD reported as -8.14 ± 5.46
g Mean final score ± SD reported as 8 ± 4
h Mean final score ± SD reported as 8 ± 8
i Mean final score ± SD reported as 11.50 ± 4.28
j Mean final score ± SD reported as -1.30 ± 6.59
k Mean final score ± SD reported as 12.5 ± 5.3
l Mean final score ± SD reported as 5.7 ± 12.9
m Mean final score ± SD reported as 36 ± 13
n Mean final score ± SD reported as 27 ± 14
o Mean final score ± SD reported as 7.2 ± 5.6
p Mean final score ± SD reported as –3.6 ± 13.9
q Mean final score ± SD reported as 10.6 ± 3.8
r Mean final score ± SD reported as 29.7 ± 14.8
s Mean final score ± SD reported as 8 ± 5
t Mean final score ± SD reported as 8 ± 5
u Mean final score ± SD reported as 15 ± 6

v Mean final score ± SD reported as 17 ± 9
w Mean final score ± SD reported as 26 ± 11
x Mean final score ± SD reported as 27 ± 13
y Mean final score ± SD reported as 11 ± 10
z Mean final score ± SD reported as 12 ± 10

Table 5.2 Evidence profile for solid ankle orthosis compared with no treatment in children with hemiplegia; lower limb; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Solid ankle-foot orthosis	No solid ankle-foot orthosis	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]		MD = 13.00 higher (10.42 higher to 15.58 higher)*	MODERATE
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]		MD = 5.00 higher (2.47 higher to 7.53 higher)*	MODERATE
Ankle dorsiflexion dynamic range (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]		MD = 15.00 lower (17.73 lower to 12.27 lower)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]	-	MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW
Dorsiflexion knee flexion (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[i]	29[j]		MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 2 ± 4
b Mean final score ± SD reported as –11 ± 6
c Mean final score ± SD reported as 11 ± 5
d Mean final score ± SD reported as 6 ± 5
e Mean final score ± SD reported as 11 ± 3
f Mean final score ± SD reported as 26 ± 7
g Mean final score ± SD reported as 6 ± 4
h Mean final score ± SD reported as 5 ± 6
i Mean final score ± SD reported as 13 ± 4
j Mean final score ± SD reported as 12 ± 6

Four of the studies examined outcomes assessing optimisation of function (Buckon 2001; Buckon 2004a; Radtka 2005; Sienko-Thomas 2002).

Table 5.3 Evidence profile for solid ankle orthosis compared with no treatment in children with diplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Solid ankle-foot orthosis	**No solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-D score (standing, GMFM version not reported), better indicated by higher values)					
1 study (Buckon 2004a)	16[a]	16[b]	-	MD = 0.40 higher (1.51 lower to 2.31 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 3.50 higher (4.31 lower to 11.31 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[e]	16[f]	-	MD = 1.40 higher (0.65 lower to 3.45 higher)*	LOW
PEDI caregiver assistance scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[g]	16[h]	-	MD = 0.30 higher (0.64 lower to 1.24 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2004a)	16[i]	16[j]	-	MD = 0.04 lower (0.18 lower to 0.10 higher)*	LOW
Velocity (cm/second, better indicated by higher values)					
1 study (Radtka 2005)	40 limbs[k]	40 limbs[l]		MD = 0.40 higher (-4.03 lower to 4.83 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 35.8 ± 2.8

b Mean final score ± SD reported as 35.4 ± 2.7

c Mean final score ± SD reported as 60.6 ± 10.5

d Mean final score ± SD reported as 57.1 ± 12

e Mean final score ± SD reported as 52.6 ± 3.2

f Mean final score ± SD reported as 51.2 ± 2.7

g Mean final score ± SD reported as 34.4 ± 1.3

h Mean final score ± SD reported as 34.1 ± 1.4
i Mean final score ± SD reported as 1.04 ± 0.18
j Mean final score ± SD reported as 1.08 ± 0.22
k Mean final score ± SD reported as 63.6 ± 12
l Mean final score ± SD reported as 63.2 ± 8.4

Table 5.4 Evidence profile for solid ankle orthosis compared with no treatment in children with hemiplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Solid ankle-foot orthosis	**No solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-D score (standing, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]	-	MD = 0.40 higher (0.40 lower to 1.20 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]	-	MD = 0.50 higher (1.79 lower to 2.79 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]	-	MD = 1.40 higher (0.39 higher to 2.41 higher)*	LOW
PEDI item 54, ascent score (proportion of children who keep up with peers, better indicated by higher values)					
1 study (Sienko-Thomas 2002)	9/19	6/19	1.50 (0.66 to 3.39)	RD = 0.16 (0.15 lower to 0.46 higher)*	LOW
PEDI item 59, descent score (proportion of children who keep up with peers, better indicated by higher values)					
1 study (Sienko-Thomas 2002)	7/19	5/19	1.40 (0.54 to 3.64)	RD = 0.11 (0.19 lower to 0.40 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]		MD = 0.04 higher (0.06 lower to 0.14 higher)*	LOW
Velocity ascent (time for distance stair 1 to stair 3)					
1 study (Sienko-Thomas 2002)	19[i]	19[j]		MD = 0.01 lower (0.05 lower to 0.03 higher)*	LOW
Velocity descent (time for distance stair 3 to stair 1)					

1 study (Sienko-Thomas 2002)	19[k]	19[l]		MD = 0.04 higher (0.02 lower to 0.09 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory, RD risk difference, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 38.0 ± 1

b Mean final score ± SD reported as 37.6 ± 2

c Mean final score ± SD reported as 67.6 ± 4

d Mean final score ± SD reported as 67.1 ± 5

e Mean final score ± SD reported as 56.8 ± 2

f Mean final score ± SD reported as 55.4 ± 2

g Mean final score ± SD reported as 1.11 ± 0.17

h Mean final score ± SD reported as 1.07 ± 0.22

i Mean final score ± SD reported as 0.270 ± 0.07

j Mean final score ± SD reported as 0.280 ± 0.06

k Mean final score ± SD reported as 0.296 ± 0.10

l Mean final score ± SD reported as 0.259 ± 0.06

None of the studies reported reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Comparisons to fixed or solid ankle foot orthoses

Hinged ankle foot orthosis with plantarflexion stop versus solid ankle foot orthosis

Four of the studies identified for inclusion assessed optimisation of movement (Buckon 2001; Buckon 2004a; Radtka 2005; Rethlefsen 1999).

Table 5.5 Evidence profile for hinged ankle foot orthosis with plantarflexion stop compared with solid ankle foot orthosis in children with diplegia; lower limb; joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Hinged ankle-foot orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[a]	42 limbs[b]	-	MD = 1.00 higher (0.94 lower to 2.94 higher)*	LOW
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 0.20 lower (3.03 lower to 2.63 higher)*	LOW
Ankle dorsi/plantarflexion at initial contact (post hoc analysis, better indicated by higher values)					
1 study (Radtka 2002)	12[e]	12[f]	-	MD = 1.72 lower (6.61 lower to 3.17 higher)*	LOW
Ankle dorsiflexion, terminal stance (better indicated by higher values)					
1 study (Rethlefsen	42 limbs	42 limbs	-	MD = 5.00 higher (2.82	LOW

1999)				higher to 7.18 higher)*	
1 study (Radtka 2002)	12[g]	12[h]	-	MD = 4.63 higher (0.38 higher to 8.88 higher)*	LOW
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2004a)	16[i]	16[j]	-	MD = 6.10 higher (1.27 higher to 10.93 higher)*	MODERATE
Peak dorsiflexion time (%, better indicated by higher values)					
1 study (Buckon 2004a)	16[k]	16[l]	-	MD = 10.00 higher (3.18 higher to 16.82 higher)*	MODERATE
Peak dorsiflexion swing (better indicated by higher values)					
1 study (Buckon 2004a)	16[m]	16[n]	-	MD = 1.10 higher (2.75 lower to 4.95 higher)*	LOW
Range (better indicated by higher values)					
1 study (Buckon 2004a)	16[o]	16[p]	-	MD = 5.90 higher (2.54 higher to 9.26 higher)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2004a)	16[q]	16[r]	-	MD = 2.00 higher (2.22 lower to 6.22 higher)*	LOW
Dorsiflexion knee flexion (degree, better indicated by higher values)					
1 study (Buckon 2004a)	16[s]	16[t]	-	MD = 4.00 higher (0.90 lower to 8.90 higher)*	LOW
Knee, initial contact (degrees, better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[u]	42 limbs[v]		MD = 2.00 higher (2.92 lower to 6.92 higher)*	LOW
Knee, terminal stance (degrees, better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs[w]	42 limbs[x]		MD = 2.00 higher (2.28 lower to 6.28 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH

a Mean final score ± SD reported as 4 ± 5
b Mean final score ± SD reported as 3 ± 4
c Mean final score ± SD reported as 4.8 ± 4.6
d Mean final score ± SD reported as 5.0 ± 4.5
e Mean final score ± SD reported as 5.37 ± 7.00
f Mean final score ± SD reported as 7.09 ± 5.06
g Mean final score ± SD reported as 16.13 ± 6.17
h Mean final score ± SD reported as 11.50 ± 4.28
i Mean final score ± SD reported as 18.6 ± 8.3
j Mean final score ± SD reported as 12.5 ± 5.3
k Mean final score ± SD reported as 46 ± 5
l Mean final score ± SD reported as 36 ±13
m Mean final score ± SD reported as 8.3 ± 5.5
n Mean final score ± SD reported as 7.2 ± 5.6
o Mean final score ± SD reported as 16.5 ± 5.7
p Mean final score ± SD reported as 10.6 ± 3.8
q Mean final score ± SD reported as 10 ± 7
r Mean final score ± SD reported as 8 ± 5
s Mean final score ± SD reported as 19 ± 8
t Mean final score ± SD reported as 15 ± 6
u Mean final score ± SD reported as 28 ± 12
v Mean final score ± SD reported as 26 ± 11
w Mean final score ± SD reported as 13 ± 10
x Mean final score ± SD reported as 11 ± 10

Table 5.6 Evidence profile for hinged ankle foot orthosis with plantarflexion stop compared with solid ankle foot orthosis in children with hemiplegia; lower limb; joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Hinged ankle-foot orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]	-	MD = 1.00 higher (1.02 lower to 3.02 higher)*	LOW
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]	-	MD = 5.00 higher (2.21 higher to 7.79 higher)*	MODERATE
Ankle dorsiflexion dynamic range (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]	-	MD = 5.00 higher (3.21 higher to 6.79 higher)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]	-	MD = 1.00 higher (1.29 lower to 3.29 higher)*	LOW

Dorsiflexion knee flexion (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[i]	29[j]	-	MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 3 ± 4
b Mean final score ± SD reported as 2 ± 4
c Mean final score ± SD reported as 16 ± 6
d Mean final score ± SD reported as 11 ± 5
e Mean final score ± SD reported as 16 ± 4
f Mean final score ± SD reported as 11 ± 3
g Mean final score ± SD reported as 7 ± 5
h Mean final score ± SD reported as 6 ± 4
i Mean final score ± SD reported as 14 ± 6
j Mean final score ± SD reported as 13 ± 4

All five of the studies identified for inclusion examined optimisation of function (Buckon 2001; Buckon 2004a; Radtka 2005; Rethlefsen 1999; Sienko-Thomas 2002).

Table 5.7 Evidence profile for hinged ankle foot orthosis with plantarflexion stop compared with solid ankle foot orthosis in children with diplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Hinged ankle-foot orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-D score (standing, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2004a)	16[a]	16[b]	-	MD = 0.30 lower (2.31 lower to 1.71 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 0.40 higher (7.02 lower to 7.82 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[e]	16[f]	-	MD = 0.70 lower (2.78 lower to 1.38 higher)*	LOW
PEDI caregiver assistance scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[g]	16[h]	-	MD = 0.10 higher (0.73 lower to 0.93 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2004a)	16[i]	16[j]	-	MD = 0.06 lower (0.20 lower to 0.08 higher)*	LOW

Velocity (cm/second, better indicated by higher values)					
1 study (Radtka 2002)	12[k]	12[l]		MD = 4.93 higher (12.12 lower to 21.98 higher)*	LOW
Velocity (m/minute, better indicated by higher values)					
1 study (Rethlefsen 1999)	40 limbs[m]	40 limbs[n]		MD = 0.90 higher (3.75 lower to 5.55 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 35.5 ± 3.0
b Mean final score ± SD reported as 35.8 ± 2.8
c Mean final score ± SD reported as 61.0 ± 10.9
d Mean final score ± SD reported as 60.6 ± 10.5
e Mean final score ± SD reported as 51.9 ± 2.8
f Mean final score ± SD reported as 52.6 ± 3.2
g Mean final score ± SD reported as 34.5 ± 1.1
h Mean final score ± SD reported as 34.4 ± 1.3
i Mean final score ± SD reported as 0.98 ± 0.21
j Mean final score ± SD reported as 1.04 ± 0.18
k Mean final score ± SD reported as 99.63 ± 20.53
l Mean final score ± SD reported as 94.70 ± 22.07
m Mean final score ± SD reported as 64.5 ± 9
n Mean final score ± SD reported as 63.6 ± 12

Table 5.8 Evidence profile for hinged ankle foot orthosis with plantarflexion stop compared with solid ankle foot orthosis in children with hemiplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Hinged ankle-foot orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-D score (standing, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]	-	MD = 0.10 lower (0.61 lower to 0.41 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]	-	MD = 1.00 higher (0.79 lower to 2.79 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]	-	MD = 0.10 lower (1.11 lower to 0.91 higher)*	LOW
PEDI item 54, ascent score (proportion of children who keep up with peers, better indicated by higher values)					

1 study (Sienko-Thomas 2002)	12/19	9/19	1.33 (0.74 to 2.39)	RD = 0.16 higher (0.15 lower to 0.47 higher)*	LOW
PEDI item 59, descent score (proportion of children who keep up with peers, better indicated by higher values)					
1 study (Sienko-Thomas 2002)	10/19	7/19	1.43 (0.69 to 2.96)	RD = 0.16 higher (0.15 lower to 0.47 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]	-	MD = 0.03 higher (0.05 lower to 0.11 higher)*	LOW
Velocity ascent (time for distance stair 1 to stair 3)					
1 study (Sienko-Thomas 2002)	19[i]	19[j]	-	MD = 0.01 higher (0.03 lower to 0.06 higher)*	LOW
Velocity descent (time for distance stair 3 to stair 1)					
1 study (Sienko-Thomas 2002)	19[k]	19[l]	P = No significant difference (reported)	MD = 0.02 lower (0.07 lower to 0.04 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 37.9 ± 1.0

b Mean final score ± SD reported as 38.0 ± 1.0

c Mean final score ± SD reported as 68.1 ± 3

d Mean final score ± SD reported as 67.6 ± 4

e Mean final score ± SD reported as 56.7 ± 2

f Mean final score ± SD reported as 56.8 ± 2

g Mean final score ± SD reported as 1.14 ± 0.16

h Mean final score ± SD reported as 1.11 ± 0.17

i Mean final score ± SD reported as 0.281 ± 0.07

j Mean final score ± SD reported as 0.270 ± 0.07

k Mean final score ± SD reported as 0.280 ± 0.08

l Mean final score ± SD reported as 0.296 ± 0.10

None of the studies reported reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Posterior leaf spring ankle foot orthosis versus solid ankle foot orthosis

Two of the studies identified for inclusion examined outcomes for optimisation of movement (Buckon 2001; Buckon 2004a).

Table 5.9 Evidence profile for posterior leaf spring ankle foot orthosis compared with solid ankle foot orthosis in children with diplegia; lower limb; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Posterior leaf spring ankle-foot orthosis	Solid ankle-foot orthosis	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Buckon 2004a)	16[a]	16[b]	-	MD = 0.20 lower (3.35 lower to 2.95 higher)*	LOW
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 2.30 higher (2.12 lower to 6.72 higher)*	LOW
Peak dorsiflexion time (%, better indicated by higher values)					
1 study (Buckon 2004a)	16[e]	16[f]	-	MD = 2.00 higher (7.01 lower to 11.01 higher)*	LOW
Peak dorsiflexion swing (better indicated by higher values)					
1 study (Buckon 2004a)	16[g]	16[h]	-	MD = 0.30 lower (3.85 lower to 3.25 higher)*	LOW
Range (better indicated by higher values)					
1 study (Buckon 2004a)	16[i]	16[j]	-	MD = 4.00 higher (1.11 higher to 6.89 higher)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2004a)	16[k]	16[l]	-	MD = 0.00 higher (3.83 lower to 3.83 higher)*	LOW
Dorsiflexion knee flexion (degrees (better indicated by higher values)					
1 study (Buckon 2004a)	16[m]	16[n]	-	MD = 3.00 higher (2.30 lower to 8.30 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 4.8 ± 4.6
b Mean final score ± SD reported as 5.0 ± 4.5
c Mean final score ± SD reported as 14.8 ± 7.3
d Mean final score ± SD reported as 12.5 ± 5.3
e Mean final score ± SD reported as 38 ± 13
f Mean final score ± SD reported as 36 ± 13
g Mean final score ± SD reported as 6.9 ± 4.6

h Mean final score ± SD reported as 7.2 ± 5.6
i Mean final score ± SD reported as 14.6 ± 4.5
j Mean final score ± SD reported as 10.6 ± 3.8
k Mean final score ± SD reported as 8 ± 6
l Mean final score ± SD reported as 8 ± 5
m Mean final score ± SD reported as 18 ± 9
n Mean final score ± SD reported as 15 ± 6

Table 5.10 Evidence profile for posterior leaf spring ankle foot orthosis compared with solid ankle foot orthosis in children with hemiplegia; lower limb; joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Posterior leaf spring ankle-foot orthosis	Solid ankle-foot orthosis	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion initial contact (better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]		MD = 2.20 lower (4.49 lower to 0.09 higher)*	LOW
Peak dorsiflexion stance (better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]		MD = 5.00 higher (2.21 higher to 7.79 higher)*	MODERATE
Ankle dorsiflexion dynamic range (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]		MD = 4.00 higher (2.21 higher to 5.79 higher)*	MODERATE
Ankle range dorsiflexion knee extension (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]	-	MD = 1.00 higher (1.02 lower to 3.02 higher)*	LOW
Dorsiflexion knee flexion (degrees, better indicated by higher values)					
1 study (Buckon 2001)	29[i]	29[j]		MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as -0.2 ± 5
b Mean final score ± SD reported as 2 ± 4
c Mean final score ± SD reported as 16 ± 6
d Mean final score ± SD reported as 11 ± 5
e Mean final score ± SD reported as 15 ± 4
f Mean final score ± SD reported as 11 ± 3
g Mean final score ± SD reported as 7 ± 4
h Mean final score ± SD reported as 6 ± 4
i Mean final score ± SD reported as 14 ± 6
j Mean final score ± SD reported as 13 ± 4

All three studies identified for inclusion examined optimisation of function (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002).

Table 5.11 Evidence profile for posterior leaf spring ankle foot orthosis compared with solid ankle foot orthosis in children with diplegia; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Posterior leaf spring ankle-foot orthosis	Solid ankle-foot orthosis	Relative (95% CI)	Absolute (95% CI)	
GMFM-D score (standing, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2004a)	16[a]	16[b]	-	MD = 0.20 lower (2.25 lower to 1.85 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2004a)	16[c]	16[d]	-	MD = 0.20 higher (7.01 lower to 7.41 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[e]	16[f]	-	MD = 0.30 higher (1.72 lower to 2.32 higher)*	LOW
PEDI caregiver assistance scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2004a)	16[g]	16[h]	-	MD = 0.10 lower (1.19 lower to 0.99 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2004a)	16[i]	16[j]	-	MD = 0.07 higher (0.06 lower to 0.20 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory, SD standard deviation
* Calculated by the NCC-WCH
a Mean final score ± SD reported as 35.6 ± 3.1
b Mean final score ± SD reported as 35.8 ± 2.8
c Mean final score ± SD reported as 60.8 ± 10.3
d Mean final score ± SD reported as 60.6 ± 10.5
e Mean final score ± SD reported as 52.9 ± 2.6
f Mean final score ± SD reported as 52.6 ± 3.2
g Mean final score ± SD reported as 34.3 ± 1.8
h Mean final score ± SD reported as 34.4 ± 1.3
i Mean final score ± SD reported as 1.11 ± 0.19
j Mean final score ± SD reported as 1.04 ± 0.18

Table 5.12 Evidence profile for posterior leaf spring ankle foot orthosis compared with solid ankle foot orthosis in children with hemiplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Posterior leaf spring ankle-foot orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-D score (standing, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[a]	29[b]	-	MD = 0.20 lower (0.71 lower to 0.31 higher)*	LOW
GMFM-E score (walking, running and jumping, GMFM version not reported, better indicated by higher values)					
1 study (Buckon 2001)	29[c]	29[d]	-	MD = 0.50 higher (1.29 lower to 2.29 higher)*	LOW
PEDI functional skills scale, mobility domain score (better indicated by higher values)					
1 study (Buckon 2001)	29[e]	29[f]	-	MD = 0.20 lower (1.21 lower to 0.81 higher)*	LOW
PEDI item 54, ascent score (proportion of children who keep up with peers, better indicated by higher values)					
1 study (Sienko-Thomas 2002)	8/19	9/19	0.89 (0.44 to 1.81)	RD = 0.05 lower (0.37 lower to 0.26 higher)*	LOW
PEDI item 59, descent score (proportion of children who keep up with peers, better indicated by higher values)					
1 study (Sienko-Thomas 2002)	6/19	7/19	0.86 (0.35 to 2.08)	RD = 0.05 lower (0.35 lower to 0.25 higher)*	LOW
Velocity (m/second, better indicated by higher values)					
1 study (Buckon 2001)	29[g]	29[h]		MD = 0.07 higher (0.02 lower to 0.16 higher)*	LOW
Velocity ascent (time for distance stair 1 to stair 3)					
1 study (Sienko-Thomas 2002)	19[i]	19[j]		MD = 0.03 higher (0.01 lower to 0.08 higher)*	LOW
Velocity descent (time for distance stair 3 to stair 1)					
1 study (Sienko-Thomas 2002)	19[k]	19[l]		MD = 0.03 higher (0.04 lower to 0.09 higher)*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PEDI Pediatric Evaluation of Disability Inventory, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 37.8 ± 1

b Mean final score ± SD reported as 38.0 ± 1

c Mean final score ± SD reported as 68.1 ± 3

d Mean final score ± SD reported as 67.6 ± 4

e Mean final score ± SD reported as 56.6 ± 2

f Mean final score ± SD reported as 56.8 ± 2

g Mean final score ± SD reported as 1.18 ± 0.17

h Mean final score ± SD reported as 1.11 ± 0.17

i Mean final score ± SD reported as 0.304 ± 0.07

j Mean final score ± SD reported as 0.270 ± 0.07

k Mean final score ± SD reported as 0.323 ± 0.11

l Mean final score ± SD reported as 0.296 ± 0.10

None of the studies reported reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Supramalleolar foot orthosis versus solid ankle foot orthosis

The only study identified for inclusion (Carlson 1997) examined outcomes assessing optimisation of movement.

Table 5.13 Evidence profile for supramalleolar foot orthosis compared with solid ankle foot orthosis in children with diplegia; joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Supramalleolar orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ankle dorsiflexion angle at foot strike (degrees, group mean, better indicated by higher values)					
1 study (Carlson 1997)	11[a]	11[b]	-	MD = 6.70 lower (12.15 lower to 1.25 lower)*	MODERATE

CI confidence interval, MD mean difference, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 3.3 ± 7.0

b Mean final score ± SD reported as 10.0 ± 6.0

Table 5.14 Evidence profile for supramalleolar foot orthosis compared with solid ankle foot orthosis in children with diplegia; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Supramalleolar orthosis	**Solid ankle-foot orthosis**	**Relative (95% CI)**	**Absolute (95% CI)**	
Velocity (m/second, group mean, better indicated by higher values)					
1 study (Carlson 1997)	11[a]	11[b]	-	MD = 0.00 (0.16 lower to 0.16 higher)*	LOW

CI confidence interval, MD mean difference, SD standard deviation

* Calculated by the NCC-WCH

a Mean final score ± SD reported as 1.00 ± 0.20

b Mean final score ± SD reported as 1.00 ± 0.19

The study did not report reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Elastomere arm splint versus no orthosis

The only study identified for inclusion examined outcomes assessing optimisation of function (Elliott 2011).

Table 5.15 Evidence profile for elastomere arm splint compared with no orthosis in children with quadriplegia and hemiplegia; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Elastomere arm splint	No orthosis	Relative (95% CI)	Absolute (95% CI)	
GAS T-score (mean change score, better indicated by higher values)					
1 study (Elliott 2011)	8[a]	8[b]	-	MD = 18 (12.15 higher to 23.85 higher)*	HIGH

CI confidence interval, GAS T-score Goal Attainment Scaling T-score, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean change score ± SD reported as 53 ± 5.0
b Mean final score ± SD reported as 35 ± 6.8
c The authors note that a change score ≥50 represented the expected change in goal attainment over the 3 month period.

The study did not report outcomes for reduction of tone, range of movement, reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Evidence statement

Solid ankle foot orthosis versus no treatment (weight bearing or non-weight bearing)

Five cross-over RCTs examined outcomes assessing optimisation of movement.

Diplegia

With regard to range of movement at the ankle joint, one cross-over RCT provided evidence that there was a statistically significant increase in mean ankle dorsiflexion at initial contact at 3 months when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes. (MODERATE; group mean comparison across groups) Two further cross-over RCTs provided evidence of statistically significant increases in mean ankle dorsiflexion at initial contact at 4-6 weeks with SAFO use compared to bare feet or shoes; one study analysed results by limb and the other reported a post hoc analysis of data. (LOW; group mean comparison across groups)

Two cross-over RCTs examined ankle dorsiflexion at terminal stance at 4-6 weeks when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes. Whilst one cross-over RCT provided evidence of no difference between the groups (this study analysed results by limb and the outcome was not statistically significant; LOW), the other cross-over RCT provided evidence of a statistically significant increase in ankle dorsiflexion at terminal stance when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes (post hoc analysis of data). (LOW; group mean comparison across groups)

One cross-over RCT provided evidence that there was an increase in peak dorsiflexion in stance and in percentage peak dorsiflexion time at 3 months when children and young people with diplegia wore a SAFO compared to when they wore shoes, although neither of these differences was statistically significant (LOW; group mean comparison across groups) The same cross-over RCT provided evidence that there was a statistically significant increase in peak dorsiflexion swing and a statistically significant decrease in range of movement at 3 months when children and young people with diplegia wore a SAFO compared to when they wore shoes. (MODERATE; group mean comparison across groups)

One cross-over RCT provided evidence of no difference in ankle dorsiflexion range with knee extended at 3 months when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes. This finding was not statistically significant. (LOW; group mean comparison across groups) The same cross-over RCT provided evidence that there was an increase in ankle dorsiflexion range with knee flexed at 3 months when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes, but this finding was not statistically significant. (LOW; group mean comparison across groups) With regard to range of movement at the knee joint, one cross-over RCT provided evidence that there were decreases in knee position at initial contact and at terminal stance when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to range of movement at the ankle joint, one cross-over RCT provided evidence that there were statistically significant increases in ankle dorsiflexion at initial contact and peak dorsiflexion and a statistically significant decrease in ankle dorsiflexion dynamic range at 3 months when children and young people with hemiplegia wore a SAFO compared when they had bare feet or wore shoes. (MODERATE; group mean comparison across groups)

The same cross-over RCT provided evidence that there were increases in range of ankle dorsiflexion with knee extended or flexed at 3 months when children and young people with hemiplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW; group mean comparison across groups)

Four cross-over RCTs examined outcomes assessing optimisation of function.

Diplegia

With regard to optimisation of function, one cross-over RCT provided evidence that there were increases in GMFM-D and GMFM-E scores, and in PEDI mobility domain scores within the functional skills and caregiver assistance scales, at 3 months when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that there was a decrease in walking velocity at 3 months when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes, but this finding was not statistically significant. (LOW; group mean comparison across groups)

A second cross-over RCT provided evidence that that there was an increase in walking velocity at 4-6 weeks when children and young people with diplegia wore a SAFO compared to when they had bare feet or wore shoes, but this finding was not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to optimisation of function, two publications based on one cross-over RCT examined outcomes regarding optimisation of function. One publication provided evidence that there were increases in GMFM-D and GMFM-E scores, and in PEDI mobility domain scores within the functional skills scales, at 3 months when children and young people with hemiplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW; group mean comparison across groups) The same RCT provided evidence that there was an increase in walking velocity at 3 months when children and young people with hemiplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW; group mean comparison across groups)

A subgroup analysis of 19 trial participants who were able to climb up and down stairs in bare feet with or without the use of a handrail provided evidence that although more children and young people were able to keep up with their peers going up and down stairs when wearing a SAFO compared to when in bare feet or wearing shoes, the difference was not statistically significant. (LOW) The subgroup analysis also provided evidence that the time taken to go up or down three stairs was decreased and increased, respectively, when children and young people with hemiplegia wore a SAFO compared to when they had bare feet or wore shoes, but these findings were not statistically significant. (LOW)

No evidence was identified relating to reduction of pain, quality of life, acceptability and tolerability, or adverse effects.

Comparisons to fixed or solid ankle foot orthoses

Hinged ankle foot orthosis with plantarflexion stop versus solid ankle foot orthosis

Four cross-over RCTs assessed optimisation of movement.

Diplegia

With regard to range of movement at the ankle joint, one cross-over RCT (which analysed results by limb) provided evidence that there was an increase in mean ankle dorsiflexion at initial contact at 4-6 weeks when children and young people with diplegia wore a HAFO compared to a SAFO, but that this finding was not statistically significant. (LOW; group mean comparison across groups) Two further cross-over RCTs provided evidence of decreases in mean ankle dorsiflexion at initial contact at 4 weeks (post hoc analysis of data) and 3 months when children and young people with diplegia wore a HAFO compared to a SAFO, however these findings were not statistically significant. (LOW; group mean comparison across groups)

Two cross-over RCTs provided evidence that there was a statistically significant increase in ankle dorsiflexion at terminal stance at 4-6 weeks when children and young people with diplegia wore a HAFO compared to a SAFO, although one study analysed results by limb and the other reported a post hoc analysis of data. (LOW; group mean comparison across groups)

One cross-over RCT provided evidence that there were statistically significant increases in peak dorsiflexion at stance, peak dorsiflexion time percentage (no definition reported) and range at 3 months when children and young people with diplegia wore a HAFO compared to a SAFO. (MODERATE; group mean comparison across groups) The same cross-over RCT provided evidence that there were increases in peak dorsiflexion swing, ankle dorsiflexion range with knee extended and flexed at 3 months when children and young people with diplegia wore a HAFO compared to a SAFO although these findings were not statistically significant. (LOW; group mean comparison across groups)

With regard to range of movement at the knee joint, one cross-over RCT provided evidence that there were increases in knee position at initial contact and at terminal stance when children and young people with diplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to range of movement at the ankle joint, one cross-over RCT provided evidence that there were statistically significant increases in peak dorsiflexion at stance and active range of ankle dorsiflexion at 3 months when children and young people with hemiplegia wore a HAFO compared to a SAFO. (MODERATE; group mean comparison across groups)

The same cross-over RCT provided evidence that increases in ankle dorsiflexion at initial contact, and in range of ankle dorsiflexion with knee extended and flexed, at 3 months when children and young people with hemiplegia wore a HAFO compared to a SAFO were not statistically significant. (LOW; group mean comparison across groups)

Five cross-over RCTs examined optimisation of function.

Diplegia

With regard to optimisation of function, one cross-over RCT provided evidence that there was a decrease in GMFM-D and an increase GMFM-E at 3 months when children and young people with diplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that PEDI mobility domain scores within the functional skills scale were decreased, and those within the caregiver assistance scale were increased, at 3 months when children and young people with diplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that there was a decrease in walking velocity at 3 months when children and young people with diplegia wore a HAFO compared to a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups)

Two further cross-over RCTs (one of which analysed results by limb) provided evidence of increases in walking velocity at 4-6 weeks when children and young people with diplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to optimisation of function, two publications based on one cross-over RCT examined outcomes regarding optimisation of function. One publication provided evidence that there was a decrease in GMFM-D and an increase in GMFM-E at 3 months when children and young people with hemiplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that PEDI mobility domain scores within the functional skills scale were decreased at 3 months when children and young people with hemiplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups) The same RCT provided evidence that there was an increase in walking velocity at 3 months when children and young people with hemiplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

A subgroup analysis of 19 trial participants who were able to climb up and down stairs in bare feet with or without the use of a handrail provided evidence that although more children and young people were able to keep up with their peers going up and down stairs when wearing a HAFO compared to a SAFO, the difference was not statistically significant. (LOW) The subgroup analysis also provided evidence that the time taken to go up and down three stairs was increased and decreased, respectively, when children and young people hemiplegia wore a HAFO compared to a SAFO, but these findings were not statistically significant. (LOW)

Posterior leaf spring ankle foot orthosis versus solid ankle foot orthosis

Two studies examined outcomes for optimisation of movement.

Diplegia

With regard to range of movement at the ankle joint, one cross-over RCT provided evidence that there were decreases in mean ankle dorsiflexion at initial contact and in peak dorsiflexion swing at 3 months when children and young people with diplegia wore a PLSAFO compared to when they wore a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that that there was a statistically significant increase in range of ankle dorsiflexion at 3 months when children and young people with diplegia wore a PLSAFO compared to when they wore a SAFO. (MODERATE; group mean comparison across groups) However, increases in peak dorsiflexion at stance and percentage peak dorsiflexion time when a PLSAFO was compared to a SAFO were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence of no difference in ankle dorsiflexion range with knee extended between treatment groups at 3 months, but there was an increase in ankle dorsiflexion range with knee flexed at 3 months in children and young people with diplegia wearing a PLSAFO compared to a SAFO which was not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to range of movement at the ankle joint, one cross-over RCT provided evidence that there was a decrease in mean ankle dorsiflexion at initial contact at 3 months when children and young people with hemiplegia wore a PLSAFO compared to when they wore a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups) The same cross-over RCT provided evidence that there were statistically significant increases in mean ankle dorsiflexion in stance and in range at 3 months when children and young people with hemiplegia wore a PLSAFO compared to when they wore a SAFO. (MODERATE; group mean comparison across groups) The same cross-over RCT provided evidence that there were statistically significant increases in mean ankle dorsiflexion range with knee extended or flexed when children and young people with hemiplegia wore a PLSAFO compared to when they wore a SAFO, but these finding were not statistically significant. (LOW; group mean comparison across groups) Three studies examined outcomes for optimisation of function.

Diplegia

With regard to optimisation of function, one cross-over RCT provided evidence that there was a decrease in GMFM-D and an increase in GMFM-E at 3 months when children and young people with hemiplegia wore a PLSAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that PEDI mobility domain scores within the functional skills scale were increased, and those within the caregiver assistance scale were decreased, at 3 months when children and young people with diplegia wore a PLSAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that there was a increase in walking velocity at 3 months when children and young people with diplegia wore a PLSAFO compared to a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups)

Hemiplegia

With regard to optimisation of function, two publications based on one cross-over RCT examined outcomes regarding optimisation of function. One cross-over RCT provided evidence that there was a decrease in GMFM-D and an increase in GMFM-E at 3 months when children and young people with hemiplegia wore a PLSAFO compared to a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups)

The same cross-over RCT provided evidence that PEDI mobility domain scores within the functional skills scale were decreased at 3 months when children and young people with hemiplegia wore a PLSAFO compared to a SAFO, but these findings were not statistically significant. (LOW; group mean comparison across groups) The same RCT provided evidence that there was an increase in walking velocity at 3 months when children and young people with hemiplegia wore a PLSAFO compared to a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups)

A subgroup analysis of 19 trial participants who were able to climb up and down stairs in bare feet with or without the use of a handrail provided evidence that although fewer children and young people were able to keep up with their peers going up and down stairs when wearing a PLSAFO compared to a SAFO, the difference was not statistically significant. (LOW) The subgroup analysis also provided evidence that the time taken to go up and down three stairs was increased when children and young people with hemiplegia wore a HAFO compared to a SAFO, but this finding was not statistically significant. (LOW; group mean comparison across groups)

Supramalleolar foot orthosis versus solid ankle foot orthosis

One cross-over RCT provided evidence that ankle dorsiflexion angle at foot strike was statistically significantly decreased at 1 month when children wore a SMO compared to when they wore a SAFO. (MODERATE; group mean comparison across groups) The same cross-over RCT provided evidence that there was no difference in velocity at 1 month when children wore a SMO compared to when they wore a SAFO and that this finding was not statistically significant. (LOW; group mean comparison across groups)

Elastomere arm splint versus no orthosis

One parallel RCT provided evidence that, compared to baseline, there was a statistically significant improvement in GAS-T scores at 3 months in children and young people with hemiplegia or quadriplegia who wore an elastomere arm splint compared to those who did not wear a splint. (HIGH)

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion:

- wrist-hand orthosis versus no treatment
- thumb abduction orthosis versus no treatment
- knee orthosis versus no treatment
- hip abduction orthosis versus no treatment
- prescribed footwear or orthopaedic boots versus no treatment
- anterior GRAFO versus AFO
- foot orthosis or heel cup versus AFO
- any orthosis versus another treatment not involving an orthosis.

Health economics

No economic evaluations of orthoses were identified in the literature search conducted for the guideline. The clinical evidence for this review question was limited and of low quality. A simple cost description was conducted to understand the costs associated with having an orthosis fitted. In this description a child or young person is offered the following appointments:

- an initial assessment which takes 20-30 minutes with a physiotherapist or occupational therapist (this includes taking measurements)
- a follow-up appointment which takes 20-30 minutes and occurs about 2 weeks after the initial assessment
- a further follow-up appointment to check that everything is correct (usually only for a child or young person who has not had an orthosis previously).

Using the cost per hour of client contact with a physiotherapist[§§] (band 5 median) to represent the cost of an orthotist the appointments would cost from £27 (for 40 minutes) to £62 (for 1.5 hours) to supply and fit an orthosis if the orthotist were employed by the NHS. The cost of a single AFO is about £120 to £300.

An orthosis will need to be replaced every 10-12 months or sooner depending on the child or young person's rate of growth. The straps on the orthosis usually wear out after about 12 months. If the orthosis does not fit well and is uncomfortable then the child or young person will not wear it.

An important consideration highlighted by the GDG related to the comfort and cosmesis of orthoses. If an orthosis is not comfortable or the child or young person does not like wearing it then they will not wear it and this will result in poor use of resources. If there is a significant delay between assessment for an orthosis and making and fitting it then the child or young person will be more likely to have grown and the orthosis may no longer be suitable. This would also represent poor use of resources.

The costs for an orthosis are low, but there is considerable uncertainty surrounding benefits based on the clinical evidence available. The GDG commented on the need to monitor children and young people using orthoses to assess goals and record tolerability and side effects. Such information may be useful for assessing the cost effectiveness of orthoses when the guideline is updated.

[§§] £42 per hour of client contact with a community physiotherapist or £40 with a hospital physiotherapist; the mean cost was used. Source: Unit costs of health and social care 2010, Personal and Social Service Research unit (PSSRU).

Evidence to recommendations

Relative value of outcomes

Depending on an individual child or young person's needs and difficulties, orthoses may be employed in order to achieve improved function and posture. They are used with the aim of preventing contractures and deformity. The outcomes of importance vary depending on the specific goal. The GDG agreed the following outcomes to be important: measures of optimisation of function, including the GMFM, the PEDI and GAS; improving or maintaining range of movement; improving posture and preventing deformity; AROM and PROM; and quality of life, as measured by the CHQ. Based on their clinical experience, the GDG considered muscle spasticity as an outcome since orthoses may reduce muscle spasm and pain indirectly. Possible harms include discomfort, inconvenience or cosmetic concerns, and pain and discomfort associated with an ill-fitting orthosis.

Studies have used foot and knee position as indicators of effectiveness in relation to stance and gait efficiency. Lower limb orthoses are frequently used to improve standing posture and especially to improve walking, for example in GMFCS level I, II or III. However, the GDG also considered that movement was an important indicator, assessed by measuring speed of walking and walking distance. In the case of lower limb orthoses aimed at correcting abnormal foot posture during walking, formal gait analysis is widely employed. Foot movement as measured by improvement in dorsiflexion in the various gait phases was considered an important outcome measure. In relation to children and young people in GMFCS level IV or V or MACS levels 4 or 5 there is a greater risk of deformity. Here, PROM is important as an indicator of contractures and fixed deformity.

The GDG also considered that acceptability and tolerability and the occurrence of adverse effects should be included as important outcomes.

Trade-off between clinical benefit and harms

The studies identified for inclusion provided some evidence supporting a beneficial effect with various forms of AFO (notably the SAFO, HAFO and PLSAFO) in relation to ankle dorsiflexion during the gait cycle in children and young people with unilateral or bilateral spasticity affecting the legs. The findings were, however, often inconsistent across studies. Although there were some increases in walking velocity and improvements in function as measured by the GMFM or PEDI none of these was statistically significant. Despite the lack of high-quality evidence, based on their understanding of the underlying principles and the rationale for orthotic interventions, and based on their clinical experience the GDG believed that the use of orthoses has a major role in the management of spasticity in children and young people.

The GDG consensus was that orthoses can have an important role in improving posture, facilitating upper limb function, improving walking efficiency, preventing or slowing the development of contractures and hip migration, relieving discomfort or pain and preventing or treating tissue injury, for example, by relieving pressure points. The group therefore recommended that orthoses should be used with these goals in mind. The GDG acknowledged that while these were common objectives, there may be other, more specific, objectives for the use of orthoses. On the other hand, the group considered that, on balance, the level of detail in the recommendations was appropriate because it reflected their clinical practice and was therefore likely be useful to the majority of users of the guideline. Also it did not provide unduly nuanced advice that was neither underpinned by evidence nor reflective of their expertise and experience. Thus, the group recommended that all children and young people should have access to a network of care that provides expertise in orthotics (see Chapter 4). The group also noted that goals for the use of orthoses should be considered in relation to the individual child or young person and informed through a careful assessment to ensure that they are appropriate for the individual.

No adverse effects were identified in the evidence considered for the guideline review and no evidence was identified regarding acceptability or tolerance of orthoses. In the GDG's experience, however, adverse effects were deemed to have a major impact on the child or young person's ability and willingness to accept or tolerate an orthosis. There was also consensus in the group that discomfort, skin injury, sleep disturbance, etc are more likely to occur if orthoses are badly designed, ill-fitting or worn, but that adverse effects should mainly be preventable with careful design and fitting of the devices.

The GDG therefore concluded that where necessary advice should be sought from an orthotist from within the network team to ensure that orthoses are appropriately designed for the individual child or young person and are sized and fitted correctly. The GDG considered that another key aspect of preventing avoidable adverse effects was limiting delays in the supply of an orthosis after measurements for fitting have been made, or in repairing the orthoses. While there was no evidence to support this it was considered to be a rational assertion because changes which could cause orthoses to fit badly (for example, growth or progression of spasticity) would be more likely to occur if there was a long gap. Consequently the GDG thought that it was necessary to specify that network care pathways be designed to minimise delay in the supply of orthoses.

A longer-term risk of muscle wasting and weakness resulting from immobilisation was also identified. The GDG recommended that this possibility be kept in mind, and the risk needed to be balanced against the potential benefit of the orthosis based on an individual assessment.

The GDG also recommended that when prescribing an orthosis it was important to consider whether the device might lead to difficulties with self-care or care by others, including difficulties with maintaining hygiene. Finally, the GDG recognised that it was very important to take into account the views of the child or young person and their parents or carers regarding any cosmetic concerns about the appearance of orthoses.

Based on their expertise and experience, and taking account of the available evidence, the GDG considered that it was appropriate to make recommendations for the use of orthoses in a variety of specific circumstances described below. Again, the GDG considered that it was only appropriate to provide guidance for some of the more common clinical indications for certain orthoses as the users of the guideline might have varying levels of expertise in the prescription of orthoses, and it would not be appropriate to make recommendations that were too technically specific given the paucity of evidence. In all cases the choice of an orthosis should be dependent on the individual child or young person and informed by expert advice where necessary.

Lower limb orthoses

The GDG recommended that for children and young people in GMFCS level IV or V consideration be given on an individual basis to the use of AFOs to achieve an improved foot position if this is likely to facilitate sitting, transfers, or assisted standing.

In children and young people in whom foot equinus deformity is impairing gait, the GDG recommended that the use of AFOs be considered. There was some research evidence in support of the effectiveness of AFOs in this setting. Comparing the effect of the SAFO and the HAFO, the latter allows greater dorsiflexion but has no greater impact on dorsiflexion swing during walking. The PLSAFO also increases the range of ankle dorsiflexion compared with the SAFO but is used less commonly, especially in those with foot eversion or inversion because such orthoses are less supportive. The GDG agreed that if the child or young person has good control of knee and hip extension then a HAFO should be considered, but if not then a SAFO might be preferred as this would be less likely to cause over-extension. The GDG also agreed that AFOs may not be beneficial in those with secondary complications of spasticity (such as joint contractures and abnormal torsion).

It was believed that those individuals who have a crouch posture due to flexion at the hips or knees combined with good PROM at the hips and knees might benefit from the use of GRAFOs to assist walking, provided their posture was due to muscle tone rather than fixed deformities (contractures). The tibial pressure exerted by the GRAFOs could encourage a more upright posture.

Upper limb orthoses

One study evaluating the effectiveness of elastomere arm splints was identified for inclusion. The GDG was concerned that although a statistically significant improvement in function was reported at 3 months, other outcomes particularly relevant to these types of orthosis were not reported (acceptability and tolerability). There was no published evidence on which to base recommendations on the use of other type of orthosis for the upper limb. Again, based on rational principles and on their clinical experience, the GDG recommended that consideration be given to the use of upper limb orthoses in various situations.

In children and young people with excessive elbow flexion the use of an elbow gaiter could help maintain an extended posture and this could help with upper limb function. For example, by holding the elbow in extension, a child or young person might be able to support themselves whilst sitting or might be able to manage the controls of a powered wheelchair.

Wrist and hand function can be affected by spasticity: the wrist may tend to ulnar deviation and it may be flexed; the thumb may be adducted or flex across the palm; and the fingers may take on abnormal postures. Rigid wrist orthoses could be useful to prevent hand and finger flexion deformity and the development of fixed contractures. However, a dynamic (non-rigid) orthosis should be considered to help with hand function. For example, a non-rigid thumb abduction splint for those with a 'thumb in palm' deformity may be helpful.

The GDG noted that it is a common view that AFOs should be worn for at least 6 hours each day to provide sustained calf muscle stretch, and although they recognised there was no evidence in relation to the optimal duration of use they believed this to be generally reasonable. The group concluded that that despite the limited trial evidence, based on the mechanisms of action of orthoses, it made sense that orthoses designed to maintain stretch to prevent contractures were likely to be more effective if worn for longer periods of time and that 6 hours represented a reasonable timeframe in their clinical experience. However, the same rationale did not apply to orthoses designed to support a specific function, and the group therefore recommended that these should only be worn when needed.

The GDG considered that in the case of prolonged use, it might be appropriate for orthoses to be used overnight. The goals for overnight use of orthoses should reflect the subset of the general goals identified above that are concerned with maintaining stretch of orthoses (that is, improving posture, preventing or delaying contractures and preventing or delaying hip migration). The GDG considered that checking that an orthosis does not cause injury or sleep disturbance during overnight use would be especially important because the child or young person might be unattended for longer periods of time. The group also noted that sometimes the position of the body during sleep provides an opportunity to stretch muscles that control two joints in a way that would not be practicable during the day. A good example of this is the gastrocnemius muscle in the calf, which can be stretched by simultaneous knee and ankle extension; these effects are more easily achieved when the child or young person is lying down.

Body trunk orthoses

There was an absence of evidence regarding the use of body trunk orthoses. The GDG considered that while TLSOs are probably not sufficient to prevent progression of scoliosis in children and young people with spasticity, they may slow the process. Based on their clinical experience, the GDG agreed that TLSOs can be helpful in stabilising an individual's posture and they may provide a useful level of support facilitating activities such as feeding or using a switch.

Made-to-measure orthoses constructed from elasticated fabric (elastane) can be difficult to be made to fit well and may impact adversely on ease of care. The GDG expressed concerns over the level of comfort of this type of orthosis, which is being used increasingly with children and young people with spasticity, despite mixed evidence regarding their effectiveness. The GDG concluded that there was insufficient evidence to recommend the use of such orthoses.

Monitoring and assessment of orthoses

The GDG made recommendations on the need for regular monitoring of orthosis use and on giving advice to the child or young person and their parents or carers regarding the use of orthoses. These recommendations were made to reduce risk and optimise effectiveness, including acceptability and tolerability.

An appropriate member of the network team should discuss with the child or young person and their parents or carers how to apply and wear orthoses, when to wear them and for how long, and when and from whom to seek advice if concerns arise. Once fitted, there should be regular reviews of the orthosis to ensure maximum efficiency in achieving individualised goals. The reviews should cover all aspects of the use of an orthosis that were considered when the device was first prescribed, including acceptability and appropriateness to the child or young person, checks of the condition, fit and correct use of the orthosis, and that it is not causing pain, discomfort, sleep disturbance, or injury. A regular review should also cover any difficulties with self-care or hygiene and any cosmetic or other concerns that the child or young person might have that would affect the value of the orthosis to that individual. The healthcare professional undertaking the review should also look for signs of muscle wasting or reduced sensation.

The GDG consensus was that if an orthosis causes pain for which there is no immediate remedy it should be removed without delay. The group therefore recommended that children and young people and their parents or carers should be advised that they may remove an orthosis that is causing pain that is not relieved despite their repositioning the limb in the orthosis or adjusting the strapping.

The GDG was aware, based on their experience, that rigid orthoses may sometimes cause discomfort or pressure injuries in a child or young person with a marked dyskinesia. These children and young people should be monitored closely to ensure that the orthosis is not causing such difficulties.

Trade-off between net health benefits and resource use

A single orthosis costs £200 to £300 on average, with the cost rising considerably for some types of elasticated garments, and additional costs being associated with the involvement of an orthotist or physical therapist in assessment, supply, fitting, and regular reviews. Although the evidence considered for the guideline did not identify statistically significant improvements in quality of life or function, the GDG considered that improved gait efficiency would contribute to subtle improvements in energy expenditure, and in time these would impact on the child or young person's activity levels and ability to participate in activities. Although the degree of participation may not equal that of the child or young person's peers in some instances, the net health benefits of delayed soft tissue adaptation and contractures and improved gait represent clinically important long-term outcomes. Delaying the often inevitable soft tissue surgery or bony surgery will save NHS resources.

Quality of the evidence

The GDG recognised that there was a deficit in the evidence base underpinning the use of orthoses in the context of this guideline. Seven RCTs were included in the guideline review, six of which examined the effectiveness of various types of AFO in children and young people with unilateral or bilateral spasticity affecting the legs. The sequence of treatments was randomly allocated to children and young people in these studies and for all the outcomes investigated the quality of the evidence was rated as low. The GDG considered that the findings from the studies should, therefore, be treated with caution.

A further RCT examined the effectiveness of an elastomere arm splint in children and young people with unilateral or bilateral spasticity affecting the arms. The only reported outcome relevant to the guideline review was GAS-T scores for which the quality was rated as high. There was no evidence suitable for inclusion in relation to the use of wrist or hand orthoses, thumb abduction orthoses, knee orthoses, spinal orthoses (TLSOs), hip abduction orthoses, or prescribed footwear.

Other considerations

Orthoses in association with other treatment options

None of the evidence identified for inclusion compared the use of orthoses with other treatments. The GDG noted that orthoses are usually used with other interventions and should, therefore, be considered in terms of the child or young person's overall management programme. It was also noted that that BoNT injections can be a particularly useful adjunct to treatment with orthoses by improving the tolerability of the orthoses. Conversely orthoses can help to maximise the benefit that is derived from BoNT treatment (see Chapter 7).

Recommendations

Number	Recommendation
	Orthoses
	General principles
37	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.
38	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.
39	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.
40	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.
41	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.
42	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.

43	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.

44	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
45	Consider the following orthoses for children and young people with upper limb spasticity:

Number	Recommendation
	• 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).
46	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.
47	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.
48	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.
49	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.
50	Consider body trunk orthoses for children and young people with co-existing scoliosis or kyphosis if this will help with sitting.
51	Consider the overnight use of orthoses to: • improve posture • prevent or delay hip migration • prevent or delay contractures.
52	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.
53	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
54	Review the use of orthoses at every contact with the network team. 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.

Number	Research recommendation
7	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?
8	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?
9	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?
10	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?
11	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?

6 Oral drugs

Introduction

Oral drugs are used frequently as an adjuvant treatment to alleviate symptoms associated with spasticity that are not amenable to physical therapy alone (for example, distress or restricted function). Oral drugs may reduce spasticity, muscle spasms, pain and discomfort, and perhaps improve function and quality of life. The GDG's view was, therefore, that it was important to examine the evidence regarding the effectiveness and safety of these treatments.

Diazepam is thought to directly augment gamma-aminobutyric acid (GABA) postsynaptic action, increasing an inhibitory effect at the spinal cord reflex arc, as well as at the supraspinal level and reticular formation.

Baclofen acts at the level of the spinal cord, binding to GABA-B receptor sites, agonising the site and suppressing the release of excitatory neurotransmitters. Augmenting GABA-ergic activity reduces spasticity. Baclofen is absorbed orally, metabolised by the liver, and secreted by the kidneys, with a half-life of 2-4 hours.

Dantrolene has an action at the level of the muscle itself. It works by inhibiting the release of calcium ions from the sarcoplasmic reticulum, therefore diminishing the force of the muscles contractions, but it is not selective in the muscles it acts upon. It is metabolised by the liver and excreted by the kidneys; it can be hepatotoxic.

Trihexyphenidyl has been used traditionally in the treatment of Parkinson's disease and reduction of dystonia. It is an anticholinergic medication that acts on the central muscarinic receptors. It is thought that in situations where the nervous system is damaged the injury leads to a decrease in the effect or numbers of neurones which are dopaminergic, resulting in an imbalance or preservation of cholinergic interneurons. Treatment with trihexyphenidyl is thought to reduce cholinergic transmission and redress the balance leading to a decrease in dystonia.

Other oral drugs prioritised by the GDG for consideration included tizanidine, clonidine, tetrabenazine, and levodopa.

No related NICE guidance was identified for this review question.

Review question

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?

Description of included studies

Eight studies reported in nine publications were identified for inclusion for this review question (Denhoff 1975; Haslam 1974; Joynt 1980; Mathew 2005a; Mathew 2005b; McKinlay 1980; Milla 1977; Rice 2008; Scheinberg 2006). The studies addressed the following four comparisons.

- Diazepam versus placebo in children and young people aged under 12 years (most of whom were aged under 5 years) with spasticity of varying severities was evaluated in one parallel RCT (Mathew 2005a; Mathew 2005b). In this study the effect of a single bedtime dose of diazepam was compared to placebo. Children and young people who were in distress due to painful spasms were excluded from the study.

- Baclofen versus placebo in children and young people with spasticity of different severities was evaluated in three cross-over RCTs (McKinlay 1980; Milla 1977; Scheinberg 2006). In the first study (McKinlay 1980) the participants were aged 7-16 years, in the second study (Milla 1977) they were aged 2-16 years, and in the third study (Scheinberg 2006) they were aged 1-15 years.
- Dantrolene versus placebo in children and young people with spasticity of different severities was evaluated in three RCTs (Denhoff 1975; Haslam 1974; Joynt 1980). The first study (Denhoff 1975) was a cross-over RCT in which the participants were aged 18 months to 12 years. The second study (Haslam 1974) was a cross-over RCT in which the participants were aged 18 months to 17 years. The third study (Joynt 1980) was a parallel RCT in which the participants were aged 4-15 years.
- Trihexyphenidyl versus placebo in children and young people aged 2-18 years with spasticity of different severities was evaluated in one cross-over RCT (Rice 2008).

Evidence profiles

Oral diazepam versus placebo or no treatment

The only study identified for inclusion provided evidence on reduction of spasticity in one publication (Mathew 2005b).

Table 6.1 Evidence profile for bedtime doses of oral diazepam compared with placebo in children with spasticity of different severities; tone assessment

Number of studies	Number of participants		Effect		Quality
	Diazepam	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean reduction of muscle tone score (MAS score) at 15-20 days, bedtime half dose of diazepam (0.5 mg if bodyweight <8.5kg, 1 mg if bodyweight >8.5kg) versus placebo (better indicated by higher values)					
1 study (Mathew 2005b)	59[a]	55[b]	-	MD = 8.00[c]	MODERATE
Mean reduction of muscle tone score (MAS score) at 15-20 days, bedtime full dose of diazepam 1 mg if bodyweight <8.5kg, 2 mg if bodyweight >8.5kg versus placebo (better indicated by higher values)					
1 study (Mathew 2005b)	59[d]	55[e]	-	MD = 12.79[f]	MODERATE

ANOVA analysis of variance, CI confidence interval, MAS Modified Ashworth Scale, MD mean difference

a Mean change reported as 8.53

b Mean change reported as 0.53

c Reported p<0.001 (one way ANOVA)

d Mean change reported as 13.32

e Mean change reported as 0.53

f Reported p<0.001 (one way ANOVA)

Neither publication from the study reported outcomes relevant to optimisation of movement or function, pain (reduction of pain), or quality of life.

One publication (Mathew 2005a) provided evidence on adverse effects.

Table 6.2 Evidence profile for bedtime dose of oral diazepam compared with placebo in children with spasticity of different severities; adverse events

Number of studies	Number of participants		Effect		Quality
	Diazepam	Placebo	Relative (95% CI)	Absolute (95% CI)	
Daytime drowsiness assessed by caregivers at 15-20 days, bedtime dose of diazepam					
1 study (Mathew 2005a)	0/59 (0%)	0/55 (0%)	-	-	MODERATE

CI confidence interval

One publication (Mathew 2005a) provided evidence on outcomes relevant to acceptability and tolerability.

Table 6.3 Evidence profile for bedtime doses of oral diazepam compared with placebo in children with spasticity of different severities; treatment acceptability assessment

Number of studies	Number of participants		Effect		Quality
	Diazepam	Placebo	Relative (95% CI)	Absolute (95% CI)	
Child's disposition during activities of daily living at 15-20 days, bedtime dose of diazepam (better indicated by higher values)					
1 study (Mathew 2005a)	59[a]	55[b]	-	MD 5.93 higher (5.41 to 6.45 higher)	MODERATE
Burden of caring for the child on the family at 15-20 days, bedtime dose of diazepam (better indicated by higher values)					
1 study (Mathew 2005a)	59[c]	55[d]	-	MD 7.31 higher (6.78 to 7.84 higher)	MODERATE
Child's behavioural profile at 15-20 days, bedtime dose of diazepam (better indicated by higher values)					
1 study (Mathew 2005a)	59[e]	55[f]	-	MD 7.35 higher (6.74 to 7.96 higher)	MODERATE

CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean change in score 6.31 SD 1.94
b Mean change in score 0.38 SD 0.62
c Mean change in score 7.75 SD 1.98
d Mean change in score 0.44 SD 0.66
e Mean change in score 8.17 SD 2.14
f Mean change in score 0.82 SD 1.07

Oral baclofen versus placebo or no treatment

All three studies identified for inclusion (McKinlay 1980; Milla 1977; Scheinberg 2006) reported reduction of spasticity.

Table 6.4 Evidence profile for oral baclofen compared with placebo in children with spasticity of different severities; tone assessment

Number of studies	Number of participants		Effect		Quality
	Baclofen	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Improvement of spasticity (by 1 level of Ashworth scale) at day 28 of treatment					
1 study (Milla 1977)	9/20[a]	2/20[b]	RR 4.50 (1.11 to 18.27)*	35 more per 100 (from 1 more to 173 more)*	LOW
Improvement of spasticity (by more than 1 level of Ashworth scale) at day 28 of treatment					
1 study (Milla 1977)	5/20[c]	0/20[c]	RR 11 (0.65 to 186.62)*	-	LOW
Reduced muscle tone (Ashworth scale) reported by investigators					
1 study (McKinlay 1980)	-	-	-[d]	-	LOW
Reduced muscle tone or better movement reported by physiotherapist					
1 study (McKinlay 1980)	14/20[e]	5/20[e]	RR 2.8 (1.26 to 6.22)*	45 more per 100 (from 6 more to 130 more)*	MODERATE
Mean Tardieu scale score at week 12 of treatment (better indicated by lower values)					
1 study (Scheinberg 2006)	15[f]	15[g]	-	4.4 lower[h]	MODERATE

CI confidence interval, RR relative risk

* Calculated by the NCC-WCH, RR relative risk

a Reported Sign test p<0.001

b Reported Sign test p=0.25. The 2 patients who improved received placebo before baclofen

c Significance level was not reported. Using data from the first period only and analysing as a parallel trial, (3/10 in baclofen group versus 0/10 placebo group improved) relative risk (RR) = 7.00 (0.41 to 120.16) p=0.18

d Data not presented. Statement in report: “No significant changes between baclofen and placebo were observed in muscle tone”. The assessment period for this observation was not reported

e Reduced muscle tone or better movement was reported by physiotherapists in 14 children taking baclofen (70%), five children taking placebo (25%), p=0.064 reported, method used not reported. One child showed no change throughout. N=20

f Baseline Mean Tardieu score 20.9 (15.7 to 26.2). Final score 25.6 (19.4 – 25.8)

g Baseline Mean Tardieu score 20.9 (15.7 to 26.2). Final score 27.1 (21.0 - 33.3)

h No significant treatment, carry over or period effects found. Reported in paper as mean change = -4.4 (-10.8 to 2.0)

Two of the studies reported outcomes relevant to optimisation of function (Scheinberg 2006; McKinlay 1980).

Table 6.5 Evidence profile for oral baclofen compared with placebo in children with spasticity of different severities; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Baclofen	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean PEDI self-care domain score at week 12 of treatment (Better indicated by higher values)					
1 study (Scheinberg 2006)	15[a]	15[b]	-	1.5 lower[c]	MODERATE
Mean PEDI mobility domain score at week12 of treatment (better indicated by higher values)					
1 study (Scheinberg 2006)	15[d]	15[e]	-	1.5 lower[f]	MODERATE
Mean PEDI social function score at week 12 of treatment (better indicated by higher values)					
1 study (Scheinberg 2006)	15[g]	15[h]	-	0.2 lower[i]	MODERATE
Mean GAS T-score at week12 of treatment (better indicated by higher values)					
1 study (Scheinberg 2006)	15[j]	15[k]	-	6.6 higher[l]	MODERATE
Gait assessment performance improved (interstep distance and angle of the foot to the direction of walking)[m]					
1 study (McKinlay 1980)	8/20	4/20	RR = 2.00 (0.72 to 5.59)*[n]	20 more per 100 (from 6 fewer to 92 more)*	LOW

CI confidence interval, GAS T-score Goal Attainment Scaling T-score, PEDI Pediatric Evaluation of Disability Inventory
* Calculated by the NCC-WCH
a Baseline mean PEDI self care score: 15.2 (6.5 to 23.8). Final score 19.1 (8.8 to 29.4)
b Baseline mean PEDI self care score: 15.2 (6.5 to 23.8). Final score 20.5 (9.8 to 31.3)
c Reported in paper as mean change = -1.5 (-3.5 to 0.6). No significant treatment, carry over or period effects found
d Baseline mean PEDI mobility score: 17.5 (7.3 to 27.8). Final score 17.3 (6.9 to 27.7)
e Baseline mean PEDI mobility score: 17.5 (7.3 to 27.8). Final score 18.7 (8.1 to 29.4)
f Reported in paper as mean change = -1.5 (-3.1 to 0.2). No significant treatment, carry over or period effects found
g Baseline mean PEDI social function score: 31.8 (18.0 to 45.6). Final score 32.7 (19.8 to 45.6)
h Baseline mean PEDI social function score: 31.8 (18.0 to 45.6). Final score 32.9 (19.3 to 46.5)
i Reported in paper as mean change = -0.2 (-3.0 to 2.6) No significant treatment, carry over or period effects found
j Baseline mean GAS T-score was set at 35.0. Final score 51.3 (47.4 to 55.1)
k Baseline mean GAS T-score was set at 35.0. Final score 44.7 (39.3 to 50.0)
l Reported in paper as mean change = 6.6 (1.0 higher to 12.3).
m Physiotherapy staff asked children to walk along a roll of wallpaper on the floor after standing in black paint
n The investigators report that performance was unchanged throughout for 8/20 children

None of the studies reported outcomes relevant to pain or quality of life.

All three studies reported adverse effects (McKinlay 1980; Milla 1977; Scheinberg 2006).

Table 6.6 Evidence profile for oral baclofen compared with placebo in children with spasticity of different severities; adverse effects

Number of studies	Number of participants		Effect		Quality
	Baclofen	Placebo	Relative (95% CI)	Absolute (95% CI)	
Adverse effects					
1 study (Milla 1977)	5/20[a]	0/20	RR = 11 (0.65 to 186.62)*	-	LOW
Adverse effects (parental reports)					
1 study (McKinlay 1980)	8/20 [b]	1/20	RR = 8 (1.1 to 58.19)*	35 more per 100 (from 1 more to 100 more)*	LOW
Drowsiness (physical therapist and teacher reports)					
1 study (McKinlay 1980)	12/20	0/20	RR = 25 (1.58 to 395.48)*[c]	-	LOW
Adverse effects					
1 study (Scheinberg 2006)	6/15[d]	4/15[e]	RR = 1.5 (0.53 to 4.26)*	13 more per 100 (from 13 fewer to 87 more)*	MODERATE

CI confidence interval

* Calculated by the NCC-WCH

a Children experienced adverse effects associated with baclofen during the initial dose finding period. 4/5 children were younger than 7 years and weighed less than 19 kg and in all five children symptoms disappeared a few days after stopping treatment. One child experienced hypotonia alone, two children experienced sedation alone, and two children experienced both adverse effects. No adverse reports were reported with stepped re-introduction of baclofen from a starting dose of 10mg/day, in all but one child, who had athetosis (sedation and hypotonia experienced at 20mg/day, but child continued in study on a 10mg/day dose).

b Side effects were reported by the parents of 9/20 children. One of these reports pertained to the placebo period and the remaining 8 to the baclofen treatment period. In 4 of the 8 children reduction of dose of baclofen relieved side effects. Overall, drowsiness (5), sickness (2), dizziness (2), nocturnal enuresis (2), absence states, query epileptiform (2) slurred speech (2) and weakness (1) were reported, although the side effects are not listed by treatment period.

c The investigators report this as a statistically significant difference ($p<0.001$)

d Adverse effects reported as lethargy (1), constipation (2), seizures (2), poor appetite (1), drowsiness (1)

e Adverse effects reported as lethargy (1), constipation (2), seizures (1), hypotonia (1), difficulty passing urine (1)

Two of the studies examined the acceptability of treatment to parents (Scheinberg 2006; McKinlay 1980).

Table 6.7 Evidence profile for oral baclofen compared with placebo in children with spasticity of different severities; treatment acceptability assessment (parental report)

Number of studies	Number of participants		Effect		Quality
	Baclofen	Placebo	Relative (95% CI)	Absolute (95% CI)	
Wish to continue child's treatment (parental report)					
1 study (McKinlay 1980)	-	-	-	-[a]	LOW

Willingness to continue with the drug their child was receiving (parental report)					
1 study (Scheinberg 2006)	6/15[b]	4/15[c]	RR = 1.5 (0.53 to 4.26)*	13 more per 100 (from 13 fewer to 87 more)*	MODERATE
Positive effects (parental report)					
1 study (Scheinberg 2006)	6/15[d]	7/15[e]	RR = 0.86 (0.38 to 1.95)*	7 fewer per 100 (from 28 fewer to 44 more)*	MODERATE

CI confidence interval
* Calculated by the NCC-WCH
a One parent out of 20 said that they would continue with treatment (should their guess about active treatment be correct).
b Six parents said they would continue on baclofen therapy compared to 8 who would discontinue treatment and 1 who was unsure
c Four parents said they would continue with placebo compared to 10 who would not continue
d Six parents reported positive effects in their children whilst taking baclofen [sleeps better (3), more vocal (1), easier to dress (1), less spasms (1)]
e Seven parents reported positive effects when their children were taking placebo [sleeps better (2), more vocal (1), more relaxed/settled (3), less drooling (1)]

None of the studies reported outcomes relevant to quality of life.

Oral dantrolene versus placebo

Two of the studies (Haslam 1974; Joynt 1980) reported outcomes relevant to reduction of spasticity.

Table 6.8 Evidence profile for oral dantrolene compared with placebo in children with spasticity of different severities; tone assessment

Number of studies	Number of participants		Effect		Quality
	Dantrolene	Placebo	Relative (95% CI)	Absolute (95% CI)	
Motor tone assessment					
1 study (Haslam 1974)	59[a]	55[a]	-	0.609 higher[b]	LOW
Scissoring					
1 study (Haslam 1974)	59[a]	55[a]	-	0.381 higher[c]	LOW
Incidence of spasms (child and parental reports of improvement)					
1 study (Joynt 1980)	3/11	0/9	RR = 5.83 (0.34 to 100.03)*[d]	-	MODERATE
PROM					
1 study (Haslam 1974)	59[a]	55[a]	-	0.565 higher[e]	LOW
Spontaneous range of movement					
1 study (Haslam 1974)	59[a]	55[a]	-	0.522 higher[f]	LOW

CI confidence interval, PROM passive range of movement
* Calculated by the NCC-WCH
a No baseline or final values of assessment reported

b Mean difference between dantrolene and placebo periods reported as p>0.05 (T-test for mean ΔD-ΔP)
c Mean difference between dantrolene and placebo periods reported as p<0.05 (T-test for mean ΔD-ΔP)
d p=0.089 reported
e Mean difference between dantrolene and placebo periods reported as p>0.05 (T-test for mean ΔD-ΔP)
f Mean difference between dantrolene and placebo periods reported as p>0.05 (T-test for mean ΔD-ΔP)

Two of the studies (Denhoff 1975; Joynt 1980) reported outcomes relevant to optimisation of function.

Table 6.9 Evidence profile for oral dantrolene compared with placebo in children with spasticity of different severities; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Dantrolene	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Improvement in motor functioning					
1 study (Denhoff 1975)	10/26[a]	8/26[a]	-[b]	-	LOW
Improvement in activities of daily living and behaviour (staff assessment)					
1 study (Denhoff 1975)	11/20[c]	2/20[c]	-[d]	-	VERY LOW
Improvement in activities of daily living and behaviour (parental assessment)					
1 study (Denhoff 1975)	12/28[e]	2/28[e]	-[f]	-	LOW
Overall assessments (neurological, orthopaedic, motor, activities of daily living and behaviour)					
1 study (Denhoff 1975)	28	28	-	-[g]	LOW
Activities of daily living using multiple performance tests at 9 weeks (for example, time taken to screw and unscrew two halves of barrels of three sizes, or time taken to button and unbutton buttons of three different sizes)					
1 study (Joynt 1980)	11	9	-	-[h]	LOW

CI confidence interval
* Calculated by the NCC-WCH
a 10 children showed improvement with dantrolene (5 moderate and 5 marginal), 8 children showed improvement with placebo (2 marked, 4 moderate and 2 marginal) and 8 children showed no changes throughout the study
b The investigators report that this was not a statistically significant result (determined by binomial distribution)
c 11 children showed improvement with dantrolene (4 marked, 4 moderate and 3 marginal), 2 children showed improvement with placebo (2 marginal) and 8 children showed no changes throughout the study
d The investigators report that this was a statistically significant result (p<0.02 determined by binomial distribution).
e 12 children showed improvement with dantrolene (5 marked, 4 moderate and 3 marginal), 3 children showed improvement with placebo (1 marked, 2 moderate) and 13 children showed no changes throughout the study
f The investigators report that this was a statistically significant result (p<0.03 determined by binomial distribution).
g The investigators note that only a few children showed marked differences in assessments (neurological, orthopaedic, motor, activities of daily living and behaviour) between the drug and the placebo periods: more showed moderate differences and most showed marginal differences. For between eight and 13 of the 28 children, no discernible differences in functioning could be found between the drug and placebo treatment periods.
h The investigators report that no statistically significant differences between the treatment and placebo groups were observed for these tests

None of the studies reported outcomes relevant to pain (reduction in pain) or to quality of life.

One study (Denhoff 1975) reported outcomes relevant to adverse effects.

Table 6.10 Evidence profile for oral dantrolene compared with placebo in children with spasticity of different severities; adverse events

Number of studies	Number of participants		Effect		Quality
	Dantrolene	Placebo	Relative (95% CI)	Absolute (95% CI)	
Daytime drowsiness assessed by caregivers at 15-20 days, bedtime dose of diazepam					
1 study (Denhoff 1975)	16/28[a]	7/28[a]	-[b]	-	MODERATE

CI confidence interval
a Side effects were generally transient. These were seen in 23/28 children and included irritability, lethargy, drowsiness and general malaise.16 children experienced these during dantrolene treatment periods and 7 during placebo treatment periods. Irritability was more commonly reported during placebo periods than during dantrolene periods
b The investigators report that this was a statistically significant result (p<0.03 reported)

None of the studies reported outcomes relevant to acceptability and tolerability.

Oral trihexyphenidyl versus placebo

The only study identified for inclusion (Rice 2008) reported outcomes relevant to reduction of dystonia. The outcome reported was the Barry-Albright Dystonia Scale (BADS) score

Table 6.11 Evidence profile for trihexiphenidyl compared with placebo in children with spasticity of different severities; tone assessment

Number of studies	Number of participants		Effect		Quality
	Trihexyphenidyl	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean BADS score (better indicated by lower values)					
1 study (Rice 2008)	16[a]	16[b]	-	-[c]	LOW

BADS Barry-Albright Dystonia Scale, CI confidence interval
a Baseline mean BAD score: 18.4 (15.5 to 21.2). Final score 18.3 (14.8 to 21.8)
b Baseline mean BAD score: 18.4 (15.5 to 21.2). Final score 16.9 (13.4 to 20.4)
c Reported mean difference = 0.9 (-2.2 to 3.9)

The study reported outcomes relevant to optimisation of function, including the Quality of Upper Extremity Skills Test (QUEST) score.

Table 6.12 Evidence profile for trihexiphenidyl compared with placebo in children with spasticity of different severities; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Trihexyphenidyl	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean QUEST score (better indicated by higher values)					
1 study (Rice 2008)	16[a]	16[b]	-	-[c]	LOW
Mean GAS score (better indicated by higher values)					

1 study (Rice 2008)	16[d]	16[e]	-	-[f]	VERY LOW
Mean COPM-P score (better indicated by higher values)					
1 study (Rice 2008)	16[g]	16[h]	-	-[i]	VERY LOW

CI confidence interval, COPM-P Canadian Occupational Performance Measure – Performance, GAS Goal Attainment Scaling, QUEST Quality of Upper Extremity Skills Test
a Baseline mean QUEST score: 15.3 (-0.1 to 30.7). Final score 13.5 (1.4 to 25.5)
b Baseline mean QUEST score: 15.3 (-0.1 to 30.7). Final score 15.1 (2.8 to 27.4)
c Reported mean difference = -1.6 (-6.3 to 3.1)
d Baseline mean GAS score: 20.0. Final score 39.3 (31.8 to 46.8)
e Baseline mean GAS score: 20.0. Final score 33.3 (27.4 to 39.1)
f Reported mean difference = 6.8 (-3.7 to 17.5)
g Baseline mean COPM score (performance): 2.6 (2.2 to 3.0). Final score 4.4 (3.6 to 5.3)
h Baseline mean COPM score (performance): 2.6 (2.2 to 3.0). Final score 3.8 (3.0 to 4.7)
i Reported mean difference = 0.8 (-0.5 to 2.0)

The study did not report outcomes relevant to pain (reduction in pain) or to quality of life.

The study reported outcomes relevant to adverse effects.

Table 6.13 Evidence profile for trihexiphenidyl compared with placebo in children with spasticity of different severities; adverse events

Number of studies	Number of participants		Effect		Quality
	Trihexyphenidyl	Placebo	Relative (95% CI)	Absolute (95% CI)	
Adverse effects					
1 study (Rice 2008)	16/16[a]	6/16[b]	-	-	LOW

CI confidence interval
a Adverse effects symptoms during the active medication phase included agitation (distressed without reason or other odd behaviour), constipation, dry mouth and poor sleep. One child developed multiple adverse effects related to trihexyphenidyl (including dry mouth, confusion, agitation, inability to sleep, tachycardia, hallucinations, and urinary incontinence) requiring brief admission to hospital after the initial dose and had to withdraw from the trial.
b Six of the sixteen participants (38%) experienced side effects during the placebo phase.

The study reported outcomes relevant to acceptability and tolerability

Table 6.14 Evidence profile for trihexiphenidyl compared with placebo in children with spasticity of different severities; treatment acceptability assessment

Number of studies	Number of participants		Effect		Quality
	Trihexyphenidyl	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean COPM-S score (Better indicated by higher values)					
1 study (Rice 2008)	16[a]	16[4]	-	-[c]	LOW

CI confidence interval, COPM-S Canadian Occupational Performance Measure – Satisfaction
a Baseline mean COPM-S score 2.3 (1.8 to 2.7). Final score 4.7 (3.5 to 5.9)
b Baseline mean COPM-S score 2.3 (1.8 to 2.7). Final score 3.8 (2.8 to 4.8)

c Reported mean difference = 0.7 (-0.3 to 1.8)

Evidence statement

Oral diazepam versus placebo or no treatment

With regard to reduction of spasticity, one parallel RCT reported that, compared to baseline, there was a statistically significant reduction in muscle tone (MAS score) at 15-20 days in children and young people with spasticity of varying severities who were given a single bedtime half or full dose of diazepam compared with those who received placebo. (MODERATE)

No evidence was identified in relation to optimisation of movement or function, pain (reduction of pain) or quality of life.

With regard to adverse effects, one parallel RCT reported that daytime drowsiness was not observed over 15-20 days when children were given a bedtime dose of placebo or diazepam. (MODERATE)

With regard to acceptability and tolerability, one parallel RCT reported that, compared to baseline, there were statistically significant improvements in the child or young person's disposition during activities of daily living, the burden on the family of caring for the child or young person and the child or young person's behavioural profile at 15-20 days in children with spasticity of varying severities who were given a single bedtime half or full dose of diazepam compared with those who received placebo. (MODERATE)

Oral baclofen versus placebo or no treatment

With regard to reduction of spasticity, one cross-over RCT reported that at 28 days, statistically significantly more children and young people with diplegia, hemiplegia or quadriplegia improved by one level on the Ashworth scale when they received oral baclofen compared to when they received placebo. (LOW) The same cross-over RCT reported that at 28 days more children and young people improved by two or more levels on the Ashworth scale when they received oral baclofen compared to when they received placebo, although the difference was not statistically significant. (LOW) Another cross-over RCT reported that statistically significantly more children experienced 'reduced muscle tone or better movement' (assessed by physical therapists) when they were given baclofen compared with placebo. (MODERATE) One cross-over RCT reported that, compared to baseline, there was a reduction in MTS score at week 12 of treatment when children and young people with spastic or spastic dystonic quadriplegia received baclofen compared to when they received placebo, although the difference was not statistically significant. (MODERATE)

With regard to optimisation of function, one cross-over RCT reported that, compared to baseline, there was a reduction in PEDI self-care domain scores, mobility domain scores and social function scores at week 12 of treatment when children and young people with purely spastic or spastic dystonic quadriplegia received baclofen compared to when they received placebo, although these differences were not statistically significant. (MODERATE) One cross-over RCT reported that, compared to baseline, there was a statistically significant improvement in mean GAS-T scores at week 12 of treatment when children and young people with purely spastic or spastic dystonic quadriplegia received baclofen compared to when they received placebo. (MODERATE) One cross-over RCT reported that more children experienced improved gait performance when they received baclofen compared to when they received placebo, although the difference was not statistically significant. (LOW)

No evidence was identified in relation to pain (reduction of pain) or to quality of life.

With regard to adverse effects, one cross-over RCT reported that 25% of children and young people experienced side effects related to baclofen's therapeutic effect (four cases of sedation and one of hypotonia) within the 28-day treatment period compared to one participant (5%) in the placebo group who experienced an adverse effect. (LOW) One cross-over RCT found that 89% of parent-reported side effects were observed in children and young people receiving baclofen, and in half of these cases reducing the dose of baclofen relieved side effects. (LOW) One cross-over RCT reported that physical therapists and teachers observed that daytime drowsiness occurred statistically significantly more frequently when children and young people were taking baclofen compared to placebo. All reports of drowsiness occurred during the baclofen treatment period and drowsiness affected 60% of children and young people. (LOW) One cross-over RCT, which titrated the baclofen dose more slowly than the other two included RCTs, found that during the 12-week treatment periods, 40% of parents reported adverse effects when the child or young person was receiving baclofen compared to 27% of parents during the placebo period, although the difference was not statistically significant. (MODERATE)

With regard to acceptability and tolerability, one cross-over RCT reported that one parent (5%) would have continued with active treatment (should their prediction about the active treatment period be correct). (LOW) One cross-over RCT with 12-week treatment periods reported that 40% of parents would have continued with baclofen compared to 27% who would have continued with placebo, although the difference was not statistically significant. (MODERATE) In the same study, positive findings were reported by 40% of parents during the baclofen treatment period compared with 47% of parents during the placebo period, although the difference was not statistically significant. (MODERATE)

Oral dantrolene versus placebo

With regard to reduction of spasticity, one cross-over RCT with 3-week treatment periods reported that, compared to baseline, there was an improvement in motor tone that was not statistically significant at 4 weeks when children and young people with spasticity and learning disabilities received dantrolene compared with when they received placebo. (LOW) The same RCT reported that compared to baseline, there was an improvement in scissoring that was statistically significant when children and young people with spasticity and learning disabilities received dantrolene compared with when they received placebo. (LOW) One parallel RCT with a 6-week treatment period stated that there improvements in the incidence of spasms (as reported by the child or young person or their parent) occurred more often in children and young people with moderate or severe spasticity who received dantrolene compared to those who received placebo. (MODERATE)

With regard to optimisation of movement, one cross-over RCT with 3-week treatment periods reported that, compared to baseline, there were improvements in PROM and spontaneous range of movement that was not statistically significant at 4 weeks when children and young people with spasticity and learning disabilities received dantrolene compared with when they received placebo. (LOW)

With regard to optimisation of function, one cross-over RCT with 6-week treatment periods reported that more children and young people with mild, moderate or severe spasticity showed improved motor function when they received dantrolene compared to when they received placebo, although the difference was not statistically significant. (LOW) The same cross-over RCT reported that statistically significantly more children and young people showed improvement in activities of daily living and behaviour assessed by staff (VERY LOW) and parents (LOW) when the children or young people received dantrolene compared to when they received placebo. This cross-over RCT also reported that 8-13 of the 28 participants experienced no discernable differences in function between the drug and placebo treatment periods. (LOW) One parallel RCT with a 6-week treatment period reported that there were no significant differences in performance of multiple tests to assess activities of daily living at 6 and 9 weeks in children and young people with moderate or severe spasticity who received dantrolene compared to those who received placebo. (LOW)

No evidence was identified in relation to pain (reduction in pain) or quality of life.

With regard to adverse effects, one cross-over RCT with 6-week treatment periods reported that statistically significantly more children and young people with mild, moderate or severe spasticity experienced side effects when they received dantrolene compared to when they received placebo, although the side effects were generally transient. (MODERATE)

No evidence was identified in relation to acceptability and tolerability.

Oral trihexyphenidyl versus placebo

With regard to reduction of dystonia, one cross-over RCT reported that there was an increase in BADS scores that was not statistically significant at 12 weeks when children and young people with dystonia (and spasticity) received trihexyphenidyl compared to when they received placebo (mean final score comparison across groups). (LOW)

With regard to optimisation of function, one cross-over RCT reported that there was a reduction in QUEST scores that was not statistically significant at 12 weeks when children and young people with dystonia (and spasticity) received trihexyphenidyl compared to when they received placebo (mean final score comparison across groups). (LOW) The same RCT reported that there were increases in both GAS T-scores and COPM-P scores that were not statistically significant at 12 weeks when children and young people with dystonia (and spasticity) received trihexyphenidyl compared to placebo (mean final score comparison across groups). (VERY LOW)

No evidence was identified in relation to pain (reduction in pain) or quality of life.

With regard to adverse effects, one cross-over RCT with 12-week treatment periods reported that 16 children and young people (100%) experienced side effects when they were given trihexyphenidyl (one participant required brief hospitalisation for multiple side effects) compared to six children and young people (38%) who experienced side effects during the placebo phase. (LOW)

With regard to acceptability and tolerability, one cross-over RCT with 12-week treatment periods reported that there was an increase in COPM-S scores that was not statistically significant at 12 weeks when children and young people with dystonia (and spasticity) received trihexyphenidyl compared to when they received placebo (mean final score comparison across groups). (LOW)

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion:

- nitrazepam versus placebo or no treatment
- clonazepam versus placebo or no treatment
- any benzodiazepine versus placebo or no treatment
- tizanidine versus placebo
- tetrabenazine versus placebo or no treatment
- levodopa versus placebo or no treatment
- clonidine versus placebo or no treatment
- baclofen versus any benzodiazepine
- baclofen versus tizanidine
- baclofen versus trihexyphenidyl
- dantrolene plus baclofen versus baclofen
- diazepam plus baclofen versus baclofen
- baclofen plus dantrolene versus tizanidine
- baclofen plus dantrolene plus diazepam versus baclofen
- diazepam versus clonazepam
- nitrazepam versus clonazepam
- diazepam versus nitrazepam.

Health economics

No economic evaluations of oral drug treatment were identified in the literature search conducted for the guideline. Given the limited clinical evidence available for the oral drugs prioritised for consideration and the low cost of these drugs, an economic evaluation was not considered necessary. Even though the drugs are low cost, continuing on treatment when no benefits are found would be a poor use of resources and so when no positive effects are seen or adverse events outweigh benefits then treatment should be discontinued.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG consensus was that reduction in spasticity, pain and discomfort, and improvement in mobility and function were the most important outcomes for oral drugs. The GDG also considered the evidence of the impact of any change in physical mobility on quality of life and participation in day-to-day living. Adverse effects affect long-term acceptability and tolerability of drugs, both to the child or young person and their parents and other carers. Such outcomes were also reported in the guideline review of the literature.

Quality of evidence and trade-off between clinical benefit and harms

Evidence was identified for orally administered diazepam, baclofen, dantrolene and trihexyphenidyl only. All the included studies evaluated the effectiveness of an oral drug compared to placebo.

Diazepam

Evidence was identified from one RCT evaluating bedtime administration of diazepam. The study reported a statistically significant difference in muscle tone, but no evidence was identified in relation to improvements in movement or function, pain (reduction of pain), quality of life, or parental acceptability. The study did report that bedtime administration improved the child or young person's disposition, and that it improved the reported burden of care and the child or young person's behaviour. Bedtime administration was not associated with daytime drowsiness. However, the GDG noted that the dose of diazepam employed in the study was less than that usually used in UK practice currently and recommended in the SPC. The study did not examine the effectiveness of daytime treatment with diazepam. The GDG also observed that children and young people with painful muscle spasms were specifically excluded from the study. The group considered that with higher doses the outcomes might have been different, and the likelihood of sedation and increased oral secretions (a recognised side effect of diazepam treatment in children and young people with spasticity) might have been greater.

Baclofen

Three RCTs were identified in the guideline review. Evidence from one study reported that children and young people receiving baclofen experienced a small reduction in the level of spasticity (one level of improvement on the Ashworth scale), but this was not consistently observed in the other studies. It was not clear from the study whether the observed benefit was more likely to occur with mild or more severe spasticity. There was no evidence of any larger benefit (more than one level of improvement on the Ashworth scale). The evidence did not demonstrate benefit in terms of mobility or function, or any improvement in muscle tone. There was no reported improvement in Tardieu scale scores or optimisation of function, in GAS T-scores, in gait, or in pain reduction. No evidence was identified regarding the effectiveness of baclofen in reducing pain or regarding the possible effects of oral baclofen on quality of life or ease of care. Adverse effects of treatment were reported in all studies. Drowsiness was reported as a specific side-effect, and this appeared to be dose related.

Dantrolene

Three RCTs reported evidence of outcomes relevant to the guideline review. One study reported that scissoring was statistically significantly reduced, but otherwise there was no evidence that spasticity was reduced by dantrolene. Another study reported improved performance with daily activities and behaviour, but the others did not report this benefit. The use of dantrolene was associated with increased drowsiness, lethargy and malaise although these symptoms were reportedly transient.

Trihexyphenidyl

One RCT was included in the guideline review. The participants in this study had spasticity and co-existing dystonia. The study examined optimisation of movement and function (through BADs scores, QUEST scores, GAS T-scores, and COPM-P scores) and acceptability and tolerability (through

COPM-S scores). However, no statistically significant differences between the treatment groups were observed. No outcomes relating to pain or quality of life were reported. Adverse effects occurred more frequently in the trihexyphenidyl group, but the specific effects were not reported clearly.

The GDG noted that evidence regarding the effectiveness of oral drugs in managing spasticity and co-existing motor disorders was limited, inconsistent and often of low quality. The GDG noted that no trials in which oral drugs were directly compared were identified for inclusion. The reported trials did not provide evidence to guide optimal dosage, they were of short duration, and the GDG considered that with time, increased tolerance to the drug treatments might have developed.

Given the limitations in the clinical evidence, the GDG relied on the group's expertise and on consensus in their deliberations about whether to recommend the use of oral drugs. Despite the deficiencies and inconsistencies in the evidence the GDG believed that oral drugs do have a potentially important role in the care of some children and young people with spasticity. First, despite the limited trial evidence, based on the mechanisms of action of these drugs it is plausible to expect that they might be beneficial. Second, oral diazepam and baclofen are currently widely used in the UK to alleviate pain, distress and spasticity and, based on the clinical expertise of the GDG, benefit was regularly observed or reported by individual patients and carers. The GDG recognised oral drug treatment as a non-invasive intervention that would be of great value if it were successful in alleviating spasticity and relieving associated conditions such as pain, muscle spasms and functional disability. Any likely side effects would usually be reversible either by dosage alteration or discontinuation if necessary. For these reasons the group concluded that it was appropriate to recommend the use of certain oral drugs for the management of spasticity.

The group was, however, anxious to avoid the prescription of ineffective drugs and believed that the individual child or young person's response to oral drug treatment was unpredictable and that the benefits achieved and the adverse effects experienced might vary from one child or young person to the next. Daytime drowsiness might be a significant problem and might disturb a child or young person's sleeping pattern. On the other hand, a mild nocturnal sedative effect might sometimes be beneficial. The GDG considered that the balance of benefit versus adverse effects should be judged on an individual basis and that a cautionary approach should be taken to the use of oral drugs at all times. This cautionary approach is reflected in the wording of the recommendations through the use of the term 'consider' (rather than 'offer') and through specific advice about which drugs should be used, and how and when they should be introduced, monitored for effectiveness, and discontinued.

The GDG noted that oral benzodiazepines (especially diazepam) are frequently used in the management of spasticity in children and young people. All available trial evidence within this class was in relation to diazepam. Although the evidence of effectiveness was limited, the comparative prominence of diazepam over other benzodiazepines in the available literature reflected the group's clinical experience in terms of both its common usage, and their positive experiences of using the drug to treat spasticity that was contributing to discomfort or pain, muscle spasms and functional disability. As such the GDG believed that diazepam should be the recommended benzodiazepine of choice.

Equally, although the evidence of effectiveness of oral baclofen was limited, the GDG considered that its prominence in the available literature reflected current good practice and positive clinical experience for the same clinical indications as diazepam. The group therefore considered it was also appropriate to recommend baclofen.

Although the GDG considered that the clinical indications for considering diazepam and baclofen overlapped, the group noted that diazepam was likely to have a more rapid onset of action than baclofen. The group concluded, therefore, that diazepam would be particularly useful in a situation where rapid onset of action would be beneficial, such as in a severe pain crisis. However, if the goal was to achieve a sustained long-term effect from oral drug treatment then baclofen would be preferred. This was because the GDG was concerned about the possibility of adverse consequences from long-term administration of a benzodiazepine such as diazepam.

The GDG consensus was that a rational approach to the use of oral drugs would be to introduce them gradually with a stepwise increase in dosage aimed at optimising therapeutic benefit while minimising the risk of adverse effects such as excessive sedation. The trial evidence relating to baclofen also reported benefits associated with this approach.

The GDG view was that if oral diazepam were offered as treatment, this should begin as a bed-time dose. If necessary the dose could be increased stepwise and/or a daytime dose added. This was considered a particularly safe approach as it was the equivalent of giving one of the two divided doses recommended in the SPCs. This, in turn, reflected the reduced dosages reported in the evidence considered in the guideline review.

When using oral baclofen, again the group considered it advisable to begin with a low dose and increased stepwise over 4 weeks. The GDG's view was that this was the appropriate time period to achieve the intended therapeutic goal with minimal side-effects.

If oral diazepam was chosen at the outset because of its expected rapid onset of action, the GDG's view was that consideration should be given to changing to oral baclofen later as this may have a more satisfactory long-term outcome.

The GDG concluded that if an oral drug were found to have a useful effect in an individual child or young person (that is, it achieves a desired goal and is well tolerated) it should be continued as medium-term or long-term maintenance therapy. However, unnecessary and possibly ineffective prescribing in the longer term should be avoided. Therefore, the GDG advised that consideration should be given as to whether a particular drug treatment is still necessary on each occasion when a child or young person is reviewed. Such a review of treatment should take place at least 6-monthly.

In the event that an oral drug leads to side-effects such as drowsiness, consideration should be given either to reducing the dose or discontinuing treatment. Likewise, if there is no worthwhile effect with diazepam and baclofen individually within a period of 4-6 weeks then consideration should be given to a trial of combined treatment with both diazepam and baclofen. Although no evidence was identified to support the effectiveness of such combined treatment, the GDG considered that this was a rational approach given the different mechanisms of action of the two drugs.

The GDG considered that there were potential adverse effects associated with withdrawal of diazepam and baclofen after a long period of treatment. The group therefore recommended that discontinuation after several weeks' use should be accomplished through staged reductions in dose to avoid withdrawal symptoms.

The GDG considered that neither the evidence of the effectiveness of dantrolene nor their clinical experience of its use was sufficient to allow them to make a recommendation on its use for reduction of spasticity.

Given the absence of clinical trial evidence in relation to oral drugs other than diazepam, baclofen and dantrolene examined in the guideline review, and the group's limited experience of using trihexyphenidyl or the other drugs for which no evidence was identified for inclusion where spasticity is the main cause for concern, the GDG made no recommendations for oral drug treatment for this indication other than using diazepam or baclofen.

The GDG was, however, aware that oral drugs are commonly used in the management of dystonia in children and young people with spasticity. Dystonia may be more problematic than spasticity in some children and young people, have a greater effect on motor function and independence, and also cause problems with posture and pain. If an oral drug could diminish involuntary movements and/or improve motor control, then the child or young person may benefit. In this case, despite the absence of clinical trial evidence for specific drugs other than trihexyphenidyl the GDG took account of their personal experience. The group was of the view that some drugs are often used in the treatment of dystonia in such circumstances and can be effective.

Baclofen can be effective in reducing dystonia through similar mechanisms to its use in spasticity, although higher doses may be needed with the greater risk of side effects.

Trihexyphenidyl, which is an anticholinergic agent, can be effective in treating dystonia and other involuntary movements in progressive brain disorders and where dystonia occurs as a side effect of other medications. Again the GDG therefore considered it reasonable to consider a trial of trihexyphenidyl in children and young people with spasticity and co-existing dystonia.

Levodopa is used in conditions where the production of dopamine by the brain is insufficient. The GDG recognised that it is highly effective in treating dopa-responsive dystonia, a genetic condition.

The group concluded that it was reasonable to expect that it might also reduce dystonia in children and young people with spasticity.

The GDG concluded, therefore, that it was appropriate to recommend a trial of oral drug treatment with a drug such as trihexyphenidyl, levodopa or baclofen in children and young people in whom dystonia contributes significantly to problems with posture, function and pain. The exact choice of drug in such children and young people would be best determined using clinical judgement based on the side effect profile of each potential drug and the likely impact on the specific child or young person. As with the recommendations for management of pure spasticity, the group considered that a cautionary, trial-based approach was necessary to avoid the prescription of ineffective drugs.

Trade-off between net health benefits and resource use

Diazepam, baclofen and dantrolene are inexpensive drugs and, if clinically effective, the GDG considered that they would be cost effective. The current cost of 28 diazepam tablets is £0.89 for 2 mg tablets, £0.90 for 5 mg tablets, and £0.92 for 10 mg tablets (British National Formulary for Children (BNFc) 2011-12). The maximum daily dose is 40 mg, which would cost £48 per year if the drug were administered tablets. As an oral solution diazepam 2 mg/5 ml costs £6.08/100 ml. A strong oral solution is also available, diazepam 5 mg/5 ml, net price of a 100 ml pack is £6.38. The current cost of baclofen is £0.02 per 10 mg tablet and £7.16 for 300 ml of oral solution (5 mg/5 ml; BNFc 2011-12) Given that the maximum daily dose of baclofen is 60 mg this amounts to an annual cost of £41 if tablets are given.

Other considerations

The GDG noted that a proportion of children with spasticity receive anticonvulsant medication for epilepsy, and the possibility of interactions needs to be borne in mind.

The GDG also noted that, while pain is a common clinical indication for the use of oral drugs BoNT-A might be considered a preferable alternative for focal pain in some children and young people. The GDG concluded that it would be difficult to give precise guidance on which of these pharmacological interventions (oral drugs or BoNT-A) would be preferred in an individual child or young person because, for example, more than one indication might lead to a decision to use a particular form of drug treatment.

The GDG acknowledged that, as with all treatments recommended in the guideline, oral drugs should be prescribed by a relevant member of the network team. Furthermore, the use of oral drugs should be considered in the context of the child or young person's overall management programme, which is formulated in conjunction with the child or young person and their parents or carers.

Recommendations

Number	Recommendation
	Oral drugs
55	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).
56	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.

Number	Recommendation
	Baclofen is particularly useful if a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).
57	If oral diazepam is initially used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.
58	Give oral diazepam treatment as a bedtime dose. If the response is unsatisfactory consider: • increasing the dose **or** • adding a daytime dose.
59	Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect.
60	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.
61	If adverse effects (such as drowsiness) occur with oral diazepam or oral baclofen, think about reducing the dose or stopping treatment.
62	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.
63	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.
64	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[***], levodopa[†††] or baclofen[‡‡‡].

Number	Research recommendation
12	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?
13	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?
14	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?

[***] At the time of publication (June 2012), trihexiphenidyl 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

[†††] At the time of publication (June 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

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

7 Botulinum toxin

Introduction

BoNT is a neurotoxic protein produced by the bacterium *Clostridium botulinum*. There are seven serologically distinct toxin types but only toxins A and B are used to treat spasticity in the UK. When injected intramuscularly BoNT attaches rapidly to receptors in the presynaptic nerve membrane where it binds irreversibly and blocks the release of the neurotransmitter achetylcholine. Without achetylcholine the muscle cannot be triggered to contract and flaccid paralysis is produced. In spastic muscles this relaxation is the intended effect of treatment and it can help alleviate some of the problems associated with upper motor neurone disorders such as cerebral palsy. The blockage of the neuromuscular junction triggers neuronal sprouting which re-establishes impulse transmission and therefore muscle activity and spasticity return at around 3 months.

BoNT-A is licensed in the UK for use in focal spasticity in children 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. However, it is frequently used 'off licence' by many practitioners. There is variation in its use across the UK in terms of assessment of patients, administration and follow up pathways. For this reason the GDG prioritised a review of the available evidence relating to BoNT-A with the aim of formulating recommendations to guide practice.

BoNT is one of a number of strategies available for the management of spasticity in children and young people with non-progressive brain disorders and it is not usually used in isolation. It is believed that the temporary reduction in spasticity offers clinicians a window of opportunity to address issues of weakness and functional difficulties brought about by the abnormal muscle tone. It may also unmask weak muscles and cause a temporary deterioration in function. This, along with the possible side effects of the toxin, makes careful assessment very important. Good patient selection criteria and individualised patient goals are essential when planning a course of treatment with BoNT.

BoNT-A is the primary toxin used in the UK although, some centres have used type B (BoNT-B) when response to BoNT-A is inadequate.

The review conducted for this guideline prioritised the following aspects of treatment with BoNT.

- The effectiveness of a single dose of BoNT-A given in combination with a programme of physical therapy appropriate to the child or young person's needs compared to:
  - physical therapy alone
  - oral antispasmodic medication and physical therapy.
- The effectiveness of BoNT-A treatment repeated every 4 months compared to every 12 months.
- The comparative effectiveness of BoNT-A treatment when administered using the following localisation techniques to identify muscle injection sites:
  - palpation of the spastic muscle
  - electrical stimulation guided-injection
  - ultrasound-guided injection.
- The comparative effectiveness of BoNT-A and BoNT-B.

No related NICE guidance specific to BoNT treatment in children and young people with spasticity was identified for this review question. The GDG recognised, however, the importance of analgesia, anaesthesia or sedation to minimise distress during the injection of BoNT and noted that 'Sedation in children and young people' (NICE clinical guideline 112) provides guidance in relation to the use of sedation during diagnostic and therapeutic procedures.

Review question

What is the effectiveness of the long-term use of intramuscular BoNT-A or BoNT-B in combination with other interventions (physical therapy or orthoses) as compared to other interventions in reducing spasticity, maintaining motor function and preventing secondary complications in children and young people with spasticity with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder?

Description of included studies

Eight studies were identified for inclusion for this review question (Ackman 2005; Hoare 2010; Kanovsky 2009; Kay 2004; Kwon 2010; Olesch 2010; Reddihough 2002; Xu 2009). The studies addressed the following four comparisons.

- BoNT-A and physical therapy versus physical therapy alone was evaluated in five studies (Ackman 2005; Hoare 2010; Kay 2004; Olesch 2010; Reddihough 2002). One study was a Cochrane systematic review relating to treatment of upper limbs in children and young people with cerebral palsy (Hoare 2010). The Cochrane systematic review synthesised data from seven parallel RCTs (Boyd 2004; Fehlings 2000; Greaves 2004; Lowe 2006; Russo 2007; Speth 2005; Wallen 2007), in which the participants were aged 5-15 years, 2.5-10 years, 22-58 months, 2-8 years; 3-16 years, 4-16 years, and 2-14 years, respectively. Some of the data reported in the Cochrane systematic review had been obtained through direct contact with the study authors, rather than being extracted from published articles. A further parallel RCT (Olesch 2010) published after the Cochrane systematic review evaluated treatment of upper limbs in children with hemiplegia; the participants in this study were aged 1 year 10 months to 4 years 10 months. Three parallel RCTs evaluated treatment of lower limbs in children and young people with cerebral palsy (Ackman 2005; Kay 2004; Reddihough 2002). The participants in the first study (Ackman 2005) were aged 3-9 years, those in the second study (Kay 2004) were aged 4.3-13.8 years, and those in the third study (Reddihough 2002) were aged 22-80 months.
- BoNT-A every 4 months versus BoNT-A every 12 months was evaluated in one parallel RCT (Kanovsky 2009) involving children aged 1-8 years with cerebral palsy. In this study BoNT-A was injected into the gastrocnemius muscles to treat the lower limb.
- Electrical muscle stimulation versus palpation of the spastic muscle group for guiding the delivery of BoNT injections was evaluated in one parallel RCT (Xu 2009) involving children aged 2-10 years with cerebral palsy. In this study BoNT-A was used to treat ankle plantarflexor spasticity.
- Ultrasound versus electrical muscle stimulation for guiding the delivery of BoNT injections was evaluated in one quasi-randomised controlled trial (Kwon 2010) involving children aged under 7 years with cerebral palsy. In this study BoNT-A was injected into calf muscles.

Evidence profiles

Botulinum toxin type A and physical therapy versus physical therapy alone

The Cochrane systematic review (Hoare 2010) and the RCT published after the Cochrane systematic review (Olesch 2010) relating to treatment of the upper limb reported outcomes relevant to reduction of spasticity and optimisation of movement.

Table 7.1 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; upper limb; tone and joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and occupational therapy	**Occupational therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
MAS score, shoulder adductors at 4 months					
1 study (Greaves 2004)	9	9	OR 0.20 (0.03, 1.15)†	-	LOW
MAS score, elbow flexors at 3 months					
2 studies (Russo 2007; Wallen 2007)	41	39	OR 0.16 (0.06 to 0.43)†	-	MODERATE
MAS score, elbow flexors at 6 months					
2 studies (Russo 2007; Wallen 2007)	41	39	OR 0.33 (0.13 to 0.86)†	-	LOW
MTS score (mean change from baseline), elbow flexors at 4 months (better indicated by lower values)					
1 study (Greaves 2004)	9	9	-	MD 43.89 lower (92.99 lower to 5.21 higher)†	LOW
MTS score (mean final score), elbow flexors at 4 months, cycle 1 (better indicated by lower values)					
1 study (Olesch 2010)	11[a]	11[b]	-	MD 34.3 lower (70.67 lower to 2.07 higher)*	MODERATE
MTS score (mean final score), elbow flexors, cycle 2 (better indicated by lower values)					
1 study (Olesch 2010)	11[c]	11[d]	-	MD 36 lower (71.3 to 0.7 lower)*	MODERATE
MTS score (mean final score), elbow flexors, cycle 3 (better indicated by lower values)					
1 study (Olesch 2010)	11[e]	11[f]	-	MD 42.8 lower (86.48 lower to 0.88 higher)*	MODERATE
PROM elbow extension (change from baseline) at 3 months (better indicated by higher values)					
2 studies (Fehlings 2000; Wallen 2007)	34	31	-	MD 0.11 higher (2.96 lower to 3.19 higher)†	LOW
PROM elbow extension (change from baseline) at 6 months (better indicated by higher values)					
2 studies (Fehlings 2000; Wallen 2007)	34	32	-	MD 0.15 lower (3.38 lower to 3.07 higher)†	LOW

MAS score, pronators at 3 Months					
1 study (Wallen 2007)	20	17	OR 1.58 (0.45 to 5.52)†	-	MODERATE
MAS score, pronators at 4 Months					
1 study (Greaves 2004)	9	9	OR 0.13 (0.02 to 0.97)†	-	LOW
MAS score, pronators at 6 Months					
1 study (Wallen 2007)	20	17	OR 1.5 (0.22 to 10.16)†	-	LOW
MTS score (mean change from baseline), forearm pronators at 4 months, cycle 1 (better indicated by lower values)					
1 study (Olesch 2010)	11[g]	11[h]	-	MD 4 higher*	LOW
MTS score (mean change from baseline), forearm pronators, cycle 2 (better indicated by lower values)					
1 study (Olesch 2010)	11[i]	11[j]	-	MD 5.8 lower*	LOW
MTS score (mean change from baseline), forearm pronators, cycle 3 (better indicated by lower values)					
1 study (Olesch 2010)	11[k]	11[l]	-	MD 18.5 lower*	LOW
AROM supination (change from baseline) at 3 months (better indicated by higher values)					
1 study (Speth 2005)	10	10	-	MD 16.3 lower (33.01 lower to 0.41 higher)†	MODERATE
AROM supination (change from baseline) at 6 months (better indicated by higher values)					
1 study (Speth 2005)	10	10	-	MD 8.4 lower (36.74 lower to 19.94 higher)†	MODERATE
PROM forearm supination (change from baseline) at 3 months (better indicated by higher values)					
2 studies (Fehlings 2000, Wallen 2007)	34	31	-	MD 3.64 higher (0.92 lower to 8.2 higher)†	LOW
PROM forearm supination (change from baseline) at 6 months (better indicated by higher values)					
2 studies (Fehlings 2000, Wallen 2007)	34	32	-	MD 0.97 higher (4.45 lower to 6.39 higher)†	LOW
MAS score, wrist flexors at 3 months					
2 studies (Russo 2007, Wallen 2007)	0/0 (0%)	0/0 (0%)	OR 0.1 (0.03 to 0.29)†	-	MODERATE
MAS score, wrist flexors at 4 months					
1 study (Greaves	0/0 (0%)	0/0 (0%)	OR 0.36 (0.07	-	LOW

2004)			to 1.87)†		
MAS score, wrist flexors at 6 months					
2 studies (Russo 2007, Wallen 2007)	0/0 (0%)	0/0 (0%)	OR 0.2 (0.08 to 0.51)†	-	LOW
MTS score (mean change from baseline), wrist flexors at 4 months (better indicated by lower values)					
1 study (Greaves 2004)	10	10	-	MD 10.56 lower (30.83 lower to 9.71 higher)†	LOW
MTS score (mean final score), wrist flexors at 4 months, cycle 1 (better indicated by lower values)					
1 study (Olesch 2010)	11[m]	11[n]	-	MD 18.5 lower (37.78 lower to 0.78 higher)*	MODERATE
MTS score (mean final score), wrist flexors, cycle 2 (better indicated by lower values)					
1 study (Olesch 2010)	11[o]	11[p]	-	MD 18.5 lower (37.78 lower to 0.78 higher)*	MODERATE
MTS score (mean final score), wrist flexors, cycle 3 (better indicated by lower values)					
1 study (Olesch 2010)	11[q]	11[r]	-	MD 20.9 lower (38.27 to 3.53 lower)*	HIGH
AROM wrist extension (change from baseline) at 3 months (better indicated by higher values)					
1 study (Speth 2005)	10	10	-	MD 14.7 higher (7.92 lower to 37.32 higher)†	MODERATE
AROM wrist extension (change from baseline) at 6 months (better indicated by higher values)					
1 study (Speth 2005)	10	10	-	MD 15.6 higher (6.36 lower to 37.56 higher)†	MODERATE
PROM wrist extension (change from baseline) at 3 months (better indicated by higher values)					
1 study (Fehlings 2000)	14	15	-	MD 3.31 higher (4.7 lower to 11.32 higher)†	LOW
PROM wrist extension (change from baseline) at 6 months (better indicated by higher values)					
1 study (Fehlings 2000)	14	15	-	MD 0.07 lower (9.85 lower to 9.71 higher)†	LOW
PROM palmar thumb abduction (change from baseline) at 3 months (better indicated by higher values)					
1 study (Fehlings 2000)	14	15	-	MD 2.06 higher (4.69 lower to 8.81 higher)†	LOW
PROM palmar thumb abduction (change from baseline) at 6 months (better indicated by higher values)					
1 study (Fehlings 2000)	14	15	-	MD 1.56 higher (3.96 lower to 7.08 higher)†	LOW

AROM active range of movement, CI confidence interval, MAS Modified Ashworth Scale, MD mean difference, MTS Modified Tardieu Scale, OR odds ratio, PROM passive range of movement, SD standard deviation
* Calculated by the NCC-WCH
† Data from Hoare 2010 Cochrane systematic review
a Mean final score ± SD reported as 43.0 ± 45.7
b Mean final score ± SD reported as 77.3 ± 39.3
c Mean final score ± SD reported as 54.5 SD ± 44.1
d Mean final score ± SD reported as 90.5 SD ± 40.3
e Mean final score ± SD reported as 34.5 SD ± 48.0
f Mean final score ± SD reported as 77.3 SD ± 56.2
g Mean final score ± SD reported as 48.5 ± 37.2
h Mean final score ± SD reported as 75.5 ± 31.7
i Mean final score ± SD reported as 39.5 ± 40.6
j Mean final score ± SD reported as 77.3 ± 22.8
k Mean final score ± SD reported as 22.7 ± 33.2
l Mean final score ± SD reported as 72.7 ± 28.7
m Mean final score ± SD reported as 11.0 ± 17.4
n Mean final score ± SD reported as 29.5 ± 27.6
o Mean final score ± SD reported as 7.3 ± 9.3
p Mean final score ± SD reported as 25.0 ± 30.7
q Mean final score ± SD reported as 3.2 ± 7.2
r Mean final score ± SD reported as 24.1 ± 28.5

All three RCTs relating to treatment of the lower limb reported outcomes relevant to reduction of spasticity and optimisation of movement (Ackman 2005; Kay 2004; Reddihough 2002).

Table 7.2 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; lower limb; tone and joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
MAS score, plantarflexor spasticity (reduction in spasticity), mean change at 3 months (better indicated by higher values)					
1 study (Kay 2004)	16 limbs[a]	20 limbs[b]	-	MD 0.2 higher (0.52 lower to 0.92 higher)*	LOW
MAS score, plantarflexor spasticity (reduction in spasticity), mean change at 6 months (better indicated by higher values)					
1 study (Kay 2004)	16 limbs[c]	20 limbs[d]	-	MD 0.94 higher (0.14 to 1.74 higher)*	LOW
Ashworth score at ankle (reduction in spasticity), mean change at 3 months (better indicated by higher values)					
1 study (Ackman 2005)	12[e]	13[f]	-	MD 0.3 higher	LOW
Ashworth score at ankle (reduction in spasticity), mean change at 6 months (better indicated by higher values)					
1 study (Ackman	12[g]	13[h]	-	MD 0.0	LOW

2005)				lower/higher	
Active dorsiflexion at ankle, mean change at 3 months (better indicated by higher values)					
1 study (Ackman 2005)	12[i]	13[j]	-	MD 2 more	LOW
Active dorsiflexion at ankle, mean change at 6 months (as reported, read from graph, better indicated by higher values)					
1 study (Ackman 2005)	12[k]	13[l]	-	MD 3 higher	LOW
PROM ankle dorsiflexion (knee flexion) at 3 months (mean change from baseline, better indicated by higher values)					
1 study (Ackman 2005)	12[m]	13[n]	-	MD 0.5 lower	LOW
PROM ankle dorsiflexion (knee flexion) at 6 months (mean change from baseline, better indicated by higher values)					
1 study (Ackman 2005)	12[o]	13[p]	-	MD 1.5 higher	LOW
PROM ankle dorsiflexion (knee extension) at 3 months (mean change from baseline, better indicated by higher values)					
1 study (Ackman 2005)	12[q]	13[r]	-	MD 1 higher	LOW
PROM ankle dorsiflexion (knee extension) at 6 months (mean change from baseline, better indicated by higher values)					
1 study (Ackman 2005)	12[s]	13[t]	-	MD 1.5 higher*	LOW
PROM ankle dorsiflexion at 3 months (mean change from baseline, better indicated by higher values)					
1 study (Kay 2004)	16[u]	20[v]	-	MD 4.5 higher (3.22 lower to 12.22 higher)*	LOW
PROM ankle dorsiflexion at 6 months (mean change from baseline, read from graph, better indicated by higher values)					
1 study (Kay 2004)	16[w]	20[x]	-	MD 1.5 lower	LOW
PROM right ankle dorsiflexion (knee extension) at 3 months (mean change from baseline, better indicated by higher values)					
1 study Reddihough 2002)	11[y]	11[z]	-	MD 8.63 higher (2.23 to 15.03 higher)*	LOW
PROM right ankle dorsiflexion (knee flexion) at 6 months (mean change from baseline, better indicated by higher values)					
1 study Reddihough	34[A]	34[B]	-	MD 8.53 higher (0.27 lower to	VERY LOW

2002)				17.33 higher)*	
MAS score, left calf, mean change at 6 months (better indicated by lower values)					
1 study Reddihough 2002)	35[C]	35[D]	-	0.52 lower (0.89 to 0.15 lower)*	VERY LOW
MAS score, left adductor, mean change at 6 months (better indicated by higher values)					
1 study Reddihough 2002)	8[E]	8[F]	-	1.63 lower (2.53 to 0.71 lower)*	VERY LOW
MAS score, right adductor, mean change at 6 months (better indicated by higher values)					
1 study Reddihough 2002)	-[G]	-[H]	-	-[I]	VERY LOW
MAS total score, mean change at 3 months (better indicated by higher values)					
1 study Reddihough 2002)	18[J]	18[K]	-	2.51 lower (3.22 to 1.8 lower)	MODERATE

AROM active range of movement, CI confidence interval, MAS Modified Ashworth Scale, MD mean difference, MTS Modified Tardieu Scale, PROM passive range of movement, SD standard deviation
* Calculated by the NCC-WCH
a Mean change from baseline ± SD = 0.9 ± 1.0
b Mean change from baseline ± SD = 1.1 ± 1.2
c Mean change from baseline ± SD = 0.26 ± 1.14
d Mean change from baseline ± SD =1.2 ± 1.3
e Estimated baseline = 2.6±0.9, estimated final score 2.4±0.5
f Estimated baseline = 2.6±1.0, estimated final score 2.1±0.8
g Estimated baseline = 2.6±0.9, estimated final score 2.2±0.6
h Estimated baseline = 2.6±1.0, estimated final score 2.2±0.7
i Estimated baseline = -18°±16, estimated final score -15°±20
j Estimated baseline = -12°±14, estimated final score -11°±20
k Estimated baseline = -18°±16, estimated final score -11°±14
l Estimated baseline = -12°±14, estimated final score -8°±13
m Estimated change from baseline = 3.5
n Estimated change from baseline = 4
o Estimated change from baseline = 4.5
p Estimated change from baseline = 3
q Estimated change from baseline = 3.5
r Estimated change from baseline = 2.5
s Estimated change from baseline = 4.5
t Estimated change from baseline = 3
u Mean change from baseline reported as 18.4 ± 11.7
v Mean change from baseline reported as 13.9 ± 11.8
w Estimated change from baseline = 10.5 ± 10.5
x Estimated change from baseline = 12 ± 12
y Mean change from baseline ± SD = 1.36 ± 7.45
z Mean change from baseline ± SD = -7.27 ± 7.86
A Mean change from baseline reported as -0.09 ± 0.78
B Mean change from baseline reported as 13.9 ± 11.8
C Mean change from baseline ± SD = -0.09 ± 0.78
D Mean change from baseline ± SD = 0.43 ± 0.81
E Mean change from baseline ± SD = -0.63 ± 1.06
F Mean change from baseline ± SD = 1 ± 0.76
G Worsening of approx 0.5-1 MAS reported

H Improvement of approx 1 MAS point reported
I p <0.05 reported by authors
J Mean change from baseline ± SD = -1.13 ± 0.83
K Mean change from baseline ± SD = 1.38 ± 1.30

The Cochrane systematic review (Hoare 2010) and the RCT published after the Cochrane systematic review (Olesch 2010) relating to treatment of the upper limb reported outcomes relevant to optimisation of function.

Table 7.3 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; upper limb; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and occupational therapy	**Occupational therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
GAS score (change from baseline, parental report at 3 months, better indicated by higher values)					
4 studies (Boyd 2004; Lowe 2006; Russo 2007; Wallen 2007)	77	75	-	MD 8.52 higher (4.42 to 12.62 higher)†	HIGH
GAS score (change from baseline, parental report at 4 months, better indicated by higher values)					
1 study (Greaves 2004)	10	10	-	MD 9.21 higher (1.06 to 17.36 higher)†	LOW
GAS score (change from baseline, parental report at 6 months (better indicated by higher values)					
3 studies (Lowe 2006; Russo 2007; Wallen 2007)	62	60	-	MD 5.04 higher (0.75 lower to 10.83 higher)†	MODERATE
GAS T-Score (final score comparison, cycle 1, better indicated by higher values)					
1 study (Olesch 2010)	11[a]	11[b]	-	MD 6.0 higher (2.32 lower to 14.32 higher)*	MODERATE
GAS T-score (final score comparison), cycle 2, better indicated by higher values)					
1 study (Olesch 2010)	11[c]	11[d]	-	MD 7.7 higher (1.16 lower to 16.56 higher)*	MODERATE
GAS T-score (final score comparison, cycle 3, better indicated by higher values)					
1 study (Olesch 2010)	11[8]	11[f]	-	MD 4.9 higher (2.11 lower to 11.91 higher)*	MODERATE
GAS T-score over whole year (better indicated by higher values)					
1 study (Olesch 2010)	11[g]	11[h]	-	MD 7 higher (0.59 to 13.41 higher)*	MODERATE

COPM-P score (change from baseline at 3 months, better indicated by higher values)					
3 studies (Boyd 2004; Lowe 2006; Wallen 2007)	56	53	-	MD 0.77 higher (0.23 to 1.31 higher)†	MODERATE
COPM-P score (change from baseline at 4 months, better indicated by higher values)					
1 study (Greaves 2004)	10	10	-	MD 0.6 higher (0.68 lower to 1.88 higher)†	LOW
COPM-P score (change from baseline at 4 months, cycle 1 change score, better indicated by higher values)					
1 study (Olesch 2010)	11[i]	11[j]	-	MD 0.7 higher (0.32 lower to 1.72 higher)*	MODERATE
COPM-P score (change from baseline, cycle 2, better indicated by higher values)					
1 study (Olesch 2010)	11[k]	11[l]	-	MD 0.9 higher (0.1 to 1.7 higher)*	MODERATE
COPM-P score (change from baseline, cycle 3, better indicated by higher values)					
1 study (Olesch 2010)	11[m]	11[n]	-	MD 1.4 higher (0.35 to 2.45 higher)*	MODERATE
COPM-P score (change from baseline over whole year, better indicated by higher values)					
1 study (Olesch 2010)	11[o]	11[p]	-	MD 0.8 higher (0.04 lower to 1.64 higher)*	MODERATE
COPM-P score (change from baseline at 6 months, better indicated by higher values)					
2 studies (Lowe 2006; Wallen 2007)	41	38	-	MD 0.4 higher (0.3 lower to 1.09 higher)†	MODERATE
PEDI functional skills scale, scaled score (change from baseline) at 3 months (better indicated by higher values)					
3 studies Boyd 2004; Fehlings 2000; Wallen 2007)	49	47	-	MD 0.6 higher (1.44 lower to 2.63 higher)†	LOW
PEDI functional skills scale, scaled score (change from baseline) at 6 months (better indicated by higher values)					
2 studies (Fehlings 200; Wallen 2007)	34	32	-	MD 1.09 higher (1.7 lower to 3.88 higher)†	LOW
PEDI caregiver assistance scale, scaled score (change from baseline) at 3 months (better indicated by higher values)					
1 study (Wallen 2007)	20	17	-	MD 6.3 lower (14.68 lower to 2.08 higher)†	MODERATE
PEDI caregiver assistance scale, scaled score (change from baseline) at 6 months (better indicated by					

higher values)					
1 study (Wallen 2007)	20	17	-	MD 4.4 lower (13.38 lower to 4.58 higher)†	MODERATE
QUEST parent score (change from baseline) at 3 months (better indicated by higher values)					
3 studies (Fehlings 2000; Lowe 2006; Wallen 2007)	42	42	-	MD 9.19 higher (4.84 to 13.54 higher)†	MODERATE
QUEST parent score (change from baseline) at 4 months (better indicated by higher values)					
1 study (Greaves 2004)	10	10	-	MD 4,42 lower (9.98 lower to 1.14 higher)†	LOW
QUEST parent score (change from baseline) at 6 months (better indicated by higher values)					
3 studies (Fehlings 2000; Lowe 2006; Wallen 2007)	42	42	-	MD 2.93 higher (1.58 lower to 7.45 higher)†	LOW
QUEST total score (final score comparison), cycle 1 (better indicated by higher values)					
1 study (Olesch 2010)	11[q]	11[r]	-	MD 5.50 higher (5.37 lower to 16.37 higher)*	MODERATE
QUEST total score (final score comparison), cycle 2 (better indicated by higher values)					
1 study (Olesch 2010)	11[s]	11[t]	-	MD 7.60 higher (2.42 lower to 17.62 higher)*	MODERATE
QUEST total score (final score comparison), cycle 3 (better indicated by higher values)					
1 study (Olesch 2010)	11[u]	11[v]	-	MD 6.70 higher (1.58 lower to 14.98 higher)*	MODERATE

COPM-P Canadian Occupational Performance Measure – Performance, GAS Goal Attainment Scaling, PEDI Paediatric Evaluation of Disability Inventory, QUEST Quality of Upper Extremity Skills Test, SD standard deviation

* Calculated by the NCC-WCH

† Data from Hoare 2010 Cochrane systematic review

a Mean final score ± SD reported as 54.1 ± 9.8

b Mean final score ± SD reported as 48.1 ± 10.1

c Mean final score ± SD reported as 55.0 ± 4.3

d Mean final score ± SD reported as 47.3 ± 11.6

e Mean final score ± SD reported as 54.9 ± 9.5

f Mean final score ± SD reported as 50.0 ± 7.1

g Mean final score ± SD reported as 55.8 ± 6.6

h Mean final score ± SD reported as 48.8 ± 8.6

i Mean change from baseline ± SD = 2.4 ± 1.0

j Mean change from baseline ± SD = 1.7 ± 1.4

k Mean change from baseline ± SD = 2.7 ± 0.9

l Mean change from baseline ± SD = 1.8 ± 1.0

m Mean change from baseline ± SD = 3.0 ± 1.3

n Mean change from baseline ± SD = 1.6 ± 1.2

o Mean change from baseline ± SD = 2.5 ± 1
p Mean change from baseline ± SD = 1.7 ± 0.6
q Mean final score ± SD reported as 76.3 ± 13.2
r Mean final score ± SD reported as 70.8 ± 12.8
s Mean final score ± SD reported as 76.9 ± 10.4
t Mean final score ± SD reported as 69.3 ± 13.4
u Mean final score ± SD reported as 79.6 ± 8.0
v Mean final score ± SD reported as 72.9 ± 11.5

Two of the RCTs relating to treatment of the lower limb reported outcomes relevant to optimisation of function (Kay 2004; Reddihough 2002).

Table 7.4 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; lower limb; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
GMFM-C (crawling and kneeling), GMFM-D (standing), GMFM-E (walking, running and jumping, GMFM version not reported, per cent score mean change at 3 months, better indicated by higher values)					
1 study (Kay 2004)	16 limbs[a]	20 limbs[b]		MD 3.8 higher (0.5 lower to 8.1 higher)*	LOW
GMFM-C (crawling and kneeling), GMFM-D (standing), GMFM-E (walking, running and jumping, GMFM version not reported, per cent score mean change at 6 months, better indicated by higher values)					
1 study (Kay 2004)	16 limbs[c]	20 limbs[d]		MD 1.01 higher (1.13 lower to 3.15 higher)*	LOW
GMFM total score (version not reported, mean change at 3 months, better indicated by higher values)					
1 study (Reddihough 2002)	19[e]	19[f]		MD 1.33 lower (5.12 lower to 2.46 higher)*	LOW
GMFM total score (version not reported, mean change at 6 months, better indicated by higher values)					
1 study (Reddihough 2002)	19[g]	19[h]		MD 0.16 higher (4.37 lower to 4.69 higher)*	LOW
GMFM total score with aids (version not reported), mean change at 3 months, better indicated by higher values)					
1 study (Reddihough 2002)	7[i]	7[j]		MD 3.72 higher (7.56 lower to 15 higher)	LOW
GMFM total score with aids (version not reported), mean change at 6 months, better indicated by higher values)					
1 study (Reddihough 2002)	24[k]	24[l]		MD 7.19 lower (13.64 to 0.74 lower)	LOW
Velocity (m/second, mean change at 3 months, as reported, read from graph, better indicated by higher values)					

1 study (Ackman 2005)	12[m]	13[n]		MD 0.2 higher*	LOW
Velocity (m/second, mean change at 6 months, as reported, read from graph, better indicated by higher values)					
1 study (Ackman 2005)	12[o]	13[p]		MD 0.05 higher*	LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-C Gross Motor Function Measure dimension C, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, SD standard deviation

* Calculated by the NCC-WCH

a Mean change from baseline ± SD = 2.5 ± 7.5

b Mean change from baseline ± SD = -1.3 ± 5.1

c Mean change from baseline ± SD = 2.84 ± 3.33

d Mean change from baseline ± SD = 1.83±3.17

e Mean change from baseline ± SD = 2.70 ± 4.62

f Mean change from baseline ± SD = 4.03 ± 7.05

g Mean change from baseline ± SD = 3.60 ± 7.44

h Mean change from baseline ± SD = 3.44 ± 6.79

i Mean change from baseline ± SD = 6.52 ± 4.95

j Mean change from baseline ± SD = 2.80 ± 14.40

k Mean change from baseline ± SD = 3.94 ± 11.60

l Mean change from baseline ± SD = 11.13 ± 11.18

m Mean change from baseline = 0.15 no SD reported

n Mean change from baseline = -0.05 no SD reported

o Mean change from baseline = 0.1 no SD reported

p Mean change from baseline = 0.05 no SD reported

The Cochrane systematic review (Hoare 2010) relating to treatment of the upper limb reported outcomes relevant to quality of life.

Table 7.5 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; upper limb; quality of life assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and occupational therapy	**Occupational therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
CHQ physical functioning domain score at 3 months (better indicated by higher values)					
3 studies (Boyd 2004; Russo 2007; Wallen 2007)	56	54	-	MD 3.88 lower (15.48 lower to 7.72 higher)*	MODERATE
CHQ physical functioning domain score at 6 months (better indicated by higher values)					
2 studies (Russo 2007; Wallen 2007)	41	39	-	MD 0.28 higher (12.2 lower to 12.75 higher)*	MODERATE
CHQ role emotional domain score at 3 months (better indicated by higher values)					
3 studies	56	54	-	MD 12.98	MODERATE

(Boyd 2004; Russo 2007; Wallen 2007)				higher (1.37 to 24.60 higher)*	
CHQ role emotional domain score at 6 months (better indicated by higher values)					
2 studies (Russo 2007; Wallen 2007)	41	39	-	MD 7.30 higher (7.75 lower to 22.34 higher)	MODERATE
CHQ physical functioning domain score at 3 months (better indicated by higher values)					
3 studies (Boyd 2004; Russo 2007; Wallen 2007)	56	54	-	MD 8.79 higher (3.04 lower to 20.62 higher)	MODERATE
CHQ physical functioning domain score at 6 months (better indicated by higher values)					
2 studies (Russo 2007; Wallen 2007)	41	39	-	MD 2.02 higher (13.98 lower to 18.02 higher)	MODERATE

CHQ Child Health Questionnaire, CI confidence interval, MD mean difference
* Calculated by the NCC-WCH from data in Hoare 2010 Cochrane systematic review

None of the studies relating to treatment of the lower limb reported outcomes relevant to quality of life.

The Cochrane systematic review (Hoare 2010) and the RCT published after the Cochrane systematic review (Olesch 2010) relating to treatment of the upper limb reported outcomes relevant to acceptability and tolerability.

Table 7.6 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; upper limb; treatment acceptability assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and occupational therapy	**Occupational therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
COPM-P score (change from baseline) at 3 months (better indicated by higher values)					
3 studies (Boyd 2004; Lowe 2006; Wallen 2007)	56	63	-	MD 0.81 higher (0.17 to 1.46 higher)†	MODERATE
COPM-S score (change from baseline) at 4 months (better indicated by higher values)					
1 study (Greaves 2004)	10	10	-	MD 0.76 higher (0.92 lower to 2.44 higher)†	MODERATE
COPM-S score (change from baseline) at 6 months (better indicated by higher values)					
2 studies (Lowe 2006; Wallen 2007)	41	38	-	MD 0.35 higher (0.39 lower to 1.08 higher)†	MODERATE
COPM-S score (change from baseline, cycle 1, better indicated by higher values)					
1 study	11	11	-	MD 1.2 higher	MODERATE

(Olesch 2010)				(0.15 to 2.25 higher)*	
COPM-S score (change from baseline, cycle 2, better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 1.2 higher (0.15 to 2.25 higher)*	MODERATE
COPM-S score (change from baseline, cycle 3, better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 1.4 higher (0.35 to 2.45 higher)*	MODERATE
COPM-S score (change from baseline over whole year, better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 0.8 higher (0.11 to 1.49 higher)*	MODERATE

CI confidence interval, COPM-P Canadian Occupational Performance Measure – Performance, COPM-S Canadian Occupational Performance Measure – Satisfaction, MD mean difference
* Calculated by the NCC-WCH
† Data from Hoare 2010 Cochrane systematic review

One of the RCTs relating to treatment of the lower limb reported outcomes relevant to acceptability and tolerability (Reddihough 2002).

Table 7.7 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; lower limb; treatment acceptability assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Botulinum toxin type A and occupational therapy	**Occupational therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
Parental perception 'did the parent feel that the botulinum toxin injection had been of benefit to the child?' at 3 months					
1 study (Reddihough 2002)	-	-	-	-[a]	LOW
Parental perception 'did the parent feel that the botulinum toxin injection had been of benefit to the child?' at 6 months					
1 study (Reddihough 2002)	-	-	-	-[b]	LOW

CI confidence interval
a Statistically significantly more positive responses to the question at 3 months ($\chi2 = 12.0$, $p<0.05$) 95% confidence interval not calculable. 36 of 47 parents rated the benefit as good, very good or excellent. Of 33 parents who noticed a benefit with BoNT treatment, 26 reported the maximum benefit occurring within 6 weeks of the injection. The remainder (7 parents) reported the maximum benefit occurring 6-12 weeks post-injection
b Statistically significantly more positive responses to the question at 6 months ($\chi2 = 7.16$, $p<0.05$) 95% confidence interval not calculable. 35 of 43 parents at 6 months rated the benefit as good, very good or excellent. Of 35 parents who noticed a benefit with BoNT treatment, 23 reported the maximum benefit occurring within 1-2months of the injection, 5 reported maximum benefit at 2 to 3 months and the remainder (7 parents) reported the maximum benefit occurring 3 to 6 months post-injection

The Cochrane systematic review (Hoare 2010) and the RCT published after the Cochrane systematic review (Olesch 2010) relating to treatment of the upper limb reported outcomes relevant to adverse effects.

Table 7.8 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; upper limb; adverse events

Number of studies	Number of participants		Effect		Quality
	Botulinum toxin type A and occupational therapy	Occupational therapy only	Relative (95% CI)	Absolute (95% CI)	
Adverse effects					
1 study (Hoare 2010)	-	-	-	-[a]	LOW
1 study (Olesch 2010)	11	11	-	-[b]	LOW

CI confidence interval
a 95% confidence interval not calculable. No adverse effects were reported in 2 studies (Greaves 2005: Speth 2005). No major adverse events reported in Boyd 2004 although three children were noted to have decreased extension of the index finger that resolved by 6 weeks. There were 31 adverse events reported by 15 participants and no between-group difference in Lowe 2006. There were 29 adverse events reported by 20 participants over six months in Russo 2007. Three of these events involved hospitalisation for seizures in known epileptic children, and one child had 3 hospitalisations for medical reasons. Excessive weakness in the injected limb (reported as a minor adverse effect) was reported in 5 children and was prolonged in 2 children. In the Wallen 2007 RCT, there were 5 adverse events reported in the BoNT and therapy group and four adverse events in the therapy only group
b Three adverse events were reported in BoNT/occupational therapy group of the Olesch 2010 trial - One child with a maculopapular rash (immunological test to consider if response to BoNT inconclusive), one child with weakness in index finger after BoNT administration into adductor pollicis. Both these adverse events resolved spontaneously and the children continued with treatment. One child with prolonged weakness in the finger flexors did not receive any further BoNT injections at this site, but completed the study with respect to other muscle groups

Two of the RCTs relating to treatment of the lower limb reported outcomes relevant to adverse effects (Ackman 2005; Reddihough 2002).

Table 7.9 Evidence profile for botulinum toxin type A and physical therapy compared with physical therapy alone; lower limb; adverse events

Number of studies	Number of participants		Effect		Quality
	Botulinum toxin type A and occupational therapy	Occupational therapy only	Relative (95% CI)	Absolute (95% CI)	
Parental response 'did the child experience some form of complication or side effect from the botulinum toxin?' at 3 months					
1 study (Reddihough 2002)	-	-	-	-[a]	LOW
Parental response 'did the child experience some form of complication or side effect from the botulinum toxin?' at 6 months					

1 study (Reddihough 2002)	-	-	-	-[b]	LOW
Parental response 'did the child experience any pain in their legs following injection?' at 3 months					
1 study (Reddihough 2002)	-	-	-	-[c]	LOW
Parental response 'did the child experience any pain in their legs following injection?' at 6 months					
1 study (Reddihough 2002)	-	-	-	-[d]	LOW
Adverse effects, parental report					
1 study (Ackman 2005)	1/12	0/13	-	-[e]	LOW

CI confidence interval
a 95% confidence interval not calculable.4 of 21 parents agreed that their child had experienced a complication/side effect. Those reported were some level of incontinence, short term muscle weakness and less specific complaints of the child being "out of sorts" and "a little sick and sore"
b 95% confidence interval not calculable.6 of 23 parents at 6 months agreed that their child had experienced a complication/side effect. Those reported were some level of incontinence, short term muscle weakness and less specific complaints of the child being "out of sorts" and "a little sick and sore".
c 95% confidence interval not calculable 7 of 23 parents at 3 months recalled their child having experienced pain
d 95% confidence interval not calculable 4 of 23 parents at 6 months recalled their child having experienced pain
e 95% confidence interval not calculable. One family whose child was in the BoNT and physical therapy group reported that their child fell more often immediately after treatment, although this resolved within 1 to 2 weeks. There were no pressure sores or injuries associated with the casts or their removal in either group and no casts were removed early

None of the studies reported outcomes relevant to reduction of pain in the upper or lower limb.

Botulinum toxin type A every 4 months versus botulinum toxin type A every 12 months

The only study identified for inclusion (Kanovsky 2009) did not report any relevant outcomes pertaining to the upper limb, but it did report reduction of spasticity and optimisation of movement in the lower limb.

Table 7.10 Evidence profile for botulinum toxin type A every 4 months compared with botulinum toxin type A every 12 months; lower limb; tone and joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Botulinum toxin type A and occupational therapy every 4 months	Botulinum toxin type A and occupational therapy every 12 months	Relative (95% CI)	Absolute (95% CI)	
PROM worse leg ankle dorsiflexion (knee extension) at 12 months (mean change from baseline, better indicated by lower values)					
1 study (Kanovsky 2009)	110[a]	104[b]	-	MD 2 higher*	LOW

PROM worse leg ankle dorsiflexion (knee extension) at 28 months (mean change from baseline, better indicated by lower values)					
1 study (Kanovsky 2009)	110[c]	104[d]	-	MD 2.5 higher*	LOW

CI confidence interval, MD mean difference, PROM passive range of movement
* Calculated by the NCC-WCH
a Mean change from baseline = -1
b Mean change from baseline = -3
c Mean change from baseline = -1.5
d Mean change from baseline = -4

The study also reported optimisation of function in the lower limb.

Table 7.11 Evidence profile for botulinum toxin type A every 4 months compared with botulinum toxin type A every 12 months; lower limb; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Botulinum toxin type A every 4 months	Botulinum toxin type A every 12 months	Relative (95% CI)	Absolute (95% CI)	
GMFM overall score (version not reported), median change from baseline at month 28 (better indicated by higher values)					
1 study (Kanovsky 2009)	110[a]	104[b]		2.7 higher	LOW
GMFM goal total score (version not reported), median change from baseline at month 28 (better indicated by higher values)					
1 study (Kanovsky 2009)	11[c]	104[d]		2.4 higher	LOW

CI confidence interval, GMFM Gross Motor Function Measure
a Median change from baseline = 8.6
b Mean change from baseline = 5.9
c Mean change from baseline = 12.3
d Mean change from baseline = 9

The study did not report any relevant outcomes for quality of life or acceptability and tolerability pertaining to the lower limb, but it did report adverse events relating to the lower limb.

Table 7.12 Evidence profile for botulinum toxin type A every 4 months compared with botulinum toxin type A every 12 months; lower limb; adverse events

Number of studies	Number of participants		Effect		Quality
	Botulinum toxin type A every 4 months	Botulinum toxin type A every 12 months	Relative (95% CI)	Absolute (95% CI)	
Proportion of children experiencing adverse effects at month 28					
1 study (Kanovsky	89/110 (81%)	88/104 (85%)	-	3 fewer per 100 (from 14 fewer	LOW

2009)				to 6 more)*	
Proportion of children experiencing infection at month 28					
1 study (Kanovsky 2009)	17/110 (15%)	18/104 (17%)	-	2 fewer per 100 (from 12 fewer to 8 more)*	LOW
Proportion of children experiencing weakness at month 28					
1 study (Kanovsky 2009)	15/110 (14%)	15/104 (14%)	-	1 fewer per 100 (from 10 fewer to 9 more)*	LOW
Proportion of children experiencing increased cough at month 28					
1 study (Kanovsky 2009)	15/110 (14%)	11/104 (11%)	-	3 more per 100 (from 6 fewer to 12 more)*	LOW
Proportion of children experiencing convulsions at month 28					
1 study (Kanovsky 2009)	6/110 (5%)	14/104 (13%)	-	8 fewer per 100 (from 16 fewer to 0 more)*	MODERATE
Proportion of children developing neutralising antibodies at month 28					
1 study (Kanovsky 2009)	4/109 (3.7%)[a]	1/103 (1%)[a]	-	3 more per 100*	LOW
Proportion of children experiencing pain at month 28					
1 study (Kanovsky 2009)	19/110 (17%)	22/104 (21%)	-	4 fewer per 100*	LOW

CI confidence interval
* Calculated by the NCC-WCH
a Neutralising antibodies: Two patients were noted to have neutralising antibodies at entry to the study. A further 5 patients (2%) in total developed neutralising antibodies over the 2 year study period (4 monthly group = 4/110 and annual group = 1/104). In six patients the levels of antibodies were low or low-intermediate. In one patient 4 monthly group) the levels of antibodies were high although no contractures developed during the 28 month follow up and global assessments of efficacy (as subjectively assessed by physician and parent/guardian) indicated improvement

The study did not report any relevant outcomes for reduction of pain in the lower limb.

Electrical stimulation versus palpation

The only study identified for inclusion (Xu 2009) reported reduction of spasticity and optimisation of movement.

Table 7.13 Evidence profile for electrical stimulation compared with palpation as guidance techniques for botulinum toxin type A administration; tone and joint movement assessment

Number of studies	Number of participants		Effect		Quality
	Electrical stimulation and physiotherapy	Palpation and physiotherapy	Relative (95% CI)	Absolute (95% CI)	
MAS score, change from baseline at 3 months (better indicated by lower values)					
1 study (Xu 2009)	23[a]	22[b]	-	MD = 0.5 (0.74 to 0.26) lower*	MODERATE
PROM, change from baseline at 3 months (degrees, better indicated by higher values)					
1 study (Xu 2009)	23[c]	22[d]	-	MD = 3.8 (0.79 to 6.81) higher*	MODERATE

CI confidence interval, MAS Modified Ashworth Scale, MD means difference, PROM passive range of movement
* Calculated by the NCC-WCH
a Mean change ± SD = -1.9 ± 0.3
b Mean change ± SD = -1.4 ± 0.5
c Mean change ± SD = 20.0 ± 5.2
d Mean change ± SD = 16.2 ± 5.1

The study also reported optimisation of movement and function.

Table 7.14 Evidence profile for electrical stimulation compared with palpation as guidance techniques for botulinum toxin type A administration; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Electrical stimulation and physiotherapy	Palpation and physiotherapy	Relative (95% CI)	Absolute (95% CI)	
GMFM-D (standing) and GMFM-E (walking, running and jumping), change from baseline at 3 months (better indicated by higher values)					
1 study (Xu 2009)	23[a]	22[b]	-	MD = 7.3 (5.5 to 9.10) higher*	HIGH
Walking velocity, change from baseline at 3 months (m/second, better indicated by higher values)					
1 study (Xu 2009)	23[c]	22[d]	-	MD = 0.07 (0.04 to 0.10) higher*	HIGH

CI confidence interval, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Mean change ± SD = 8.6 ± 4.0
b Mean change ± SD = 11.3 ± 1.8
c Mean change ± SD = 0.15 ± 0.06
d Mean change ± SD = 0.08 ± 0.04

The study did not report quality of life, acceptability and tolerability, adverse effects or reduction of pain.

Ultrasound versus electrical stimulation

The only study identified for inclusion (Kwon 2010) reported reduction of spasticity.

Table 7.15 Evidence profile for ultrasound compared with electrical stimulation as guidance techniques for botulinum toxin type A administration; tone assessment

Number of studies	Number of participants		Effect		Quality
	Ultrasound	Electrical simulation	Relative (95% CI)	Absolute (95% CI)	
MAS score with knee extended, change from baseline at 3 months (better indicated by lower values)					
1 study (Kwon 2010)	14[a]	16[b]	-	-[c]	LOW
MAS score with knee flexed, change from baseline at 3 months (better indicated by lower values)					
1 study (Kwon 2010)	14[d]	16[e]	-	-[f]	LOW

CI confidence interval, MAS Modified Ashworth Scale
a Pre-treatment median (Range, 25 percentile ,75 percentile) = 3 (2-4, 3,3), Median at 3 months = 3 (1-4,2,3)
b Pre-treatment median (Range, 25 percentile ,75 percentile) = 3 (1-4, 2,3), Median at 3 months = 3 (1-4,2,3)
c The authors report that the difference between the groups was not statistically significant (Mann-Whitney U test)
d Pre-treatment median (Range, 25 percentile ,75 percentile) = 2 (1-4, 2,3), Median at 3 months = 2 (1-3,2,2)
e Pre-treatment median (Range, 25 percentile ,75 percentile) = 2 (1-3, 2,3), Median at 3 months = 1 (1-4,2,2)

The study also reported optimisation of movement and function.

Table 7.16 Evidence profile for ultrasound compared with electrical stimulation as guidance techniques for botulinum toxin type A administration; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Ultrasound	Electrical simulation	Relative (95% CI)	Absolute (95% CI)	
Change in physician's rating scale (speed of gait) at 3 months from baseline (m/second, better indicated by higher values)					
1 study (Kwon 2010)	14[a]	16[b]	-	-[c]	LOW

CI confidence interval
a Pre-treatment median (Range, 25 percentile ,75 percentile) = 0 (0-1, 0,1), Median at 3 months = 1 (0-1, 0,1)
b Pre-treatment median (Range, 25 percentile ,75 percentile) = 0 (0-1, 0,1), Median at 3 months = 0 (0-1, 0,1)
c The authors report that the difference between the groups was not statistically significant (Mann-Whitney U test)

The study did not report quality of life, acceptability and tolerability, adverse effects or reduction of pain.

Evidence statement

Botulinum toxin type A and physical therapy versus physical therapy alone

Regarding reduction of spasticity and optimisation of movement in the upper limb, one RCT provided evidence that compared to baseline there was an improvement in spasticity (MAS scores) in shoulder adductor muscles at 4 months in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but this finding was not statistically significant. (LOW)

Pooled results of two RCTs provided evidence that compared to baseline there was a statistically significant improvement in spasticity in the elbow flexor muscles (MAS scores) at 3 months (MODERATE) and 6 months (LOW) in children and young people who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone.

One RCT provided evidence that compared to baseline there was an improvement in spasticity (MTS scores) in elbow flexor muscles at 4 months in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but this was not statistically significant. (LOW) Another RCT provided evidence that although there were improvements in spasticity (MTS scores) in elbow flexor muscles at 4 and 12 months (after one and three cycles of treatment, respectively) in children who received treatment with BoNT-A and physical therapy compared those who received physical therapy alone, but these findings were not statistically significant. (MODERATE; mean final score comparison across groups) The same RCT provided evidence of a statistically significant improvement in spasticity (MTS scores) in elbow flexor muscles at 8 months (after two cycles of treatment) in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone. (MODERATE; mean final score comparison across groups)

Pooled results of two RCTs provided evidence that compared to baseline there was an improvement in elbow extension PROM at 3 months and a deterioration at 6 months in children and young people who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone, but these findings were not statistically significant. (LOW)

One RCT provided evidence that compared to baseline there was a deterioration in spasticity (MAS scores) in forearm pronator muscles at 3 months (MODERATE) and 6 months (LOW) in children and young people who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but that the differences were not statistically significant. One RCT provided evidence that compared to baseline there was a statistically significant improvement in spasticity (MAS scores) in forearm pronator muscles at 4 months in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone. (LOW) Another RCT provided evidence that compared to baseline there was a deterioration in spasticity (MTS scores) in forearm pronator muscles at 4 months (after one cycle of treatment) in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The same RCT provided evidence that compared to baseline there were improvements in spasticity (MTS scores) in forearm pronator muscles at 8 and 12 months (after two and three cycles of treatment) in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (LOW)

One RCT provided evidence that compared to baseline there was a reduction in supination AROM at 3 months (MODERATE) and 6 months (MODERATE) in children and young people who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but these findings were not statistically significant. Pooled results from two RCTs provided evidence that compared to baseline there was an improvement in forearm supination passive range of movement at 3 months (LOW) and 6 months (LOW) in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but these findings were not statistically significant. (LOW)

Pooled results from two RCTs provided evidence that compared to baseline there was a statistically significant improvement in spasticity in the wrist flexor muscles (MAS scores) at 3 months (MODERATE) and 6 months (LOW) in children and young people who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone. One RCT provided evidence that compared to baseline there was an improvement in spasticity in wrist flexor muscles (MAS and MTS scores) at 4 months in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but this finding was not statistically significant. (LOW) One RCT provided evidence that although there were improvements in spasticity (MTS scores) in wrist flexor muscles at 4 and 8 months (after one and two cycles of treatment) in children who received treatment with BoNT-A and physical therapy compared those who received physical therapy alone, these findings were not statistically significant. (MODERATE; mean final score comparison across groups) However, the same RCT provided evidence of a statistically significant improvement in spasticity (MTS scores) in wrist flexor muscles at 12 months (after three cycles of treatment) in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone. (HIGH; mean final score comparison across groups)

One RCT provided evidence that compared to baseline there was an improvement in wrist extension AROM at 3 months and 6 months in children and young people who received treatment with BoNT-A and physical therapy compared with those who received physical therapy alone, but these findings were not statistically significant. (MODERATE)

One RCT provided evidence that compared to baseline there was an improvement at 3 months and a reduction at 6 months in wrist extension PROM in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone, but these findings were not statistically significant. (LOW)

One RCT provided evidence that compared to baseline there were improvements in palmar thumb abduction PROM at 3 months and 6 months in children who received treatment with BoNT-A and physical therapy compared with those who received physical therapy alone, but these findings were not statistically significant. (MODERATE)

Regarding reduction of spasticity and optimisation of movement in the lower limb, one RCT provided evidence that compared to baseline there was a smaller reduction in plantarflexor spasticity (mean MAS score) at 3 months in children who received treatment with BoNT-A and serial casting as compared to those who received serial casting alone, but this finding was not statistically significant. (LOW) The same RCT provided evidence that compared to baseline there was a smaller reduction in plantarflexor spasticity (mean MAS score) at 6 months in children who received treatment with BoNT-A and serial casting as compared to those who received serial casting alone and that this finding was statistically significant. (LOW)

One RCT provided evidence that compared to baseline there was a smaller reduction in spasticity at the ankle (Ashworth scores) at 3 months in children who received treatment with BoNT-A and casting as compared to those who received placebo and casting, but the statistical significance of this finding could not be determined. (LOW) The same RCT provided evidence that compared to baseline there was a similar reduction in spasticity at the ankle (Ashworth scores) at 6 months in children who received treatment with BoNT-A and casting as compared to those who received placebo and casting, but the statistical significance of this finding could not be determined. (LOW) One RCT provided evidence that compared to baseline there were improvements in active ankle dorsiflexion at 3 and 6 months in children who received treatment with BoNT-A and casting as compared to those who received placebo and casting, but the statistical significance of these findings could not be determined. (LOW) The same RCT provided evidence that compared to baseline there was a reduction in passive ankle dorsiflexion (knee flexed) at 3 months, and an increase at 6 months in children who received treatment with BoNT-A and casting as compared to those who received placebo and casting, but the statistical significance of these findings could not be determined. (LOW) The same RCT provided evidence that compared to baseline there was an improvement in right ankle dorsiflexion (knee extension) PROM at 3 and 6 months in children who received treatment with BoNT-A and casting as compared to those who received placebo and casting but the statistical significance of these findings could not be determined. (LOW)

One RCT provided evidence that compared to baseline there was an increase in passive dorsiflexion at 3 months in children who received treatment with BoNT-A and serial casting as compared to those who received serial casting alone, but this finding was not statistically significant. (LOW) The same RCT provided evidence that compared to baseline there was a reduction in passive dorsiflexion at 6 months in children who received treatment with BoNT-A and serial casting as compared to those who received serial casting alone. One RCT provided evidence that compared to baseline there was a statistically significant increase in passive dorsiflexion of the right ankle (knee extension) at 3 months in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone, (LOW) The same RCT provided evidence that compared to baseline there was an increase in passive dorsiflexion of the right ankle (knee extension) at 6 months in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone, but this finding was not statistically significant, (VERY LOW)The same RCT provided evidence that compared to baseline there was a statistically significant reduction in tone in the left calf and the left adductors (MAS scores) at 6 months in children who received treatment with BoNT-A and physical therapy as compared to those who received physical therapy alone. However, the same RCT reported that compared to baseline there was a statistically significant increase in tone in the right adductors (MAS scores) at 6 months in children who received treatment with BoNT-A and physical therapy as compared to those that received physical therapy alone. (VERY LOW) The same RCT provided evidence that compared to baseline there was a statistically significant improvement in tone (MAS total score) at 3 months in children who received BoNT-A and physical therapy as compared to those who received treatment physical therapy. (MODERATE)

Regarding optimisation of function in the upper limb, pooled results from two RCTs provided evidence that compared to baseline there was a statistically significant improvement in upper limb function (GAS parent reports) at 3 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy only. (HIGH) One RCT provided evidence that compared to baseline there was a statistically significant improvement in upper limb function (GAS parent reports) at 4 months in children who received BoNT-A and physical therapy compared to those who received physical therapy only. (LOW) Pooled results from three RCTs provided evidence that compared to baseline there was an improvement in upper limb function (GAS parent reports) at 6 months between children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy only, but this finding was not statistically significant. (MODERATE) One further RCT provided evidence that there were improvements in upper limb functioning (GAS T-scores) at 4, 8 or 12 months (after one, two or three treatment cycles) in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but these findings were not statistically significant. (MODERATE; mean final score comparison across groups) A further analysis of GAS T-scores over the whole study period of 1 year provided evidence that compared to baseline there was a statistically significant improvement in upper limb functioning (GAS T-scores) in children receiving BoNT and physical therapy compared to those receiving physical therapy alone. (MODERATE; mean final score comparison across groups)

Pooled results from three RCTs provided evidence that compared to baseline there was a statistically significant improvement in upper limb function (COPM-P scores) at 3 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone. (MODERATE) One RCT provided evidence that compared to baseline there was an improvement in upper limb function (COPM-P scores) at 4 months in children who received BoNT-A and physical therapy compared to those who received physical therapy only, but this finding was not statistically significant. (LOW) Pooled results from two RCTs provided evidence that compared to baseline there was an improvement in upper limb function (COPM-P scores) at 6 months in children and young people who received BoNT-A and physical therapy compared to those who received physical therapy only, but this finding was not statistically significant.(MODERATE). One further RCT provided evidence that there were improvements in COPM-P scores at 4, 8 and 12 months, and over the whole study period of 1 year (after one, two and three treatment cycles, respectively) in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but the findings were only statistically significant at 8 and 12 months (MODERATE; mean final score comparison across groups)

Pooled results from three RCTs and from two RCTs provided evidence that compared to baseline there were improvements in upper limb function (COPM-P scores) at 3 and 6 months, respectively, in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy only, but these findings were not statistically significant. (LOW)

One RCT provided evidence that compared to baseline there was a reduction in function (PEDI caregiver assistance scaled scores) at 3 and 6 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy only, but these findings were not statistically significant. (MODERATE)

Pooled results from three RCTs provided evidence that compared to baseline there was a statistically significant improvement in parent-reported QUEST scores at 3 months, (MODERATE) but that improvement at 6 months (LOW) was not statistically significant in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy. One RCT provided evidence that compared to baseline that there was an improvement in parent-reported QUEST scores at 4 months in children who received treatment with BoNT-A and physical therapy compared to those who received physical therapy alone, but this finding was not statistically significant. (LOW) One RCT provided evidence that there were improvements in QUEST scores at 4, 8 and 12 months (after one, two and three treatment cycles, respectively) in children who received treatment with BoNT-A and physical therapy compared to children who received physical therapy alone, but these findings were not statistically significant (MODERATE)

Regarding optimisation of function in the lower limb, one RCT provided evidence that compared to baseline there was an increase in lower limb function (GMFM-C, GMFM-D, and GMFM-E percentage scores) in children and young people who received BoNT-A and serial casting compared to those who received serial casting alone at 3 months or at 6 months, but these findings were not statistically significant. (LOW) One RCT provided evidence that compared to baseline there was a reduction in lower limb function (GMFM total score) at 3 months when children and young people who received treatment with BoNT-A and physical therapy were compared to those who received physical therapy alone, but this finding was not statistically significant. (LOW) The same RCT provided evidence that compared to baseline there was an increase in lower limb function (GMFM total score) at 6 months when children and young people who received treatment with BoNT-A and physical therapy were compared to those who received physical therapy alone, but this finding was not statistically significant. (LOW) The same RCT provided evidence that compared to baseline there was an increase in lower limb function using aids (GMFM total score) at 3 months in children who received treatment with (BoNT-A and casting compared to those who received casting alone, but this finding was not statistically significant. (LOW) The same RCT provided evidence that compared to baseline there was a statistically significant reduction in lower limb function using aids (GMFM total score) at 6 months in children who received treatment with BoNT-A and casting compared to those who received casting alone. (LOW) One RCT provided evidence that compared to baseline there were increases in walking speed (velocity) at 3 and 6 months in children who received BoNT-A and casting compared to those who received serial casting alone, although the statistical significance of these findings could not be determined (LOW)

Regarding acceptability and tolerability of treatment to the upper limb, pooled results from three RCTs provided evidence that compared to baseline there was a reduction in CHQ physical functioning domain scores at 3 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone, but this finding was not statistically significant. (MODERATE) Pooled results from two RCTs provided evidence that compared to baseline there was an increase in CHQ physical functioning domain scores at 6 months (LOW) in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone, but this finding was not statistically significant. (MODERATE)

Pooled results from three RCTs provided evidence that compared to baseline there was an increase in CHQ emotional role domain scores at 3 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone, but this finding was not statistically significant. (MODERATE) Pooled results from two RCTs provided evidence that compared to baseline there was a statistically significant increase in CHQ emotional role domain scores at 6 months (LOW) in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone. (MODERATE)

Pooled results from three RCTs and two RCTs provided evidence that compared to baseline there were increases in CHQ physical role domain scores at 3 and 6 months, respectively, in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone, but these findings were not statistically significant. (MODERATE)

Pooled results from three RCTs provided evidence that compared to baseline there was a statistically significant increase in COPM-S scores at 3 months in children and young people who received BoNT-A and physical therapy as compared to those who received physical therapy alone. (MODERATE) One RCT provided evidence that compared to baseline that there was an improvement in COPM-S scores at 4 months in children who received treatment with BoNT-A and physical therapy compared to children who received physical therapy alone, but this finding was not statistically significant. (MODERATE) Pooled results from two RCTs provided evidence that compared to baseline there was an improvement in COPM-S scores at 6 months in children and young people who received BoNT-A and physical therapy as compared to the physical therapy group only, but this finding was not statistically significant. (MODERATE) One further RCT provided evidence that compared to baseline there were statistically significant improvements in COPM-S scores at 4, 8, and 12 months (after one, two and three treatment cycles) and over the whole study period of 1 year in children who received treatment with BoNT-A and physical therapy compared to children who received physical therapy alone. (MODERATE)

Regarding acceptability and tolerability in the lower limb, in one cross-over RCT a statistically significant number of parents reported benefit of BoNT at both 3 and 6 months post-injection for the treatment of the lower limb; 75.6% of parents at 3 months and 81.4% of parents at 6 months rated the benefit of treatment as good, very good or excellent (LOW) while 78.8% of parents at 3 months and 65.7% of parents at 6 months estimated the maximum effect of the BoNT injection had occurred within 6 weeks of the injection or within 1-2 months of the injection at 3 and 6 months, respectively. (LOW)

Regarding adverse effects reported in studies of the upper limb, four children experienced a serious adverse event requiring hospitalisation after treatment of the upper limb (Russo 2007). One child with epilepsy had two hospital admissions for seizures; three other children had hospital admissions for unspecified medical reasons. Three children with a history of epilepsy were admitted to hospital for seizure management shortly after injection. Grip weakness was reported in four studies (Boyd 2004; Fehlings 2000; Olesch 2010; Russo 2007). Other reports included nausea, vomiting, influenza symptoms, coughing, soreness at the injection site, respiratory infections, headache, fainting episodes (on a hot day), anxiety, depression (past history), alopecia and fatigue. (LOW)

Regarding adverse effects reported in studies of the lower limb, in one cross-over RCT there were 10 reports of adverse affects in total over the 6-month period following BoNT treatment for the lower limb (Reddihough 2002). (LOW) In the same RCT, 30.4% of parents at 3 months and 9.3% of parents at 6 months recalled their child having experienced leg pain following the injection. (LOW) In one RCT there was one report of a child in the BoNT and casting group falling more often immediately after treatment and no reports of adverse effects associated with casts. (LOW)

No evidence was identified for reduction of pain.

Botulinum toxin type A every 4 months versus botulinum toxin type A every 12 months

One RCT involving treatment of the lower limb was identified for inclusion. Regarding reduction of spasticity and optimisation of movement, the RCT provided evidence that compared to baseline there was an increase in ankle dorsiflexion (in the worse-affected leg, knee extension) PROM at 12 or 28 months in children who received 4-monthly BoNT treatment compared to those who received annual BoNT-A treatment, although the statistical significance of these findings could not be determined. (LOW)

Regarding optimisation of function, the RCT provided evidence that compared to baseline there was an increase in GMFM overall scores and GMFM goal total scores at 28 months in children who received 4-monthly BoNT treatment compared to those who received annual BoNT-A treatment, although the statistical significance of these findings could not be determined. (LOW)

No evidence was identified for quality of life or acceptability and tolerability.

Adverse events were reported in 81% of the 4-monthly treatment group and in 85% of the yearly treatment group. (LOW) The RCT provided evidence that fewer children who received 4-monthly BoNT-A treatment compared to those who received annual BoNT-A treatment experienced infection, weakness or pain at 28 months, but these findings were not statistically significant. (LOW) The RCT also provided evidence that fewer children who received 4-monthly BoNT-A treatment compared to those who received annual BoNT-A treatment experienced convulsions at 28 months and that these findings were statistically significant. (MODERATE) The RCT provided evidence that more children who received 4-monthly BoNT-A treatment compared to those who received annual BoNT-A treatment experienced increased cough, but these findings were not statistically significant. (LOW) Neutralising antibodies were present in two children at baseline and developed in a further five children by the end of the 28-month follow up. Four of these children were in the 4-monthly treatment group (not statistically significant). (LOW)

No evidence was identified for reduction of pain.

Electrical stimulation versus palpation

Regarding reduction of spasticity, one RCT provided evidence that compared to baseline there was a statistically significant reduction in spasticity (MAS scores) at 3 months in children who received BoNT-A administered using electrical stimulation-guided injection and physical therapy as compared to children who received BoNT-A administered using injection guided by palpation of the spastic muscle group and physical therapy (MODERATE) The same RCT provided evidence that compared to baseline there was a statistically significant improvement in PROM at 3 months in children who received BoNT-A administered using electrical stimulation-guided injection and physical therapy as compared to children who received BoNT-A administered using injection guided by palpation of the spastic muscle group and physical therapy. (MODERATE)

Regarding optimisation of function, one RCT provided evidence that compared to baseline there was a statistically significant increase in gross motor function (GMFM-D and GMFM-E) and walking velocity at 3 months in children who received BoNT-A administered using electrical stimulation-guided injection and physical therapy as compared to children who received BoNT-A administered using injection guided by palpation of the spastic muscle group and physical therapy. (HIGH)

No evidence was identified for quality of life, acceptability and tolerability, adverse events or reduction of pain.

Ultrasound versus electrical stimulation

Regarding reduction of spasticity, one quasi-randomised controlled trial reported that compared to baseline there was no change in tone with knee extended (MAS scores) at 3 months in children who received BoNT-A administered using ultrasound-guided injection and physical therapy or in those who received BoNT-A administered using electrical stimulation-guided injection and physical therapy, and that this finding was not statistically significant. (LOW) The same study reported that, compared to baseline, there was no reduction in tone with knee flexed (assessed using MAS scores) at 3 months in children who received BoNT-A administered using ultrasound-guided injection and physical therapy, but there was a reduction in tone in those who received BoNT-A administered using electrical stimulation-guided injection and physical therapy; however, the difference between the two treatment groups was not statistically significant. (LOW)

Regarding optimisation of movement and function, one quasi-randomised controlled trial reported that compared to baseline there was an increase in gait speed (assessed using the Physician's Rating Scale) at 3 months in children who received BoNT-A administered using ultrasound-guided injection and physical therapy, but no change in children who received BoNT-A administered using electrical stimulation-guided injection and physical therapy, although the difference between the treatment groups was not statistically significant. (LOW)

No evidence was identified for quality of life, acceptability and tolerability, adverse events or reduction of pain.

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion:

- BoNT-A and physical therapy versus oral antispasmodic medication and physical therapy
- BoNT-A versus BoNT-B.

Health economics

No UK-based economic evaluations of BoNT-A or BoNT-B treatment were identified in the literature search conducted for the guideline. A cost analysis was conducted based on descriptions of BoNT treatment services at Leeds and Great Ormond Street Hospital (see Chapter 11). The GDG agreed that assessment would be performed by a consultant. An NHS reference cost was used for the outpatient visits for the injection as BoNT is a high-cost drug. The reference cost for 2010-11 was £321. There is also a specialist uplift to tariffs for children of 60%, and applying this increases the cost to £514. The reference cost includes all costs related to the procedure, the day-case admission, drug costs, and staff costs. It was assumed that assessment and follow-up would incur additional costs.

The analysis presented a baseline cost for a child or young person having two sets of injections in 1 year with only one follow-up assessment (£2,000 per child or young person). The costs would increase if more repeat injections were given in 1 year, and with the increased likelihood of adverse events.

It is important to consider costs alongside the benefits of treatment. The clinical evidence for this review question was limited and there was no conclusive evidence to show BoNT would increase function or reduce pain, which would be the most useful outcomes for developing an economic analysis. Therefore, the analysis was presented using the NICE cost effectiveness threshold to determine the levels of effectiveness the treatment would need to offer in terms of reduction in pain or discomfort, improvements with self care, improvements performing their usual activities, or conversely prevention of deterioration in self-care or usual activities. Although no cost effectiveness results could be reported for this review question, the analysis presented a framework to allow the GDG to make decisions on when they should consider BoNT injections would be beneficial enough to recommend (further details of this analysis are presented in Chapter 11).

The GDG considered the effectiveness of casting after BoNT treatment as part of the physical therapy review question (see Chapter 4). There was limited clinical evidence of low quality which reported a statistically significant reduction in spasticity in children who received casting immediately after BoNT treatment as opposed to those who received casting 4 weeks after BoNT treatment. However, 50% of children who had casting immediately after injection experienced pain and required a change of cast within 48 hours.

The clinical evidence for serial casting compared to no casting identified that there was no statistically significant difference in walking speed between the two treatment groups. A statistically significant improvement in PROM for ankle dorsiflexion (knee flexed) was reported, but the difference was not significant for ankle dorsiflexion (knee extended).

It is difficult to consider the cost effectiveness of casting in addition to BoNT treatment based on the available clinical evidence. There is considerable uncertainty around its effectiveness compared to no casting. If casting were found to be effective, then the timing of casting would be another consideration with resource implications, whether an additional appointment would be needed for a cast to be performed after BoNT treatment, or if casting performed immediately after BoNT treatment needed to be replaced due to pain. Further research in relation to these issues is needed, and such research should consider resource use.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG believed that the pharmacological activity of BoNT was unlikely to extend beyond 4 months, and for that reason the group was primarily interested in examining outcomes measured within that time interval. Outcomes observed after 4 months were also considered, however, to examine any potential carry-over effect.

The group also felt that AROM was more informative than PROM because AROM can be a reflection of muscle strength (an outcome not described in the literature) and functional ability. A small but measurable improvement in AROM (that is, a change of 5-10 degrees) may have an effect on a child or young person’s ability to control upper limb movement and function. The GDG believed that PROM might have a part to play in the ability of a child or young person to reach for objects effectively and better lower limb posture when standing and walking. However, the group's view was that strength remains key to improved functional ability.

Patient-important outcomes, including estimates of acceptability and tolerability or pain reduction, were prioritised because the invasive nature of BoNT-A treatment may not be acceptable for all children and young people if functional gains are not significant. This can, in turn, lead to a lack of motivation to participate in BoNT-A treatment and associated physical therapy.

GAS scores, which reflect the individual goals of the child or young person, were thought to be more likely to detect a statistically significant effect in this context than other scores and were, therefore, prioritised by the GDG.

There are some adverse effects that particularly pertain to BoNT treatment and a few deaths after treatment have been reported. The GDG was particularly interested in investigating breathing and swallowing difficulties when injections are given in the shoulder or neck muscles. Despite such events being rare, with none reported in the evidence reviewed for the guideline, the GDG felt it important to highlight these potentially life-threatening adverse effects in the recommendations (see below). Great care needs to be taken with any treatment in a child or young person in whom some spasticity is needed to support function because too much weakness (too big an effect of the treatment) would lead to loss of function. Weakness as an adverse event was thus also prioritised by the GDG.

Trade-off between clinical benefits and harms

The GDG took account of the complexities of evidence and interpretation when considering the clinical importance of trial results. It was noted that no statistically significant benefit was observed in relation to various outcomes in many of the studies. Nevertheless, there were several reports of potential significance supporting the effectiveness of BoNT-A in reducing spasticity and achieving patient-important outcomes.

Muscle tone and range of movement

Upper limb

Although results often varied between studies, there was evidence that in the upper limb BoNT-A can reduce spasticity in the elbow and wrist flexor muscles and in the forearm pronators. Most of the trials excluded children and young people with significant contractures. That is, the participants still had a full range of passive movement and correspondingly there was no evidence that PROM improved significantly more when BoNT was administered in addition to physical therapy alone. One of the RCTs included in a Cochrane systematic review and meta-analysis considered for the guideline did examine supination and wrist AROM, but there were no statistically significant differences between the treatment groups at either 3 or 6 months.

Lower limb

The quality of the evidence from the three trials examining BoNT-A for the lower limb was low or very low. One trial reported a greater improvement in plantarflexor tone at 6 months with serial casting when compared to the combination of serial casting and BoNT. One small cross-over study reported improvements in tone in the calf and adductors at 6 months and at 3 months when an total Ashworth score was used, however, there was likely to have been selective reporting of outcomes with these results. The available trials did not, therefore, provide compelling evidence for a reduction in muscle tone with BoNT-A treatment.

Optimisation of function

Upper limb

There was evidence of functional benefit associated with BoNT-A treatment for the upper limb from a meta-analysis of four trials and from two further trials that reported statistically significant improvements in GAS scores at 3 and 4 months (following one cycle of BoNT-A treatment), as expected. However, no carry-over effect was observed at 6 months when the pharmacological effect of the toxin would have ceased. Improvement with addition of BoNT-A treatment was also observed in one RCT at 1 year (following three cycles of treatment with BoNT-A) compared to physical therapy alone. A meta-analysis of three trials reported a statistically significant improvement (compared to physical therapy alone) in COPM-P scores at 3 months, and one trial reported this benefit at 8 and 12 months (following two and three cycles of treatment, respectively). There were no statistically significant differences between the treatment groups in a meta-analysis or one further trial that reported PEDI scores, although a meta-analysis of QUEST scores showed a statistically significant improvement with BoNT-A treatment at 3 months only.

Lower limb

The evidence for the lower limb was of low quality and was based on GMFM scores and walking speed. There was little evidence from two trials of improved functioning (higher GMFM scores) when BoNT-A was administered in addition to physical therapy or serial casting. The GDG believed that the varied approaches to reporting of GMFM scores (for example, varied sub-scores) and the sensitivity of this assessment tool may account for the lack of positive benefit identified. It was unclear from another RCT if the reported improvement in walking speed amounted to clinically important effects for children and young people.

Quality of life

There was little evidence that BoNT-A injections had a significant effect on quality of life. In the upper limb, there was evidence for a possible improvement in the CHQ emotional role, but no improvements were seen for the other dimensions of the assessment tools that were examined. The only supportive evidence for benefit from BoNT-A treatment of the lower limb came from a single cross-over RCT in which parental perception of benefit was reported.

Acceptability and tolerability

Upper limb

There was moderate quality evidence of improved acceptability and tolerability associated with BoNT-A treatment for the upper limb measured using COPM-S scores. This was from a meta-analysis of three trials (at 3 months, although no carry-over effect was observed at 4 months or at 6 months, by which time the pharmacological effect of the toxin would have ceased). Another trial reported a statistically significant improvement in GAS scores at 4, 8 and 12 months and 1 year (following one, two and three cycles of BoNT-A treatment, respectively), These findings provided the most consistent evidence of benefit of additional BoNT-A treatment of all the outcomes examined in the guideline review, and they suggest that sustained improvement requires repeated cycles of a programme combining BoNT-A injections and physical therapy.

Lower limb

In one RCT examining the lower limb, parents felt that BoNT-A was of benefit at 3 and 6 months after the injection. No other evidence was identified for inclusion.

Adverse effects

Four serious adverse events (requiring hospitalisation) were reported in one upper limb RCT within the Cochrane systematic review and meta-analysis considered for the guideline. These all occurred in children and young people known to have co-existing medical conditions. Severe adverse events of concern, but not reported in the evidence reviewed, included swallowing and breathing difficulties following injection around the shoulder, neck and thorax. Other reported adverse effects included short-term muscle weakness and less specific complaints.

In the lower limb, adverse events were reported in two studies. These included pain after the BoNT-A injection, increased frequency of falls, incontinence, short-term muscle weakness and other less specific complaints. The GDG felt that these side effects were important to note when seeking consent for the procedure, but that they are infrequently reported and usually short lived.

Botulinum toxin type A versus botulinum toxin type B

No evidence was identified for inclusion in relation to the comparative effectiveness of BoNT-A and BoNT-B. In the absence of head-to-head trials of BoNT-A versus BoNT-B (nor even trials of BoNT-B versus placebo or usual care) the GDG felt unable to make recommendations regarding the use of BoNT-B.

Location of injection site

There was evidence from one small RCT of a small reduction in spasticity and an improvement in gross motor function in children and young people in whom BoNT-A injections were guided using electrical muscle stimulation as compared to children and young people in whom the injections were guided by palpation of the spastic muscle group. The GDG noted, however, that no was evidence reported regarding acceptability or tolerability of the procedure. In addition, there was evidence from one quasi-randomised controlled trial of a statistically significant improvement in walking speed in children and young people whose BoNT-A injections were guided using ultrasound as compared to those whose injections were guided using electrical muscle stimulation. Again, no evidence was reported for acceptability or tolerability of the procedure. In addition to the modest benefits reported, the GDG felt that improvements in injection-site identification with use of ultrasound might help to reduce the risk of intravascular injection of BoNT-A with consequent adverse effects.

Summary

Despite the difficulty of interpreting the evidence, the GDG felt that, on balance and taking account of their clinical experience, the positive effects of BoNT-A were likely to outweigh the possible side effects for certain clinical indications and, therefore, it was appropriate to recommend BoNT-A provided that careful consideration be given to patient selection.

The GDG considered that children and young people who were particularly likely to benefit from BoNT-A treatment would be those in whom focal spasticity was causing a particular problem in relation to fine motor function in the upper limb or was impeding gross motor function in the lower limb. The group also concluded that the alleviation of focal spasticity through BoNT-A treatment could potentially assist in the application of other interventions, including physical therapy and the use of orthoses (for example, injecting BoNT-A can improve the tolerability of an AFO by reducing tone, thus enabling better positioning of the limb in the orthosis). The GDG was aware that none of the available trials provided evidence that BoNT-A treatment could alleviate the pain associated with spasticity. Nevertheless, the GDG believed, based on their clinical experience, that a trial of BoNT-A should be considered where focal spasticity was associated with significant pain, discomfort or abnormal posture, especially if this was disturbing sleep. The GDG noted that pain is also a common clinical indication for the use of oral drugs. The group concluded that it would be difficult to give precise guidance on which pharmacological interventions (BoNT-A or oral drug treatment) would be preferred in an individual child or young person because, for example, more than one indication might lead to a decision to use a particular form of drug treatment. In some children and young people the restrictions of movement and abnormal postures associated with spasticity can compromise care and lead to difficulties with skin hygiene. The group agreed that in selected children and young people BoNT-A treatment might alleviate these difficulties. The group also noted that postural difficulties associated with spasticity are sometimes a source of distress and embarrassment to children and young people, and in such cases alleviation of these cosmetic concerns could be an indication for BoNT-A treatment. The GDG believed that BoNT-A injections could assist in the treatment of rapid-onset spasticity that causes discomfort, abnormal postures, and difficulty with positioning following an acquired non-progressive brain injury. Finally, the GDG noted that a trial of BoNT-A treatment might be appropriate for children and young people experiencing difficulties with pain, function and posture due to focal dystonia.

In contrast, the GDG considered that children and young people in certain clinical scenarios were less likely to be suitable for treatment with BoNT-A. The group recommended that caution should be exercised when considering BoNT-A in those with contractures because the drug may alleviate spasticity, but the effect on range of movement might be limited in such children and young people (although, as noted previously, BoNT-A may still have a role by facilitating other interventions to better effect muscle length, for example, serial casting or tolerance of orthoses). Likewise the effect of BoNT-A might be limited in those with bony deformity. The group concluded that, if a deformity was established and negatively affecting gait and posture, then it would be unlikely to improve with BoNT-A injections. Careful assessment of a child or young person’s musculoskeletal system, as well as their gait, would be essential in determining the degree of bony deformity. Caution should be considered when injecting more than one muscle group for the first time in children and young people as underlying muscle weakness might be unmasked. Careful assessment of selective muscle control and strength should be made to establish whether the child or young person is able to maintain antigravity postures once spasticity has been eliminated.

In all cases, the GDG acknowledged that, based on their clinical experience and the trials in the guideline review, the line between positive and negative effects with BoNT-A treatment is very fine and careful consideration of all influencing variables is essential. The group also acknowledged that the possible adverse effects arising from incorrect administration were serious. For example, if the drug is injected into the wrong muscle then function may deteriorate; if the wrong dose is given or the drug is injected intravascularly then serious life-threatening side effects might occur. The group also noted that effectiveness could only be assured if the child or young person was receiving an appropriately adapted programme of physical therapy. In short, the GDG considered that the key components of a successful BoNT-A treatment programme were choosing an appropriate child or young person, choosing an appropriate muscle, accurate placement of the injection, and choosing an appropriate form of concomitant physical therapy.

With these issues in mind, the GDG concluded that the decision to treat with, and the administration of, BoNT-A should be performed by a team with experience in child neurology and musculoskeletal anatomy, and informed by a careful assessment of the contributions of muscle tone, muscle strength, and muscle shortening to the motor problem. Healthcare professionals with such expertise would be skilled enough to identify children and young people who are likely to benefit from BoNT-A treatment, and they would be to able minimise the risk of potential side effects through accurate placement of injections. Their assessments would provide the information needed to judge whether BoNT-A treatment is an appropriate intervention for the individual child or young person, to ensure accurate injection of the drug, to avoid unnecessary adverse effects, and to provide a baseline against which to assess the response to treatment. The involvement of a physiotherapist or occupational therapist was considered to be particularly important to the understanding of how BoNT-A treatment fits into the child or young person's overall therapeutic programme and developmental trajectory. The GDG also recommended (based on the evidence and their clinical consensus) that ultrasound and muscle stimulation should be considered to further facilitate accurate injection.

The GDG agreed that it was important for the effects of injections to be carefully assessed, and this would be best carried out during the peak pharmacological effect at 6-12 weeks after the injection. The group concluded that a satisfactory response would be judged according to whether or not the intended goals of treatment had been achieved. In light of the variable assessment techniques and their interpretations the GDG felt the same clinician who had conducted the initial (pre-injection) assessment should perform the reassessment. However, the group appreciated that this would not always be possible due to service constraints and they advocated careful documentation of assessment findings to allow comparison where possible.

If the response to treatment is poor then careful consideration should be given to possible explanations. An unsatisfactory response might be due to poor muscle identification, insufficient dose, misinterpretation of the initial assessment, or poor adherence to adjunctive treatments, such as physical therapy or the use of orthoses. Careful reassessment and identification of the root cause would be important and careful goal planning for future BoNT-A treatment would be essential to ensure any repeat injections would be likely to benefit the child or young person.

Frequency of injections

With regard to frequency of injections, the evidence identified for inclusion in the guideline review was limited to two studies. Although the studies demonstrated a statistically significant improvement in upper limb tone after 4-monthly BoNT-A injections and occupational therapy compared to occupational therapy alone, the effect did not continue after the next treatment cycle at 12 months. A 6-monthly injection cycle showed a statistically significant improvement across a number of measures at 6 months and 12 months. Neither treatment group reported serious side effects related to BoNT-A treatment. In the lower limb studies neither 4-monthly nor 12-monthly treatment cycles resulted in a statistically significant improvement in the outcome measures evaluated, and side effect frequency was similar for both treatment groups. However, the identification of neutralising antibodies in four participants in the 4-monthly injection cycle group might be worth consideration when planning treatment cycles and care pathways for BoNT-A services.

In the GDG's experience, careful reassessment after injections is essential regarding decision-making for ongoing BoNT-A treatment. The evidence did not give rise to strong recommendations on whether to re-inject at 4, 6, or 12 months, however, the risk of developing neutralising antibodies was thought likely to be higher with earlier and more frequent injections. Conversely, if the gap between reassessment and injections were 12 months, the opportunity for maintaining range of movement and improving function might be diminished or lost. In the absence of clear evidence, the GDG made a recommendation that was informed by the pharmacological half-life of the drug (which suggests that there will no longer be a clinically important effect after 6 months after the injection). The recommendation also reflects the group's clinical experience that the response would vary between individuals, and their consensus view that if the response were good and continued to provide benefit for the child or young person then repeat injections should not be given, thus reducing the risk of side effects. The time frames given in the recommendation reflect the group's experience of variation in response times in clinical practice.

Single versus multi-level injections

The GDG recognised the potential benefits of injection into more than one muscle, but felt this approach would be appropriate only if a clear goal was identified. The group also highlighted the importance of not exceeding the maximum dose and of the child or young person and their parents or carers understanding the possible side effects of BoNT-A treatment.

Information for children and young people and their parents and carers

The GDG considered that, given the invasive nature of BoNT-A treatment, it was important to provide detailed information for children and young people and their parents and carers before undertaking treatment. This information should include the risks and benefits of the treatment (for example, the likelihood of goals being attained and the possible adverse effects), as well as practical information about what the treatment entails in terms of the frequency of hospital visits and subsequent injections, whether analgesia, anaesthesia or sedation will be used, and details of any other adjunctive treatments. For safety reasons the group also concluded that children and young people and their parents or carers should be informed of serious side effects, how to recognise them, and what action to take should such complications occur.

Trade-off between net health benefits and resource use

With regard to the upper limb, the alternatives to BoNT-A treatment in children and young people with upper arm spasticity are continuation of physical therapy and intermittent use of casting and splinting. The use of BoNT-A treatment does not necessarily diminish the need for physical therapy. The studies included in the guideline review provided an accompanying programme of tailored physical therapy that might have been more than the child or young person received before the study. The ideal situation would be where the child or young person gained significant long-term functional benefit to diminish the need for physical therapy or assistance with tasks of daily living (for example, by allowing them to gain greater independence).

Health benefits were identified in only two areas: reducing spasticity for elbow and wrist flexors and improving function as measured by GAS scores. The reduction in spasticity for elbow and wrist flexors lasted beyond the pharmacological activity for BoNT-A when combined with physical therapy however this combined approach has resource implications. The reported functional improvements were noted only at the 3-month stage and did not continue to 6 months. This may mean that regular reinjection with BoNT-A every 3-4 months combined with physical therapy would be beneficial. However, the incidence of adverse effects should be considered carefully as grip weakness was often reported in the studies included in the guideline review, and this might play an important role in increasing disability.

With regard to the lower limb, health benefits were identified in only two areas: acceptability and tolerability as reported by parents and spasticity reduction in the left calf and adductors. Both these areas were significantly improved at the 6-month stage, which is beyond the range of pharmacological activity for BoNT-A. Both BoNT-A combined with physical therapy and physical therapy alone demonstrated statistically significant improvements in function at 6 months, which may indicate the value of targeted physical therapy with or without BoNT-A to improve a child or young person's function. The GDG felt that the reported reduction in spasticity which is also observed in clinical practice might have an impact on improving a child or young person's activity levels and participation which was not recognised in the evidence reviewed for the guideline.

In summary, although BoNT-A may not result in statistically significant improvements in function as a treatment itself, it can alleviate spasticity and when used alongside other treatments it might increase the benefits. The GDG considered that patient selection is key to the effectiveness of BoNT-A treatment and, therefore, in appropriately selected children and young people BoNT-A would be considered to be a cost effective treatment. Moreover, the GDG noted that BoNT-A is already used in clinical practice and the absence of unequivocal evidence of cost effectiveness is not sufficient to direct a change in practice away from the use of this treatment.

Quality of evidence

The GDG recognised that the available evidence regarding the use of BoNT-A in children and young people with spasticity was of low or moderate quality and, in many respects, complex to interpret from a clinical perspective. There was much variation in the patients studied, the goals of treatment, the mode of BoNT-A administration, and especially in the specific outcomes investigated. Inevitably, the outcomes varied considerably between trials.

Assessors (and in one lower limb placebo-controlled study, parents) were blinded to treatment allocation for some outcomes, but not all of them. Absence of blinding introduced a significant possibility of bias, particularly in those outcomes with a strong subjective component.

Eight trials were available to inform the review on upper limb treatment. However, only three of the trials involved more than 40 participants. The studies of BoNT-A treatment for upper limb spasticity included children and young people with unilateral spasticity, although other patterns were sometimes included. For use of BoNT-A in lower limb spasticity five trials were available to inform the guideline review, all of which had limitations. All but one of the trials involved fewer than 60 participants. The predominant characteristic of all the study participants was bilateral spasticity affecting the arms (approximately 88%), although two studies also included unilateral spasticity affecting the arms (8%) and two included bilateral spasticity affecting the arms and the legs (<1%). The GDG was aware that variation in response might well be observed in such diverse groups. The effectiveness of BoNT-A treatment might well vary in different muscle groups, and depending on the intended goal of treatment. Such individual variation might not be recognised in groups of children and young people with differing degrees of spasticity and patterns of involvement.

In each of the trials involving treatment for the upper limb BoNT-A was administered by multilevel injections into various muscle groups during a single therapeutic session. The GDG was concerned that if BoNT-A was administered into relatively mildly affected muscle groups it might not be possible to detect a measurable reduction in spasticity, and this might not reflect any inherent lack of effectiveness for the muscle group concerned. It was, therefore, thought to be important to be cautious in interpreting negative results for specific treatment sites.

The GDG noted that there was variation between trials in the dilution of BoNT-A and in the maximum dose administered. In some trials the site of administration into the muscle was chosen based on clinical judgement, whereas in others electrical stimulation or electromyography was additionally employed. There was variation with regard to the nature, intensity and duration of physical therapy provided in both the treatment and comparison groups.

The included trials reported a very varied range of outcome measures, including measures of spasticity, AROM and PROM, and a range of measures of function. The sensitivity of the various outcome measures in detecting a clinically important response might vary, and their relevance to individual therapeutic goals would differ. The GDG considered that this also rendered interpretation of the trial results somewhat complex.

Evidence for the effectiveness of repeated injections of BoNT-A was of low quality. One RCT compared injection 4-monthly injections with annual injections for 2 years. The main outcome prioritised for this part of the guideline review was adverse effects, which were reported in 81% and 85% of participants, respectively. These figures were felt by the GDG to be very high when compared to clinical experience in the UK, and thus were not felt to provide a reason for not recommending repeated injections where clinical circumstances indicated they may be appropriate (for example, if the problem that prompted treatment returned after the initial effect of BoNT-A had worn off, or where new treatment goals were identified).

Other considerations

Need for analgesia, anaesthesia or sedation

BoNT-A treatment may cause discomfort or pain and so consideration should be given to using topical or systemic analgesia. Children and young people may also be anxious or frightened and so consideration should be given to the possible need for sedation both to prevent distress and to facilitate accurate injection placement. In some cases general anaesthesia might be preferable to sedation. Where sedation is used 'Sedation in children and young people' (NICE clinical guideline 112) provides guidance relevant to the age group covered by this guideline, although it contains no guidance specific to children and young people with spasticity.

Need for orthoses or serial casting

The GDG noted that the use of orthoses following BoNT-A treatment may be helpful to enhance stretching of the temporarily weakened muscle and to enable the child or young person to practice functional skills. The decision about whether to use an orthosis would need to be made on an individual basis as the need may not always be apparent until after the treatment has been given. If an orthosis is needed then timely access to orthotic services should be ensured to reduce the likelihood of delays that could result in the orthosis being poorly tolerated (see Chapter 5).If the use of an orthosis is indicated, but limited PROM would make this difficult, the GDG agreed that it would be appropriate to consider serial casting to stretch the muscle. To improve the child or young person's ability to tolerate the cast, and to improve muscle stretching, the GDG recommended delaying casting until 2-4 weeks after the BoNT-A injection (see Chapter 4).

Epilepsy

Many children and young people with cerebral palsy and acquired brain injuries have co-existing epilepsy, although this varies in severity. Although the evidence identified for inclusion did not suggest an adverse effect on epilepsy control with BoNT-A treatment, the SPCs for BoNT-A highlight undesirable effects reported in controlled clinical trials. These include new-onset or recurrent seizures, typically reported in patients predisposed such events. The SPCs also state that the exact relationship between seizures and BoNT-A injection has not been established, but that the reported events occurred predominantly in children and young people with cerebral palsy who were undergoing treatment for spasticity.

Respiratory disorders (including apnoea, airway obstruction and chronic aspiration)

The GDG was aware that BoNT can spread to muscles adjacent to the injection site, and so there is an increased risk of swallowing and breathing difficulties if it is injected into muscles around the shoulders and neck. The GDG was also aware that BoNT can spread from distant sites, such as the legs, and so if a child or young person already has disordered breathing and swallowing, a further small reduction in these functions might precipitate respiratory failure or aspiration and, therefore, care should be taken whichever muscle BoNT is injected into. Careful explanation of BoNT-A side effects (in particular, respiratory compromise) should, therefore, be given to the child or young person and their parents or carers before seeking consent for the procedure. Advice about management should such an event occur should also be given.

Feeding difficulties (including enteral tube feeding)

Careful consideration of adverse effects of BoNT injections should be given to patients with pre-existing swallowing difficulties (see above).

Cognitive and learning ability

The GDG noted that consideration should be given to administration techniques used for children and young people with impaired cognition and those of a young age or learning ability. Methods to reduce stress and improve tolerance should be used, and this might include the use of topical anaesthesia with additional sedation, systemic analgesia or anaesthesia for children and young people who are unable or unlikely to cooperate (see above).

Allergies

An allergic response may cause serious harm to the child or young person and repeated injections should not be given when allergies to BoNT-A have been identified.

Aminoglycosides

The SPCs for BoNT-A report that the effects of the drug may be enhanced by other drugs that affect neuromuscular function, including aminoglycoside antibiotics. The SPCs advise that such drugs should be used with caution in patients treated with BoNT-A. The GDG noted this increased risk of weakness in the muscles involved in breathing and swallowing and reflected the need for caution in the recommendations.

Bleeding disorders

Due to the invasive nature of BoNT-A injections, the GDG highlighted the need to take great care must be taken if the child or young person is known to suffer from a bleeding disorder, for example, due to anticoagulant therapy.

Generalised spasticity

As BoNT-A injections are considered to be a treatment for focal spasticity, children and young people with generalised spasticity might not benefit from their use. The GDG highlighted the need for caution when injecting single over-active muscle groups as the antagonist muscle group may be allowed to dominate and cause further abnormal posturing.

Recommendations

Number	Recommendation
	Botulinum toxin type A
	General principles
65	Consider botulinum toxin type 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.
66	Consider botulinum toxin type 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.
67	Consider botulinum toxin type A[§§§] treatment after an acquired non-progressive brain injury if rapid-onset spasticity is causing postural or functional difficulties.
68	Consider a trial of botulinum toxin type A[****] treatment in children and young people with spasticity in whom focal dystonia is causing serious problems, such as

[§§§] At the time of publication (June 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. Where appropriate, informed consent should be obtained and documented.

Number	Recommendation
	postural or functional difficulties or pain.
69	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.

70	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 34).

71	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.

72	When considering botulinum toxin type A treatment, provide the child or young person and their parents or carers with 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
	• important adverse effects (see recommendation 74).

73	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

74	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

**** At the time of publication (June 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 often used in the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

Number	Recommendation
	the treatment and • that if these complications occur the child or young person should return to hospital immediately.
75	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).
76	Consider ultrasound or electrical muscle stimulation to guide the injection of botulinum toxin type A.
77	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.
78	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.
79	If the use of 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.
80	Ensure that children and young people who receive treatment with botulinum toxin type A are offered timely access to orthotic services.
	Continuing assessment
81	Perform a careful 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.
82	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.

Number	Research recommendation
15	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? **Why this is important** The GDG's recommendation to consider offering botulinum toxin type A to children and young people with focal spasticity of an upper or lower limb reflected available evidence relating to the safety and effectiveness of botulinum toxin type A. In making their recommendations, the GDG emphasised the importance of

establishing individualised goals that justify the use of this potentially harmful toxin to treat spasticity. The cost of the procedure combined with the risk of side effects means that clear treatment goals that will positively influence the child or young person's life should be identified before offering this treatment. The evidence reviewed for the guideline provided limited support for botulinum toxin type A in terms of achieving clinically important goals (including those related to function), and this discouraged the GDG from making a strong recommendation to offer treatment with botulinum toxin type A to all children and young people who are at GMFCS level I, II or III. Further research is needed to evaluate the effectiveness of botulinum toxin type A in comparison with other treatment options, particularly when used over long time periods (for example, 10 years) and involving repeat injections, in this population of children and young people. Outcomes relating to improvements in gross motor function and participation in activities, and the psychological impacts of these factors, should be evaluated as part of the research.

16	What is the clinical and cost effectiveness of treatment with BoNT-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?
17	What is the clinical and cost effectiveness of botulinum toxin type A for reducing muscle pain?
18	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?

8 Intrathecal baclofen

Introduction

For many children and young people with severe spasticity, management options such as physical therapy and oral drug treatment may not prove adequate to alleviate their difficulties. In such circumstances treatment using CITB may be a useful treatment strategy.

A natural inhibitory neurotransmitter known as GABA is present in the nervous system, primarily in laminae 1 to 3 of the spinal cord dorsal horn. Baclofen is a GABA agonist (see Chapter 6). Because baclofen crosses the blood–brain barrier poorly oral administration cannot readily achieve therapeutic concentration in the cerebrospinal fluid (CSF). However, administration of ITB using doses in the order of one-hundredth of those required by the oral route may reduce spasticity while reducing the risk of dose-related adverse effects. ITB is infused continuously using a programmable pump implanted in a subcutaneous or subfascial pocket in the abdominal wall. The pump delivers baclofen via a catheter inserted into the intrathecal space. Before proceeding with pump implantation it is common practice to carry out ITB testing to assess the short-term response to ITB administration.

No related NICE guidance was identified for this review question.

Review question

In children and young people with spasticity due to a non-progressive brain disorder does ITB testing help to identify those likely to benefit from CITB?

In children and young people with spasticity due to a non-progressive brain disorder what are the benefits and risks of CITB?

Description of included studies

Eight studies reported in 10 publications were identified for inclusion across the two review questions considered in this chapter (Awaad 2003; Gilmartin 2000; Hoving 2007; Hoving 2009a; Hoving 2009b; Krach 2004; Motta 2008; Ramstad 2010; Senaran 2007; Shilt 2008).

ITB testing versus placebo was evaluated in two cross-over RCTs (Gilmartin 2000; Hoving 2007). In the first study (Gilmartin 2000), the participants were aged 4-31.3 years (median age 11.2 years) with paraplegia, diplegia or quadriplegia. In the second study (Hoving 2007), the participants were children and young people aged 7-16 years with cerebral palsy; a prospective case series (Hoving 2009b) reported follow-up data for this study. A further prospective case series which reported outcomes for people aged 4-32 years (mean age 13.69 years) with cerebral palsy who had received ITB testing was identified for inclusion (Awaad 2003).

CITB treatment was evaluated in seven studies reported in nine publications (Awaad 2003; Gilmartin 2000; Hoving 2009a; Hoving 2009b; Krach 2004; Motta 2008; Ramstad 2010; Senaran 2007; Shilt 2008). One of these studies was a parallel RCT that evaluated CITB treatment versus conventional care (Hoving 2009a) in the children and young people involved in one of the ITB testing RCTs (Hoving 2007); the prospective case series (Hoving 2009b) reported further follow-up data for this study. A prospective case series was conducted as a follow-up phase to the other ITB testing RCT (Gilmartin 2000), and a further period of follow-up was reported in a second prospective case series (Krach 2004). The other prospective case series which had reported outcomes after ITB testing (Awaad 2003) was also identified for inclusion. Two case-control studies (Senaran 2007; Shilt 2008) and two other prospective case series were also identified for inclusion (Motta 2008; Ramstad 2010).

All of these studies involved children and young people with cerebral palsy (ages ranges 5-18 years, 3.4-16.7 years, 2 years 5 months to 16 years 6 months, and 30-86 months, respectively).

Evidence profiles

Intrathecal baclofen testing

Both cross-over RCTs (Gilmartin 2000; Hoving 2007) and one prospective case series (Hoving 2009b) evaluated reduction of spasticity in the lower limb.

Table 8.1 Evidence profile for intrathecal baclofen testing follow up and compared with placebo; lower limb; tone assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Intrathecal baclofen testing	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ashworth scores 2, 4, and 6 hours after start of test treatment (better indicated by lower values)					
1 study (Hoving 2007)	17[a]	17[a]	-[b]	-[b]	VERY LOW
Ashworth scores 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009b)	17[c]	-	-[b]	-[b]	VERY LOW
Ashworth scores when receiving test treatment with baclofen 50 µg dose (better indicated by lower values)					
1 study (Gilmartin 2000)	51[d]	51[d]	-	-[e]	LOW
Ashworth scores when receiving test treatment with baclofen 75 µg dose					
1 study (Gilmartin 2000)	10[f]	-	-[b]	-[b]	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin 2000)	42[g]	-	-[e]	-[e]	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40[h]	-	-[e]	-[e]	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33[i]	-	-[e]	-[e]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation, SE standard error

a After intrathecal baclofen administration the Ashworth scores, significantly decreased in comparison with baseline for all muscle groups ($0.001 \le p \le 0.040$), except for the left hip flexors 2 hours ($p=0.080$). Ashworth scores after placebo did not change significantly in any muscle group at any test point ($0.083 \le p \le 1.000$) (MODERATE).

b No statistical comparison was given across groups
c At 12 months after CITB pump implantation (Hoving 2009b). The Ashworth score decreased significantly in 9/14 lower-extremity muscle groups (0.002 ≤ p ≤ 0.046).
d Pre-post treatment data
e When receiving 50µg baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to when they received placebo (mean, SD; SE; range) (n=51): baclofen: 2.14 (0.85); 0.12 (1.00 to 4.75) versus placebo: 3.11 (0.69); 0.14 (1.75 to 5.00); p<0.001).
f When receiving 75 µg baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline (baclofen: 2.04 (0.67); 0.21 (1.37 to 3.50) versus baseline: 3.31 (0.60);0.19 (2.00 to 4.00); p<0.001).
g When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 6 months (n=42): 2.33 (0.64); (1.0 to 3.8)
h When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 12 months (n=40): 2.15 (0.60); (1.1 to 3.3);
i When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 24 months (n=33): 2.21 (0.75); (1.0 to 3.5)

One of the cross-over RCTs (Gilmartin 2000) evaluated reduction of spasticity in the upper limb.

Table 8.2 Evidence profile for intrathecal baclofen testing follow up; upper limb; tone assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Intrathecal baclofen testing	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ashworth scores when receiving test treatment with baclofen 50 µg dose (better indicated by lower values)					
1 study (Gilmartin 2000)	51[a]	-	-[b]	-[b]	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin 2000)	42[c]	-	-[b]	-[b]	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40[d]	-	-[b]	-[b]	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33[e]	-	-[b]	-[b]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen
a Pre-post treatment data. Ashworth scores are not reported for the placebo phase.
b No statistical comparison was given across groups
c When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 6 months after implantation (n=41): 1.80 (0.72); (1.0 to 3.8)
d When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 12 months after implantation(n=40): 1.73 (0.66); (1.0 to 4.1)
e When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 24 months after implantation(n=32): 1.72 (0.69); (1.0 to 3.1)

One of the prospective case series (Awaad 2003) evaluated reduction of spasticity in the upper and lower limbs combined.

Table 8.3 Evidence profile for intrathecal baclofen testing follow up; upper and lower limb; tone assessment

Number of studies	Number of participants		Effect		Quality
	Intrathecal baclofen testing	Placebo	Relative (95% CI)	Absolute (95% CI)	
Ashworth scores when receiving test treatment with baclofen 50 μg dose (better indicated by lower values)					
1 study (Awaad 2003)	28[a]	-	-[b]	-[b]	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Awaad 2003)	-[c]	-	-[b]	-[b]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation

a After intrathecal baclofen testing the Ashworth scores significantly decreased in comparison with baseline before intrathecal baclofen testing (n=28) (mean, SD) before trial: 3.19 (0.56), after trial: 1.34 (0.50), change: -1.85 (0.51); P<0.001).

b No statistical comparison was given across groups

c Pre-post treatment data. When receiving CITB, patients had a statistically significant reduction in the mean Ashworth scores at 12 months after implantation as compared to baseline at 12 months after implantation (mean SD): Ashworth score: 1.76 (0.64), change: -1.49 (0.69); P<0.001). It is not possible to determine exactly how many children were included in the pre- and post-treatment samples

One of the cross-over RCTs (Hoving 2007) and one prospective case series (Hoving 2009b) reported ease of care as a component of optimisation of movement and functioning. One of the outcomes reported was Visual Analogue Scale (VAS) scores.

Table 8.4 Evidence profile for intrathecal baclofen testing follow up and compared with placebo; functioning assessment (ease of care)

Number of studies	Number of participants		Effect		Quality
	Intrathecal baclofen testing	Placebo	Relative (95% CI)	Absolute (95% CI)	
Ease of care, mean VAS score rated once before the test treatment started (baseline) and at the end of each test day (better indicated by higher values)					
1 study (Hoving 2007)	14[a]	13[b]	-	MD 4.20 (2.68 higher to 5.72 higher)*	HIGH
Ease of care, mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[c]	-	-[d]	-[d]	VERY LOW
Ease of care, VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[e]	-	-[d]	-[d]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, MD mean difference, SD standard deviation, VAS Visual Analogue Scale
* Calculated by the NCC-WCH
a Mean 5.1 SD (2.1) p=0.001 compared to baseline.
b Mean 0.9 SD (1.7) p=0.093 compared to baseline.
c Mean 4.4 SD (2.1) p<0.001
d No statistical comparison was given across groups
e Mean 5.2 SD (2.1) p<0.001

One prospective case series (Hoving 2009b) reported individually formulated problems as a component of optimisation of movement and functioning.

Table 8.5 Evidence profile for intrathecal baclofen testing follow up; functioning assessment (individually formulated problems)

Number of studies	Number of participants		Effect		Quality
	Intrathecal baclofen testing	Placebo	Relative (95% CI)	Absolute (95% CI)	
Accomplishment of individually formulated problems after test treatment					
1 study (Hoving 2007)	17[a]	-	-[b]	-[b]	VERY LOW
Mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[c]	-	-[b]	-[b]	VERY LOW
Mean VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[c]	-	-[b]	-[b]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, MD mean difference, SD standard deviation, VAS Visual Analogue Scale
a 14 of the 17 participants were bed bound after the test treatment (due to symptoms of lowered cerebrospinal fluid (CSF) pressure) preventing assessment of some of the individually formulated problems. The study authors noted that there were improvements for individuals in transfers, voiding, startle responses, electric wheelchair operation and arm function, and for one participant, there was improvement in hamstring pain and gait efficiency
b No statistical comparison was given across groups
c Mean 4.1 SD (2.1) p<0.001 compared to baseline
d Mean 4.7 SD (2.0) p<0.001 compared to baseline

One of the cross-over RCTs (Hoving 2007) and one prospective case series (Hoving 2009b) reported outcomes relevant to pain.

Table 8.6 Evidence profile for intrathecal baclofen testing follow up and compared with placebo; pain assessment

Number of studies	Number of participants		Effect		Quality
	Intrathecal baclofen testing	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean VAS score rated once before the test treatment started (baseline) and at the end of each test day (better indicated by higher values)					
1 study (Hoving 2007)	11[a]	10[b]	-	MD 2.2 higher (0.72 lower to 5.12 higher)*	LOW
Mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[c]	-	-[d]	-[d]	VERY LOW
Mean VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[e]	-	-[d]	-[d]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, MD mean difference, SD standard deviation, VAS Visual Analogue Scale
* Calculated by the NCC-WCH
a Mean change 3.3 SD (2.9) p=0.010 compared to baseline
b Mean change 1.1 SD (3.5) p=0.262 compared to baseline (not statistically significant)
c Mean 4.5 SD (2.6) p=0.002
d No statistical comparison was given across groups
e Mean 5.4 SD (2.7) p=0.002

Both cross-over RCTs (Gilmartin 2000; Hoving 2007) and one of the prospective case series (Awaad 2003) reported outcomes related to adverse effects and complications.

Table 8.7 Evidence profile for intrathecal baclofen testing follow up and compared with placebo; adverse events

Number of studies	Number of participants		Effect		Quality
	Intrathecal baclofen testing	Placebo	Relative (95% CI)	Absolute (95% CI)	
Drug-related adverse effects during intrathecal baclofen testing					
1 study (Hoving 2007)	8/17[a]	0/17[b]	-	-	MODERATE
Procedure-related adverse effects during intrathecal baclofen testing					
1 study (Hoving 2007)	-[c]	-	-	-	LOW
Adverse events during intrathecal baclofen testing					
1 study (Gilmartin 2000)	-[d]	-[e]	-	-	VERY LOW
1 study	-	-	-	-[f]	VERY LOW

(Awaad 2003)					

CI confidence interval
a Eight children experienced nine adverse effects associated with intrathecal baclofen during the testing (see Table M.1 - note e)
b No adverse effects were noted with placebo
c Sixteen children were affected by a total number of nineteen complications related to the procedure (see Table M.1 note g). None of these symptoms were observed in three children in whom the neurosurgeon had tunnelled the catheter subcutaneously for a few centimetres
d During the testing phase of the American study (Gilmartin 2000) reported twenty nine adverse effects, affecting eighteen patients (the respective numbers of children and adults is unclear) (see Table M.1 - note f). Twenty two adverse effects occurred during the intrathecal baclofen period and affected fourteen patients
e Seven adverse effects occurred during the placebo period and affected four patients
f No adverse effects reported during the intrathecal baclofen testing phase; but it is not clear that this was recorded, so it cannot be assumed that no adverse effects occurred

Continuous pump-administered intrathecal baclofen

The parallel RCT (Hoving 2009a) and two of the prospective case series (Gilmartin 2000; Hoving 2009b) evaluated reduction of spasticity in the lower limb.

Table 8.8 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with standard treatment; lower limb; tone assessment

Number of studies	Number of participants		Effect		Quality
	CITB and standard treatment	Standard treatment only	Relative (95% CI)	Absolute (95% CI)	
Ashworth scores 6 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009a)	9[a]	8[a]	-	-	LOW
Ashworth scores 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009b)	17[b]	-	-[c]	-[c]	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin 2000)	42[d]	-	-[c]	-[c]	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40[e]	-	-[c]	-[c]	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33[f]	-	-[c]	-[c]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation
a The 6-month score change score differed significantly in favour of the CITB group for the left hip adductors (p=0.0025) and for both hip flexors (right p=0.022; left p=0.043) but there were no significant differences for any of the other muscle groups

b At 12 months after CITB pump implantation (Hoving 2009b). The Ashworth score decreased significantly in 9/14 lower-extremity muscle groups ($0.002 \le p \le 0.046$). The actual scores were not reported

c No statistical comparison was given across groups

d When receiving CITB baclofen patients had a reduction in the mean Ashworth scores as compared to baseline (n=44) (mean, SD; range) 3.64 (0.57); (3.0 to 5.0) at 6 months (n=42): (mean, SD; range) 2.33 (0.64); (1.0 to 3.8)

e When receiving CITB baclofen patients had a significant reduction in the mean Ashworth scores as compared to baseline (n=44) (mean, SD; range) 3.64 (0.57); (3.0 to 5.0) at 12 months (n=40): (mean, SD; range) 2.15 (0.60); (1.1 to 3.3)

f When receiving CITB baclofen patients had a significant reduction in the mean Ashworth scores as compared to baseline (n=44) (mean, SD; range) 3.64 (0.57); (3.0 to 5.0) at 24 months (n=33): (mean, SD; range) 2.21 (0.75); (1.0 to 3.5)

The same studies (Gilmartin 2000; Hoving 2009a Hoving 2009b) evaluated reduction of spasticity in the upper limb.

Table 8.9 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with placebo; upper limb; tone assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	CITB	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ashworth scores 6 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009a)	9	8	-[a]	-[a]	VERY LOW
Ashworth scores 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009b)	17[b]	-	-[c]	-[c]	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin 2000)	41[d]	-	-[c]	-[c]	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40[e]	-	-[c]	-[c]	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	32[f]	-	-[c]	-[c]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen

a The 6-month-change score between both groups significantly differed in favour of the CITB group for the right wrist flexors (p=0.038). There were no significant differences for other muscle groups

b The Ashworth score decreased significantly in 5/8 upper extremity muscle groups ($0.008 \le p \le 0.046$)

c No statistical comparison was given across groups

d When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 6 months after implantation (n=41): 1.80 (0.72); (1.0 to 3.8)

e When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 12 months after implantation(n=40): 1.73 (0.66); (1.0 to 4.1)

f When receiving CITB baclofen patients had a statistically significant reduction in the mean Ashworth scores as compared to baseline at 24 months after implantation(n=32): 1.72 (0.69); (1.0 to 3.1)

One of the prospective case series (Awaad 2003) evaluated reduction of spasticity in the upper and lower limbs combined.

Table 8.10 Evidence profile for continuous pump administered intrathecal baclofen follow up; upper and lower limb; tone assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Placebo	Relative (95% CI)	Absolute (95% CI)	
Ashworth scores 12 months after CITB pump implantation					
1 study (Awaad 2003)	-[a]	-	-[b]	-[b]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation

a When receiving CITB baclofen, patients had a statistically significant reduction in the mean Ashworth scores at 12 months after implantation as compared to baseline : 12 months after implantation (mean, SD) : Ashworth score: 1.76 (0.64), change: -1.49 (0.69); P<0.001) It was not possible to determine exactly how many participants were included in the pre- and post-treatment samples

b No statistical comparison was given across groups

Another prospective case series (Motta 2008) reported outcomes relevant to reduction of dystonia and spasms. One of the outcomes reported was the Burke-Fahn-Marsden Scale (BFMS).

Table 8.11 Evidence profile for continuous pump administered intrathecal baclofen follow up; upper and lower limb; tone assessment (dystonia)

Number of studies	Number of participants		Effect		Quality
	CITB	Placebo	Relative (95% CI)	Absolute (95% CI)	
BADS score 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Motta 2008)	19[a]	-	-[b]	-[b]	VERY LOW
Overall BFMS scores 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Motta 2008)	19[c]	-	-[b]	-[b]	VERY LOW

BADS Barry-Albright Dystonia Scale, BFMS Burke-Fahn-Marsden Scale, CI confidence interval, CITB continuous pump-administered intrathecal baclofen. NS not (statistically) significant, SD standard deviation

a Assessment was conducted pre-implant and at 12 months post-implant by the same team of 2 rehabilitation therapists and same orthopaedic physician. Overall BAD scores (mean, SD) significantly improved at 12 months when compared to baseline ((mean, SD) 12 months: 17.79 ± 3.3 versus baseline: 23.84 ± 4.11; P<0.001). Individual BAD scores were not reported for each region, only p values for change. Dystonia significantly improved at 12 months when compared to baseline in all body regions assessed (eyes: <0.05; mouth: <0.01, neck: <0.001, upper limb R: <0.001, upper limb L: <0.001, trunk: <0.001, lower limb R: <0.01, lower limb L: <0.01)

b No statistical comparison was given across groups

c Overall BFM scores-movement components significantly improved at 12 months when compared to baseline ((mean, SD): 12 months: 77.60 ± 20.56 versus baseline: 98.57 ± 13.07; p<0.001).

Individual BFM scores- movement components were not reported for each region, only p values for change. Dystonia significantly improved at 12 months when compared to baseline in all body regions assessed except in the eyes and the language swallowing area (eyes: NS, mouth: <0.05, language-swallowing: NS, neck: <0.05, upper limb R: <0.05, upper limb L: <0.05, trunk: <0.001, lower limb R: <0.001, lower limb L: <0.001)

The parallel RCT (Hoving 2009a) and one of the prospective case series (Hoving 2009b) reported individually formulated problems as a component of optimisation of movement and functioning.

Table 8.12 Evidence profile for continuous pump administered intrathecal baclofen follow up; upper and lower limb; functioning assessment (individually formulated problems; dystonia)

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
Mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study Hoving 2009a)	9[a]	8[b]	-[c]	-[c]	MODERATE
Mean VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[d]	-	-[e]	-[e]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation, VAS Visual Analogue Scale
a Mean 4.0 SD (1.7) p=0.001 compared to baseline
b Mean -0.2 SD (1.3) p=not stated compared to baseline
c No statistical comparison was given across groups
d Pre-post treatment data
e Mean 4.7 SD (2.0)) p<0.001 compared to baseline

The parallel RCT (Hoving 2009a) and three of the prospective case series (Awaad 2003; Hoving 2009b; Ramstad 2010) reported outcomes relevant to optimisation of function.

Table 8.13 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with usual care; functioning assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
GMFM-66 overall score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	7[a]	5[b]	-[c]	-[c]	MODERATE
GMFM-66 total score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	32[d]	-	-[c]	-[c]	VERY LOW
GMFM-66 general score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12[e]	-	-[c]	-[c]	VERY LOW
GMFM-66 total score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad	31[f]	-	-[c]	-[c]	VERY LOW

2010)					
GMFM-A score (lying and rolling, using GMFM-88) at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	7[g]	5[h]	-	-[i]	MODERATE
GMFM-A score (lying and rolling, using GMFM-88) at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12[j]	-	-[c]	-[c]	VERY LOW
GMFM-B score (sitting, using GMFM-88) at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	7[k]	5[l]	-[c]	-[m]	MODERATE
GMFM-B score (sitting, using GMFM-88) at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12[n]	-	-[c]	-[c]	VERY LOW
GMFM-88 goal dimension score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	5[o]	4[p]	-[c]	-[q]	MODERATE
GMFM-88 goal dimension score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	9[r]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, overall score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	9[s]	8[t]	-[c]	-[u]	MODERATE
PEDI functional skills scale, overall score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[v]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, self-care domain score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	28[w]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, self-care domain score at 12 months after CITB pump implantation (better					

indicated by higher values)					
1 study (Awaad 2003)	28[x]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, self-care domain score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[y]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, mobility domain score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[z\]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, mobility domain score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28[A]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, mobility domain score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[B]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, social function domain score at 6 months after CITB implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[C]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, social function domain score at 12 months after CITB implantation (better indicated by higher values)					
1 study (Awaad 2003)	28[D]	-	-[c]	-[c]	VERY LOW
PEDI functional skills scale, social function domain score at 18 months after CITB implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[E]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, overall score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	9[F]	8[G]	-[c]	-[H]	MODERATE
PEDI caregiver assistance scale, overall score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17[I]	-	-[4]	-[4]	VERY LOW
PEDI caregiver assistance scale, self-care domain score at 6 months after CITB pump implantation					

(better indicated by higher values)					
1 study (Ramstad 2010)	23[J]	-	-[c]	-[c]	VERY LOW
P PEDI caregiver assistance scale, self-care domain score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28[K]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, self-care domain score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[L]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, mobility domain score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	28[M]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, mobility domain score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28[N]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, mobility domain score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	27[O]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, social function domain score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	28[P]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, social function domain score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28[Q]	-	-[c]	-[c]	VERY LOW
PEDI caregiver assistance scale, social function domain score at 18 months after CITB pump implantation (better indicated by higher values)					
1 study (Ramstad 2010)	26[R]	-	-[c]	-[c]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, GMFM-66 Gross Motor Function Measure 66-item scale, GMFM-88 Gross Motor Function Measure 88-item scale, GMFM-A Gross Motor Function Measure dimension A, GMFM-B Gross Motor Function Measure dimension B, NS not (statistically) significant, PEDI Paediatric Evaluation of Disability Inventory, SD standard deviation

a Mean 1.2 SD (2.3) p-value not stated compared to baseline

b Mean -1.6 SD (3.0) p=0.028 compared to baseline

c No statistical comparison was given across groups

d Baseline median (range) = 22.7 (0-48.3) n=35, at 6 months = 22.0 (0.0 – 45.9) n=32, p=0.032 reported
e Mean 1.6 SD (3.1) p=0.110 compared to baseline
f Baseline median (range) = 22.7 (0-48.3) n=35, at 18 months = 24.0 (0.0 – 47.1) n=31, p=0.005 reported
g Median 3.9 Range (-12.0 to 10.0) compared to baseline
h Median 0.0 Range (-10.0 to 0.0) compared to baseline
i p=0.512 (NS)
j Median -1.0 Range (-25.0 to 11.0). No significant difference reported compared to baseline
k Median 3.3 Range (0.0 to 10.0). p value not reported compared to baseline
l Median 0.0 Range (-7.0 to 7.0) p value not reported compared to baseline
m p=0.022
n Median 3.3 Range (-4.0 to 22.0) p=0.022 compared to baseline
o Median 3.0 Range (2.0 to 10.0) p value not reported compared to baseline
p Median 1.3 Range (-6.0 to 6.0) p value not reported compared to baseline
q p=NS reported
r Median 4.0 Range (0.0 to 26.0) p=0.007
s Median 0.0 Range (-7.4 to 5.7) p value not reported compared to baseline
t Median 0.0 Range (-5.4 to 2.1) p value not reported compared to baseline
u p=NS reported
v Median 0.0 Range (-15.0 to 15.8) No significant difference reported compared to baseline
w Baseline median (range) = 33.6 (0-58.6) n=32, at 6 months = 33.0 (0.0 – 61.8) n=28, p=0.246 reported
x Mean 6.36 SD (7.99) p=0.005
y Baseline median (range) = 33.6 (0-58.6) n=32, at 18 months = 36.0 (0.0 – 73.6) n=28, p=0.027 reported
z Baseline median (range) = 23.2 (0-53.1) n=32, at 6 months = 20.9 (0.0 – 48.8) n=27, p=0.285 reported
A Mean 2.88 SD (8.08) No significant difference reported compared to baseline
B Baseline median (range) = 23.2 (0-53.1) n=32, at 18 months = 35.9 (0.0 – 54.8) n=27, p=0.017 reported
C Baseline median (range) = 57.9 (0-96.3) n=31, at 6 months = 59.2 (0.0 – 96.3) n=27, p=0.041 reported
D Mean 5.96 SD (10.35) No significant difference reported compared to baseline
E Baseline median (range) = 57.9 (0-96.3) n=31, at 18 months = 64.1 (0.0 – 100.0) n=27, p=0.002 reported
F Median 0.0 Range (-11.7 to 4.1) p-value not reported compared to baseline
G Median 0.0 Range (-16.0 to 16.0) p value not reported compared to baseline
H p= NS reported
I Median 0.0 Range (-16.0 to 26.3) No significant difference reported compared to baseline
J Baseline median (range) = 15.9 (0-57.9) n=32, at 6 months = 11.6 (0.0 – 63.4) n=28, p=1.000 reported
K Mean 7.78 SD (21.43) No significant difference reported compared to baseline
L Baseline median (range) = 15.9 (0-57.9) n=32, at 18 months = 11.6 (0.0 – 76.7) n=28, p=0.272 reported
M Baseline median (range) = 11.7 (0-70.5) n=32, at 6 months = 29.0 (0.0 – 58.8) n=28, p=0.066 reported
N Mean 11.52 SD (19.62) p=0.028 compared to baseline
O Baseline median (range) = 11.7 (0-70.5) n=32, at 18 months = 36.9 (0.0 – 72.7) n=28, p=0.008 reported
P Baseline median (range) = 58.3 (0-100) n=30, at 6 months = 66.9 (0.0 – 100) n=28, p=0.035 reported
Q Mean 7.86 SD (19.50) No significant difference reported compared to baseline
R Baseline median (range) = 58.3 (0-100) n=30, at 18 months = 65.9 (0.0 – 100) n=26, p=0.004 reported

The parallel RCT (Hoving 2009a) and one of the prospective case series (Hoving 2009b) reported ease of care as a component of optimisation of functioning.

Table 8.14 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with usual care; functioning assessment (ease of care)

Number of studies	**Number of participants**		**Effect**		**Quality**
	CITB	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ease of care, mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving	9[a]	7[b]	-[c]	-[c]	MODERATE

2009a)					
Ease of care, mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16[d]	-	-[e]	-[e]	VERY LOW
Ease of care, mean VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16[f]	-	-[e]	-[e]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation, VAS Visual Analogue Scale

a Mean 3.9 SD (2.2) p value not reported compared to baseline

b Mean 0.1 SD (1.6) p value not reported compared to baseline

c p=0.008

d Mean 4.4 SD (2.1) p<0.001 compared to baseline

e No statistical comparison was given across groups

f Mean 5.2 SD (2.1) p<0.001 compared to baseline

The parallel RCT (Hoving 2009a) and two of the prospective case series (Motta 2008; Ramstad 2010) reported outcomes relevant to pain.

Table 8.15 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with usual care; pain assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
Pain, mean VAS score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	6[a]	6[b]	-[c]	-[c]	LOW
Pain, mean VAS score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12[d]	-	-[e]	-[e]	VERY LOW
Sleeping assessed using a non-validated questionnaire					
1 study (Motta 2008)	19[f]	-	-[e]	-[e]	VERY LOW
Pain assessed using a non-validated questionnaire					
1 study (Motta 2008)	19[g]	-	-[e]	-[e]	VERY LOW
Average frequency of awakenings during the night in previous 4 weeks at 6 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	29[h]	-	-[e]	-[e]	VERY LOW

Average frequency of awakenings during the night in previous 4 weeks at 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	30[i]	-	-[e]	-[e]	VERY LOW
Pain frequency when not sleeping in previous 4 weeks at 6 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31[j]	-	-[e]	-[e]	VERY LOW
Pain frequency when not sleeping in previous 4 weeks at 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31[k]	-	-[e]	-[e]	VERY LOW
Pain severity (using a scale 0-4) in previous 4 weeks at 6 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31[l]	-	-[e]	-[e]	VERY LOW
Pain severity (using a scale 0-4) in previous 4 weeks at 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31[m]	-	-[e]	-[e]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation, VAS Visual Analogue Scale

a Mean 4.2 SD (2.9) compared to baseline

b Mean -1.3 SD (2.4) compared to baseline

c p=0.016

d Mean 5.4 SD (2.7) p=0.002 compared to baseline

e No statistical comparison was given across groups

f 53% of patients/caregivers indicated improved sleep

g 53% of patients/caregivers indicated decreased pain h Baseline median (range) = 1.0 (0-25) n=32, at 6 months = 0.0 (0-10) n=29, p=0.005 reported

i Baseline median (range) = 1.0 (0-25) n=32, at 12 months = 0.0 (0-10) n=30, p=0.006 reported

j Baseline median (range) = 2.0 (0-3) n=35, at 6 months = 1.0 (0-3) n=31, p<0.001(reported as p=0.000)

k Baseline median (range) = 2.0 (0-3) n=35, at 12 months = 1.0 (0-3) n=31, p=0.005 reported

l Baseline median (range) = 2.0 (0-3) n=35, at 6 months = 1.0 (0-3) n=31, p=0.005 reported

m Baseline median (range) = 2.0 (0-3) n=35, at 12 months = 1.0 (0-3) n=31, p=0.011 reported

Two of the prospective case series (Hoving 2009b; Motta 2008) examined outcomes of relevance to acceptability and tolerability.

Table 8.16 Evidence profile for continuous pump administered intrathecal baclofen follow up; treatment acceptability assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Placebo	Relative (95% CI)	Absolute (95% CI)	
Satisfaction with treatment assessed using a non-validated questionnaire					
1 study (Motta 2008)	19[a]	-	-[b]	-[b]	LOW
Acceptability and tolerability assessed at least 12 months after CITB pump implantation					
1 study (Hoving 2009b)	17[c]	-	-[a]	-[a]	LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen

a 15 parents or children were satisfied with the implant, 13 said they would do it again, 3 were not totally satisfied, 3 were uncertain of whether to do it again, 1 was dissatisfied and 1 said he/she would not do it again and chose to explant the pump 4 years after implant

b No statistical comparison was given across groups

c Children and/or their parents were asked if they would participate in the test treatment and implantation procedures again. 15/17 children and/or their parents stated that they would participate in all procedures again. Two parents were not sure in spite of the achieved individual treatment goals for their children. The doubts in one case were based on both new onset seizures and the child's stress during pump refills and in another case were based on a worsened trunk and head balance

The parallel RCT (Hoving 2009a) and one of the prospective case series (Hoving 2009b) reported outcomes relevant to quality of life. One of the outcomes reported was the CHQ Parent Form 50 (CHQ-PF50).

Table 8.17 Evidence profile for continuous pump administered intrathecal baclofen follow up and compared with usual care; quality of life assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
CHQ-PF50 physical functioning domain score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	8[a]	8[b]	-[c]	-[c]	MODERATE
CHQ-PF5 psychosocial summary score at 6 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009a)	8[d]	8[e]	-[f]	-[f]	MODERATE
CHQ-PF50 physical summary score at 12 months after CITB pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16[g]	-	-[h]	-[h]	VERY LOW
CHQ-PF50 psychosocial summary score at 12 months after CITB pump implantation (better indicated					

by higher values)					
1 study (Hoving 2009b)	16[i]	-	-[h]	-[h]	VERY LOW

CHQ-PF50 Child Health Questionnaire - Parent Form 50, CI confidence interval, CITB continuous pump-administered intrathecal baclofen, SD standard deviation
a Mean 2.1 SD (10.3) compared to baseline
b Mean -7.5 SD (6.9) compared to baseline
c p=0.074
d Mean 3.4 SD (7.9)
e Mean - 5.7 SD (8.8)
f p=0.027
g Mean 4.6 SD (10.7) No significant difference reported compared to baseline
h No statistical comparison was given across groups
i Mean 5.4 SD (9.0) No significant difference reported compared to baseline

One of the prospective case series (Krach 2004) reported outcomes relevant to need for further orthopaedic surgery.

Table 8.18 Evidence profile for continuous pump administered intrathecal baclofen follow up; hip displacement assessment

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
Absolute migration percentage at 12 months after CITB pump implantation in children aged under 8 years (better indicated by lower values)					
1 study (Krach 2004)	11 (22 hips)[a]	-	-[b]	-[b]	VERY LOW
Absolute migration percentage at 12 months after CITB pump implantation in children and young people aged 8-18 years (better indicated by lower values)					
1 study (Krach 2004)	17 (34 hips)[c]	-	-[b]	-[b]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen
a Mean 0.0 standard deviation (SD) (8.4) $p<0.05$ compared to baseline
b No statistical comparison was given across groups
c Mean 1.2 SD (12.8) $p<0.05$ compared to baseline

The two case-control studies (Senaran 2007; Shilt 2008) reported outcomes relevant to adverse effects and complications (scoliosis).

Table 8.19 Evidence profile for continuous pump administered intrathecal baclofen compared with usual care; adverse events and complications

Number of studies	Number of participants		Effect		Quality
	CITB	Usual care	Relative (95% CI)	Absolute (95% CI)	
Final Cobb angles (degrees) at approximately 3 years after CITB pump insertion (better indicated by lower values)					
1 study (Shilt	50[a]	50[b]	-[c]	-[c]	VERY LOW

2008)					
Final Cobb angles (degrees) at approximately 3 years after CITB pump insertion (better indicated by lower values)					
1 study (Senaran 2007)	26[d]	25[e]	-[f]	-[f]	VERY LOW
Mean annual progression of Cobb angles (degrees, better indicated by lower values)					
1 study (Shilt 2008)	50[g]	50[h]	-[i]	-[i]	VERY LOW

CI confidence interval, CITB continuous pump-administered intrathecal baclofen, NS not (statistically) significant, SD standard deviation

a Mean 28 SD (20)

b Mean 27 SD (21)

c MD 1 higher (7.14 lower to 9.14 higher) p=NS

d Mean 65.19 SD (24.74)

e Mean 73 SD (21.81)

f MD 7.8 lower (20.95 lower to 5.33 higher) p=NS

g Mean 6.6 SD (11.3)

h Mean 5.0 SD (6.1)

i MD 1.6 lower (2 lower to 5.2 higher) p=NS

Evidence statement

Intrathecal baclofen testing

Value of intrathecal baclofen testing in predicting the response to subsequent continuous pump-administered intrathecal baclofen

No RCTs were identified that compared the outcome of CITB treatment in children and young people undergoing or not undergoing ITB testing.

No clinical studies were identified that determined the diagnostic accuracy of ITB testing in predicting the outcome of CITB treatment.

Effects of bolus intrathecal baclofen given in the setting of intrathecal baclofen testing

With regard to reduction of spasticity in the lower limb, one placebo-controlled cross-over RCT reported that, compared to baseline, there was a statistically significant reduction in tone (Ashworth scores) in most muscle groups at 2, 4 and 6 hours after children and young people received an ITB test bolus whereas, compared to baseline, there were no statistically significant changes in muscle tone in children who received a placebo bolus. An across-group comparison was not reported. (VERY LOW) One prospective case series that followed the children and young people in the above RCT who received the ITB test bolus and who went on to receive CITB reported that there was a statistically significant decrease in tone (Ashworth scores) in nine out of 14 lower-extremity muscle groups at 12 months after implantation compared to baseline. (VERY LOW)

One placebo-controlled cross-over RCT reported that, compared to baseline, there was a statistically significant reduction in tone in lower-extremity muscle groups (Ashworth scores) at 4 hours after children and young people received a 50 µg ITB test bolus compared to when they received a placebo bolus. (LOW) The same RCT reported a statistically significant reduction in tone in lower-extremity muscle groups (Ashworth scores) in children and young people who received a 75 µg ITB test bolus compared to baseline. An across-group comparison was not reported. (VERY LOW) The same placebo-controlled cross-over RCT followed the children and young people after they had received CITB and reported a statistically significant reduction in tone in lower-extremity muscle groups (Ashworth scores) at 6, 12 and 24 months after CITB compared to baseline, (VERY LOW)

With regard to reduction of spasticity in the upper limb, one placebo-controlled cross-over RCT reported a statistically significant reduction in tone in upper-extremity muscle groups (Ashworth scores) in children and young people who received a 50 µg ITB test bolus compared to baseline. (VERY LOW) The same placebo-controlled cross-over RCT followed the children and young people after they had received CITB and reported a statistically significant reduction in tone in upper-extremity muscle groups (Ashworth scores) at 6, 12 and 24 months after CITB compared to baseline, (VERY LOW)

With regard to reduction of spasticity in the upper and lower extremities combined, one prospective case series reported a statistically significant decrease in tone (average combined Ashworth scores) in lower-extremity and upper-extremity muscle groups after children and young people received a 50 µg ITB test bolus compared to baseline. (VERY LOW) The same study reported a statistically significant decrease in tone in lower-extremity and upper-extremity muscle groups at 12 months after CITB implantation compared to baseline. An across-group comparison was not reported. (VERY LOW)

With regard to ease of care, one placebo-controlled cross-over RCT provided evidence that, compared to baseline, there was a statistically significant improvement in ease of care (VAS scores) at the end of the test day when children and young people received an ITB bolus compared to when they received a placebo bolus. (HIGH) One prospective case series that followed the children and young people in the above study who received the ITB test bolus and who went on to have CITB, reported a statistically significant improvement in ease of care (VAS scores) at 6 months and 12 months after implantation compared to baseline. (VERY LOW)

With regard to individually formulated problems, one placebo-controlled cross-over RCT provided evidence that 82% of children and young people who received an ITB bolus were bed bound following the test due to symptoms of lowered CSF pressure. Compared to baseline there were improvements on the test day for individuals who received an ITB bolus in transfers, voiding, startle responses, electric wheelchair operation and arm function, and for one participant there was improvement in hamstring pain and gait efficiency. (VERY LOW) One prospective case series that followed children and young people who received an ITB test bolus and who went on to have CITB reported that, compared to baseline, there was a statistically significant improvement in individually formulated problems (VAS scores) at 6 months and 12 months after CITB implantation. (VERY LOW)

With regard to pain, one placebo-controlled cross-over RCT provided evidence that, compared to baseline, there was an improvement in pain (VAS scores) at the end of the test day when children and young people received an ITB bolus compared to when they received a placebo bolus, but that the difference between the treatment groups was not statistically significant (LOW) One prospective case series that followed the children and young people in the above study who received the ITB test bolus and who went on to have CITB reported that, compared to baseline there was a statistically significant improvement in pain (VAS scores) at 6 months and 12 months after implantation. (VERY LOW)

With regard to complications and adverse effects, one placebo-controlled cross-over RCT reported that 47% of children and young people who received ITB testing experienced a drug-related adverse effect compared to no adverse effects when a placebo bolus was received. (MODERATE) The same study reported that 94% of children and young people who received the ITB bolus test experienced a procedure-related adverse effect; most of these children and young people had lowered CSF pressure. (MODERATE) Another placebo-controlled cross-over RCT reported that 76% of adverse events occurred during ITB bolus testing compared to 24% that occurred during testing with placebo. (VERY LOW) It was unclear whether any adverse events were reported in one prospective case series. (VERY LOW)

No evidence was identified in relation to the acceptability and tolerability of ITB testing for children and young people and their families.

No evidence was identified in relation to ITB testing in children and young people with dystonia,

No evidence was identified in relation to children and young people with special concerns such as hydrocephalus, ventriculo-peritoneal shunt or those needing medical devices such as cardiac pacemakers.

Outcome with continuous pump-administered intrathecal baclofen in children and young people who had a positive response to intrathecal baclofen testing

With regard to reduction in spasticity, one RCT and two prospective case series provided evidence of a statistically significant reduction in spasticity in the upper and lower limbs at 12 months following CITB implantation compared to baseline. (VERY LOW) One RCT reported that there was a reduction in spasticity at 6, 12 and 24 months compared to baseline, although statistical significance could not be determined. (LOW)

With regard to ease of care, individually formulated problems and pain, one prospective case series provided evidence that CITB implantation leads to a statistically significant improvement at 6 and 12 months compared to baseline. (VERY LOW)

No evidence was identified in relation to acceptability and tolerability of CITB.

Continuous pump-administered intrathecal baclofen

With regard to reduction of spasticity in the lower extremities, one parallel RCT reported that, compared to baseline, there was a statistically significant improvement in tone (Ashworth scores) at 6 months for left hip adductors and both hip flexors in children and young people who received CITB and standard treatment as compared to those who received standard treatment alone. The study authors reported that there were no statistically significant differences in tone between the treatment groups for any other lower limb muscle groups. (LOW) One prospective case series (follow-up to the previous RCT) reported a statistically significant decrease in tone (Ashworth scores) in nine out of 14 lower-extremity muscle groups at 12 months after starting CITB. (VERY LOW) One cross-over RCT followed up children and young people who received a CITB implant and reported that there was a statistically significant reduction in tone (Ashworth scores) in lower-extremity muscle groups at 6, 12 and 24 months after starting CITB compared to baseline, (VERY LOW)

With regard to reduction of spasticity in the upper extremities, one parallel RCT reported that, compared to baseline, there was a statistically significant improvement in tone (Ashworth scores) at 6 months for the right wrist flexors in children and young people who received CITB and standard treatment as compared to those who received standard treatment alone. The study authors reported that there were no statistically significant differences in tone between the treatment groups for any other upper limb muscle groups. (VERY LOW) One prospective case series (follow-up to the previous RCT) reported a statistically significant decrease in tone (Ashworth scores) in five out of eight upper-extremity muscle groups at 12 months after starting CITB implantation compared to baseline. (VERY LOW) One cross-over RCT followed up children who received a CITB implant and reported a statistically significant reduction in tone (Ashworth scores) in upper extremity muscle groups over time at 6, 12 and 24 months after CITB when compared to baseline. (VERY LOW)

With regard to reduction of spasticity in lower and upper extremities combined (average combined Ashworth scores), one prospective cases series reported that there was a statistically significant decrease in tone in lower-extremity and upper-extremity muscle groups at 12 months after starting CITB compared to baseline. (VERY LOW)

With regard to reduction of dystonia, one prospective case series provided evidence of a positive effect on generalised dystonia in children and young people with cerebral palsy and a severe degree of impairment. The study provided evidence of a statistically significant improvement in overall BADS scores at 12 months after CITB when compared to baseline. (VERY LOW) There was a statistically significant improvement in dystonia in all body regions assessed 12 months after CITB when compared to baseline. (VERY LOW) The study also provided evidence of a statistically significant improvement in overall BFMS scores for movement at 12 months when compared to baseline. There was a statistically significant improvement in dystonia in all body regions assessed except for the eyes and language/swallowing area at 12 months when compared to baseline. The study reported no statistically significant difference in dystonia in the eyes and language swallowing area. The study also reported that no participants showed a statistically significant difference in BFMS scores with regard to everyday activities. (VERY LOW)

With regard to optimisation of function, one parallel RCT reported that, compared to baseline, there was a statistically significant improvement in individually formulated problems (VAS scores) in children and young people treated using a CITB pump at 6 months. Deterioration was reported in those treated with standard treatment alone (statistical significance not reported). An across-group comparison was not reported. (MODERATE) One prospective case series (follow-up to the previous RCT) reported a statistically significant improvement in individually formulated problems (VAS) at 12 months after starting CITB when compared to baseline. (VERY LOW)

With regard to optimisation of function measured using the GMFM, one parallel RCT reported an improvement in overall function (GMFM-66 overall score) in children and young people who received CITB and standard treatment at 6 months compared to baseline (statistical significance not reported). A statistically significant deterioration was reported for those who received standard treatment alone. An across-group comparison was not reported. (MODERATE) One prospective case series (follow-up to the previous RCT) reported an improvement in overall function (GMFM-66 general score) at 12 months after CITB implantation when compared to baseline which was not statistically significant. (VERY LOW) Another prospective case series reported a statistically significant improvement in overall function (GMFM-66 total score) at 6 and 18 months in children and young people treated with CITB when compared to baseline. (VERY LOW)

One parallel RCT reported that, compared to baseline, there was an improvement in GMFM-A (lying and rolling) functioning at 6 months in children and young people who received CITB and standard treatment as compared to those who received standard treatment alone, although the difference between groups was not statistically significant. (MODERATE) One prospective case series (follow-up to the previous RCT) reported deterioration in GMFM-A at 12 months after starting CITB when compared to baseline, but the difference was not statistically significant. (VERY LOW)

One parallel RCT reported that compared to baseline there was a statistically significant improvement in GMFM-B (sitting) at 6 months in children and young people who received CITB and standard treatment as compared to those who received standard treatment alone. (MODERATE) One prospective case series (follow-up to the previous RCT) reported a statistically significant improvement in GMFM-B functioning at 12 months after starting CITB when compared to baseline. (VERY LOW)

One parallel RCT reported that, compared to baseline, there was an improvement in functioning (GMFM goal dimension score) at 6 months in children and young people who received CITB and standard treatment as compared to those who received standard treatment alone, although the difference between the treatment groups was not statistically significant. (MODERATE) One prospective case series (follow-up to the previous RCT) reported a statistically significant improvement in functioning (GMFM goal dimension score) at 12 months after starting CITB when compared to baseline. (VERY LOW)

With regard to optimisation function measured using the PEDI, one parallel RCT reported that, compared to baseline, there was no change in functional skills (PEDI functional skills overall scores) in children and young people treated with CITB and standard treatment, or in those treated with standard treatment alone and that comparison of these findings across the treatment groups was not statistically significant. (MODERATE) One prospective case series (follow-up to the previous RCT) reported that there was no statistically significant change in functional skills (PEDI functional skills overall scores) at 12 months after starting CITB compared to baseline. (VERY LOW)

One prospective case series reported that, compared to baseline, that there was deterioration in self-care functioning (PEDI functional skills scale, self-care domain) at 6 months that was not statistically significant, but there was a statistically significant improvement at 18 months in children and young people who received CITB implantation. (VERY LOW) Another prospective case series reported a statistically significant improvement in self-care functioning (PEDI functional skills scale, self-care domain) at 12 months in children and young people who received CITB compared to baseline. (VERY LOW)

One prospective case series reported that, compared to baseline, there was deterioration in mobility (PEDI functional skills scale, mobility domain) at 6 months that was not statistically significant, but there was a statistically significant improvement at 18 months in children and young people who received CITB. (VERY LOW) Another prospective case series reported an improvement in mobility (PEDI functional skills scale, mobility domain) at 12 months in children and young people who received CITB compared to baseline, although this was not statistically significant. (VERY LOW)

One prospective case series reported that, compared to baseline, there was a statistically significant improvement in social functioning (PEDI functional skills scale, social function domain) at 6 and 18 months in children and young people who received CITB. (VERY LOW) Another prospective case series reported an improvement in social functioning (PEDI functional skills scale, social function domain) at 12 months in children and young people who received CITB compared to baseline, although this was not statistically significant. (VERY LOW)

With regard to optimisation of movement and function measured by PEDI caregiver assistance scores, one RCT found no statistically significant difference at 6 months in caregiver assistance between children and young people who received CITB and standard treatment, as compared to those who received standard treatment only. (MODERATE) One prospective case series (follow-up to the previous RCT) found no statistically significant difference in caregiver assistance at 12 months when compared to baseline. (VERY LOW) Another prospective case series found no statistically significant difference in the self-care and social function dimensions of caregiver assistance at 12 months, when compared to baseline. (VERY LOW) However, the same study provided evidence of a statistically significant improvement in the mobility dimension of caregiver assistance at 12 months, when compared to baseline. (VERY LOW) One further prospective case series reported no statistically significant differences in the self-care dimension (at 6 and 18 months) and the mobility dimension (at 6 months) compared to baseline, although statistically significant improvements were found at 18 months for the mobility dimension and for the social function dimension at both 6 and 18 months compared to baseline. (VERY LOW)

One parallel RCT reported that, compared to baseline, there were no changes in caregiver assistance scores (PEDI caregiver assistance scale overall scores) at 6 months in children and young people who received CITB and standard treatment or in those who received standard treatment alone and that comparison of these findings across groups was not statistically significant. (MODERATE) One prospective case series (follow-up to the previous RCT) reported that there was no statistically significant change in caregiver assistance scores (PEDI caregiver assistance scale overall scores) at 12 months after starting CITB when compared to baseline. (VERY LOW)

One prospective case series reported that, compared to baseline, there was deterioration in self-care functioning (PEDI caregiver assistance scale self-care domain) at 6 months and 18 months in children and young people who received CITB that was not statistically significant. (VERY LOW) Another prospective case series reported an improvement in self-care functioning (PEDI caregiver assistance scale self-care domain) at 12 months in children and young people who received CITB compared to baseline which was not statistically significant. (VERY LOW)

One prospective case series reported that, compared to baseline, there was an improvement in mobility (PEDI caregiver assistance scale mobility domain) at 6 months in children and young people who received CITB that was not statistically significant, but there was a statistically significant improvement at 18 months. (VERY LOW) Another prospective case series reported a statistically significant improvement in mobility (PEDI caregiver assistance scale mobility domain) at 12 months in children and young people who received CITB compared to baseline. (VERY LOW)

One prospective case series reported that, compared to baseline, there was a statistically significant improvement in social functioning (PEDI caregiver assistance scale social function domain) at 6 and 18 months in children and young people who received CITB. (VERY LOW) Another prospective case series reported a statistically significant improvement in social functioning (PEDI caregiver assistance scale social function domain) at 12 months in children and young people who received CITB compared to baseline. (VERY LOW)

With regard to optimisation of movement and functioning measured by ease of care, one parallel RCT reported that, compared to baseline, there was a statistically significant improvement in ease of care (measured using VAS scores) at 6 months in children and young people who received CITB and standard treatment, as compared to those who received standard treatment only. (MODERATE) One prospective case series (follow-up to the previous RCT) reported a statistically significant improvement in ease of care (measured using VAS scores) at 6 and 12 months in children and young people treated with CITB and standard treatment when compared to baseline. (VERY LOW)

With regard to reduction of pain, one parallel RCT reported that, compared to baseline, there was a statistically significant improvement in pain (VAS scores) at 6 months in children who received CITB and standard treatment, as compared to those who received standard treatment alone. (LOW) One prospective case series (follow-up to the previous RCT) reported a statistically significant improvement in pain (VAS scores) at 12 months when compared to baseline, indicating a reduction in pain. (VERY LOW) Another prospective case series of children and young people with cerebral palsy and with a severe degree of impairment reported that 53% of participants or caregivers indicated both decreased pain and improved sleep at follow-up (time of assessment not specified). (VERY LOW) One further prospective case series reported statistically significant decreases in the number of night awakenings, frequency of pain and severity of pain at both 6 and 12 months in children who received CITB. (VERY LOW)

With regard to acceptability and tolerability, one prospective case series involving children and young people with a severe degree of impairment receiving CITB for generalised dystonia reported that 79% of parents or caregivers were satisfied with the implant and 68% said they would have the procedure performed again. (VERY LOW) One further prospective case series involving children and young people receiving CITB reported that 88% of children and young people and/or their parents said they would participate in the test treatment and implantation procedures again. (VERY LOW)

With regard to quality of life, one parallel RCT reported that, compared to baseline, there were statistically significant improvements in physical and psychosocial functioning (CHQ-PF50) at 6 months in children who received CITB and standard treatment, as compared to those who received standard treatment alone. (MODERATE) One prospective case series (follow-up to the previous RCT), reported that there were improvements in physical and psychosocial functioning (CHQ-PF50) at 12 months in children who received CITB, when compared to baseline, but these findings were not statistically significant. (VERY LOW)

With regard to the need for further orthopaedic surgery, one prospective case series reported that there were no statistically significant changes in hip migration percentage after 12 months of CITB compared to baseline, in either children younger than 8 years or children and young people aged 8-18 years. (VERY LOW)

With regard to adverse events and complications, one case-control study provided evidence that, compared to baseline, there was a deterioration in Cobb angles at 3 years in children who received CITB implantation compared to those who received usual care, but that comparison of these findings across groups was not statistically significant. (VERY LOW) The same study provided evidence that, compared to baseline, children who received CITB implantation had a slower mean annual progression of Cobb angles compared to those who received usual care, although comparison of these findings across treatment groups was not statistically significant. (VERY LOW) Another case-control study provided evidence that, compared to baseline, there was an improvement in Cobb angles at 3 years in children who received CITB implantation compared to those who received usual care, but comparison of these findings across groups was not statistically significant. (VERY LOW)

Three prospective case series reported that for a total of 101 pumps, there were 87 complications, of which 70% were surgical complications, 30% were mechanical complications, and none were related to pump or operator failure (See Appendix L, Table L.2).

Health economics

Only one UK cost effectiveness analysis was identified from the literature search conducted for the guideline (Sampson 2002). The model compared the costs of testing, implanting the pump and follow-up visits for 5 years (representing the battery life of the pump), with the estimated benefits to quality of life. Further details are presented in Chapter 11.

The clinical effectiveness evidence used by Sampson 2002 was identified in a literature search conducted as part of that study. The studies identified used a wide variety of outcome measures and the study authors found that functional and quality of life outcomes were generally not measured using standard scores. All the studies involved people with severe disabling spasticity that could no longer be treated by oral drugs and who had responded to a bolus dose of ITB. The studies included children, young people and adults with different causes of spasticity, but the results were reported for all participants together.

As none of the studies used quality of life measures the EuroQol Group's EQ-5D instrument was used by the study authors to calculate health-related quality of life changes based on their evidence review and supported by clinical opinion. Three populations of patients were divided by severity into the following categories for the evaluation.

- Category 1: bedbound patients experiencing severe spasm-related pain.
- Category 2: bedbound patients who were not in pain.
- Category 3: wheelchair users with moderate spasm-related pain.

Cost estimates were derived from three centres in the UK where the operation was being performed. The total cost for the pump over 5 years was £15,420. Benefits of the ITB pump were assumed to last 5 years (which represents the lifespan of the pump's battery). The costs per QALY for each category of patients were as follows.

- Category 1: £6,900.
- Category 2: £12,790.
- Category 3: £8,030.

There was no comparator treatment and, therefore, the results obtained are not incremental cost effectiveness ratios (ICERs). It was found that if the QALY gain was less than approximately 0.15 or if the cost of CITB treatment was above £19,000 over the 5-year period then the cost per QALY would be greater than the NICE £20,000 threshold for willingness to pay for a QALY gain.

The published economic evaluation (Sampson 2002) was used by the GDG as the basis for developing a new health economic model. The model examined the cost effectiveness of ITB testing and implanting the ITB pump (further details are presented in Chapter 11). The costs of testing, implanting the pump and follow-up visits over 5 years were taken from Sampson 2002 (Table 11.8) and converted to 2010/11 costs (using the hospital and community health services pay and prices index uplift (Curtis 2011)).

As the model runs over 5 years, costs and benefits accrued after the first year are discounted by 3.5% for costs and 3.5% for benefits (1.5% was also used for benefits). The perspective of this evaluation is from the NHS, therefore only includes costs and benefits relevant to the NHS.

In the model the following three comparisons were considered.

- Children and young people considered suitable candidates have a pre-screening assessment and are tested before the ITB pump is implanted. Those who have a positive test result will go on to have the pump implanted. Those who have a negative test result will receive standard treatment.
- Children and young people considered suitable candidates by their healthcare professionals have a pre-screening assessment, and have the pump implanted without a test dose.
- ITB testing and pump is not available for any children and young people. Those considered suitable candidates by their healthcare professionals will continue to receive standard treatment.

No studies were identified that demonstrated the diagnostic accuracy of ITB testing. Children and young people only had a pump implanted if the test result was positive. The GDG agreed that healthcare professionals can generally predict which children and young people will benefit from ITB treatment based on their clinical characteristics. ITB testing is used to demonstrate the effectiveness of ITB to the child or young person and to help identify treatment goals.

The baseline analysis assumes no improvement in quality of life for children and young people who have the pump implanted and this is the same effect as standard treatment, a conservative assumption to reflect that little good-quality comparative evidence is available. It is assumed that staying on standard treatment resulted in no quality of life improvements, but also no deterioration. The analysis was also run using the long-term quality of life effects from Sampson 2002.

Using the baseline assumption of no improvement in health-related quality of life with CITB treatment, standard treatment should be preferred because implanting the pump is not worth the additional cost (approximately £20,000 per child or young person over 5 years). Implanting the pump without testing is cheaper and more effective than testing first using these inputs, but the differences in the overall costs and benefits is small (£21,423 versus £21,370 per child or young person, and 1.70 versus 1.71 QALYs over 5 years).

However, if the analysis is run using the quality of life outcomes from Sampson 2002 then using the ITB pump is cost-effective compared to standard treatment. The incremental cost effectiveness results for all categories of patients are as follows:

- Category 1 £19,798
- Category 2 £10,691
- Category 3 £12,431.

ITB treatment is much more expensive than standard treatment and its clinical value is uncertain. The analysis conducted for the guideline illustrates the trade-off between the benefits of treatment, the risks, and the costs. The analysis is based on very limited, low-quality data which suggests that the effectiveness, and the risks and adverse events associated with this treatment are not well known. A more detailed evaluation of costs, benefits, and risks of ITB treatment require more long-term data, especially as this analysis suggests that ITB treatment may be beneficial and cost effective in particular groups of children and young people with spasticity, rather than in all such children and young people.

Evidence to recommendations

Intrathecal baclofen testing

Relative value of outcomes

In examining the evidence regarding ITB testing the GDG noted that the most useful thing to know would be the value of ITB testing in predicting a beneficial outcome with CITB. They noted that ITB testing is a pilot for CITB in that it performs the same function of delivering the drug to the intrathecal space in a less invasive way so that effects can be observed on a more temporary basis and with lower risks to the child or young person. As such the GDG thought that it was rational to prioritise the same outcomes for both ITB testing and CITB when considering the effectiveness of each treatment.

The group considered outcomes relating to functional benefit as being of greatest importance. In particular, they were interested in improved mobility and motor function in relation to improvement in sitting, range of movement and ease of care because, in the UK, ITB is generally offered to children and young people with severe spasticity (GMFCS level IV or V). The group also concluded that the following outcomes were important:

- reduction in spasticity measured using Ashworth and MAS scores
- alleviation of pain and discomfort
- reduction of dystonia because children and young people with severe spasticity and/or dystonia have been treated with ITB
- frequency and nature of adverse events
- acceptability and tolerability (of ITB testing and CITB, respectively in the separate review questions)
- quality of life
- serious adverse events.

Trade-off between clinical benefits and harms

The GDG acknowledged that the evidence for ITB testing was very sparse. The ideal study design for evaluating the value of ITB testing in predicting a beneficial outcome with CITB would be a RCT that compared the outcomes of CITB treatment in children and young people who had either undergone, or not undergone, ITB testing. Only through a study of this type would it be possible to demonstrate whether the group who underwent ITB testing had done better with CITB treatment and thus whether

ITB testing was an effective predictor of CITB treatment success and, therefore, of help is selecting appropriate patients for CITB treatment. No such studies were identified for inclusion in the guideline review. The GDG was not surprised by the absence of such evidence because they thought it very unlikely that in clinical practice CITB treatment would ever be considered without first conducting ITB testing and, therefore, it was unlikely that an RCT as described above would be conducted as part of clinical research. Another possibility in terms of study design would be to evaluate the diagnostic accuracy of ITB testing for identifying those children and young people in whom subsequent CITB testing will be successful. However, no studies of this design were identified for inclusion either.

There was evidence from observational studies that ITB testing administered as one or more boluses can reduce spasticity. In this scenario there was also evidence that test doses can reduce pain and possibly improve ease of care by parents and other carers. There was no convincing evidence from these studies of clinically important improvement in function or change in dystonia.

The evidence from case series involving children and young people who had experienced a positive response to ITB testing and who went on to receive CITB treatment indicated that sustained reductions in spasticity and in pain could be demonstrated 12 months later, while improvements in ease of care and in individually formulated problems (as a component of optimisation of movement and functioning) were observed 6-12 months later. While this evidence does not provide conclusive evidence for the value of ITB testing in predicting a response to CITB treatment (because case studies do not evaluate the outcomes of ITB testing in comparison with any other clinical management scenario) it supports the assumption that an initial response to ITB testing can be sustained over a long period.

Despite the paucity of evidence to demonstrate that ITB testing accurately predicts the response to CITB treatment the GDG’s view was that it is reasonable, based on physiological principles, to accept that this was likely to be the case. If a child or young person did not respond to the test doses in the intended way (for example, if the intended goal of ITB treatment were to reduce pain and this was not achieved through the administration of the bolus doses during testing), a positive response from CITB in terms of the same treatment goal would be unlikely. On the other hand, if ITB testing produced a response that resulted in unexpected and disadvantageous effects (for example, if ITB testing showed that intrathecal administration of baclofen reduced spasticity that was supporting function) this would suggest that CITB would be contraindicated.

In addition to this rationale regarding the underlying physiological principles, the GDG observed that observing an immediate beneficial response to ITB testing was often helpful to parents in their decision to proceed with pump implantation for CITB treatment, and this was extremely valuable.

The GDG acknowledged that there were risks associated with ITB testing. The ITB test involves performing a lumbar puncture under general anaesthesia. The group also noted that undergoing the test involves a brief inpatient admission to administer test boluses and to assess the response.

Weighing up the evidence in the light of their clinical experience, the GDG consensus was that there was sufficient benefit to be gained from ITB testing in terms of determining the likely response to treatment goals and assessing adverse events to outweigh the risks and therefore that it was appropriate to recommend its use in this regard.

However, given the invasive nature of ITB testing the GDG felt that it was important to provide guidance to support selection of children and young people who were appropriate candidates for ITB testing. In general, the GDG believed that adverse effects associated with ITB testing would occur only occasionally and the effects would usually be minor. Nevertheless, the group agreed that ITB testing should be undertaken only in those children and young people in whom prior clinical assessment had identified them as likely candidates to proceed to CITB treatment. The GDG concluded that it should first be clarified whether the child or young person is a suitable candidate for pump placement, whether there is a real potential for that individual to benefit from ITB treatment, and that the child or young person and their parents or carers are in principle willing to proceed with CITB treatment subject to the outcomes of ITB testing being positive. These conclusions are reflected in the order of presentation of the recommendations and in their wording (see below for further details of about the GDG’s conclusions regarding patient selection for CITB). For the same reason, the group also recommended that before ITB testing, children and young people and their parents or carers should be informed about what the test will entail, adverse effects that might occur with testing, and how the test might help to indicate the response to treatment with CITB, including whether the intended goals are likely to be achieved and/or whether adverse effects might occur. The GDG considered, given the complexity of these issues, that the information should be provided in written form as well as being discussed verbally.

Although no evidence was identified regarding how ITB testing should be performed, it was the GDG's view that certain criteria were key to maximising benefit, minimising adverse effects and mitigating risks in all aspects of ITB treatment (including appropriate patient selection for testing, administration of the bolus dose(s), and accurate assessment of the test outcome). Firstly the group concluded that ITB testing should be performed in a specialist neurosurgical centre by healthcare professionals who have the expertise to carry out the necessary procedures and assessments. The group also considered that the decision to use ITB treatment, including ITB testing, should not take place in isolation, but be considered as part of a wider management programme for the child or young person and in collaboration with other experts who might have a better understanding of the child or young person's individual circumstances or needs, or would be involved in delivering post-operative care, for example, a paediatrician or a physiotherapist or occupational therapist. The GDG was aware, however, that such multidisciplinary working does not always occur in current practice. For this reason the group agreed that, although ITB is not appropriate for every child or young person with spasticity, it should not be isolated from the network of care. Instead the group recommended that the specialist neurosurgical centre should be included in the network team so that the services provided by the centre would be covered by the same stipulations regarding use of agreed care pathways, effective communication and integrated team working outlined in the recommendations about principles of care (see Chapter 4 for further details of the rationale for these recommendations).

The GDG also concluded that ITB testing should be undertaken in an inpatient setting to support a reliable process for assessing safety and effectiveness. The group also concluded that the test dose or doses of ITB should be administered using a catheter inserted under general anaesthesia to minimise distress or discomfort and to ensure accurate delivery of the drug to the intended site within the intrathecal space.

As noted above, the GDG concluded that ITB testing could only be justified in children and young people who have been identified clinically as suitable candidates for CITB treatment. The group therefore agreed that before performing ITB testing an assessment should be conducted. The assessment should take account of the intended goals of treatment because the aims of treatment in a severely affected child (GMFCS level IV or V) will usually differ from those in a more functional child or young person, but underpinning these goals should be the clinical indications for the use CITB treatment (see below for more details). The group recommended, therefore, that the pre-test assessment should take account of the intended goals using the following criteria where relevant: 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). The GDG judged that the pre-test assessment was also important as a baseline against which the response to ITB testing could be measured. The group therefore agreed that the response to ITB testing should be assessed and that the means of determining whether the response was satisfactory should reflect the pre-test assessment.

The GDG considered that if the pre-test assessment included an assessment of range of movement, it might be appropriate to perform this while the child or young person were under general anaesthetic to minimise discomfort and distress in this often severely disabled group of children and young people, while a thorough assessment of joint range is performed. The group also agreed that, ideally, both assessments should be performed by the same healthcare professionals in the specialist neurosurgical centre because variable assessment techniques and their interpretations would mean that the results would be more likely to be subject to inaccuracies if the assessments were carried out by different professionals. However, the group appreciated that this would not always be possible due to service constraints, and they advocated careful documentation of assessment findings to allow comparison where possible.

The GDG also noted that the post-test assessment should be carried out after the general anaesthetic had worn off. They recommended that, based on clinical experience, 3-5 hours would normally be an appropriate time frame for this to have taken place, but with the caveat that it might be necessary to delay the assessment until even later because children and young people being considered for this treatment were likely to take longer to recover from general anaesthesia.

The GDG concluded that children and young people and their parents or carers should be given the opportunity to discuss their views on the response to ITB testing. In particular, the group noted that it would be of value to ascertain their views on the effect of the ITB test on self-care (or ease of care by parents or carers). The GDG agreed that it might be useful to gather this information using standardised questionnaires.

Trade-off between net health benefits and resource use

The GDG considered that, although the evidence for the effectiveness of ITB testing was limited, it did, in their clinical opinion, have the potential to serve a valuable role in confirming or disproving clinically determined patient selection and treatment goals and identifying adverse effects. It also served a wider purpose in terms of facilitating fully informed consent on the part of the child or young person and their parents or carers. The group also noted that ITB testing was currently in use in clinical practice and the absence of unequivocal evidence of cost effectiveness was insufficient to direct a change in practice away from its use. For these reasons the GDG considered that ITB testing was likely to be a good use of resources for appropriately selected children and young people.

Quality of the evidence

The studies identified for inclusion frequently reported Ashworth scores as a measure of spasticity. Being an ordinal scale, the averaging of these scores is not methodologically correct but it was frequently undertaken in the included studies. Two of the three studies included in the guideline review included adults as well as children and young people, and subgroup analyses by age group and group demographics were rarely reported. In addition, the GDG noted that the included studies reported varied outcomes with ITB testing so that synthesis of data was often difficult. However, in all three studies the participants had moderate to severe bilateral spasticity (GMFCS level III, IV or V).

The GDG noted that, in the UK, oral drug treatment, including oral baclofen treatment, are generally continued during ITB testing. One of the studies conducted in the USA reported that the investigators aimed to discontinue oral drug treatment as part of the trial protocol. This constitutes a potential source of bias in the study.

Other considerations

The GDG noted that there may be specific circumstances where ITB testing would be inappropriate and that the contraindications to ITB testing would be the same as those for CITB treatment (see below).

Continuous pump-administered intrathecal baclofen

Relative value placed on the outcomes considered

In addition to the outcomes prioritised for ITB generally (see above), the GDG wished to consider evidence relating to the possible effects of CITB treatment on the risk of orthopaedic complications such as hip dislocation, scoliosis and the need for orthopaedic surgery.

Trade-off between clinical benefits and harms

The GDG noted that there was just one RCT that examined the effectiveness of CITB treatment in children and young people with spasticity. This was a small study (17 participants) involving children and young people with bilateral spasticity affecting the legs or bilateral spasticity affecting both arms and legs. Following ITB testing eight participants started CITB treatment and their outcomes were compared with the remaining nine participants who started CITB treatment 5 months later. This RCT reported a wide range of outcomes with regard to the muscle tone. Ashworth scores were reported separately for numerous muscle groups and for each separate limb. The GDG noted that 6 months after starting CITB treatment, reduced muscle tone was documented in muscles affecting the hip and wrist, but other muscle groups were not significantly altered. The CITB treatment group was followed up and assessed at 12 months with no control group comparison and muscle tone was compared with baseline. There was a reduction in muscle tone in a wider spectrum of muscle groups in both upper and lower limbs. The RCT found evidence of better outcomes with 'individually formulated problems', total GMFM scores, pain relief, ease of care, and quality of life. The study did not show evidence of better functional outcomes based on the PEDI total score.

Although this RCT reported various clinically important benefits with CIBT treatment, the GDG highlighted that the number of participants was very small, the study was inevitably an open-label design (the study investigators and participants were not blinded to which children or young people were in each treatment arm), and the GDG viewed it important to consider outcomes beyond the 6 month time point evaluated in the trial. Moreover, the group wished to look for evidence regarding the risk of adverse outcomes – particularly given the potential risks associated with pump placement and maintenance. For those reasons the GDG chose to also consider reports from non-comparative studies (cases series).

Eight prospective case series (generally involving fewer than 50 participants) in which changes from baseline were reported were identified for inclusion. The GDG noted that several of these studies reported improved muscle tone in the upper and lower limbs at 12 and/or 24 months after starting CITB treatment. One of the studies showed that CITB also had a positive effect on generalised dystonia in children and young people with cerebral palsy. Some of the studies also reported improvement in 'individually formulated problems', GMFM score (overall or in relation to specific motor skills), and ease of care. Two of the studies reported that at 12 months there was a reduction of pain or discomfort compared with baseline. Almost 90% of parents in one study stated that they would have been prepared to agree to the procedure again, indicating a high level of satisfaction.

The GDG noted that neither of two case-control studies showed an effect of CITB on the rate of scoliosis progression following CITB pump implantation. The group further noted that in one small prospective case series study of hip migration after CITB pump implantation there was only a 12 month follow-up period. In this study a 5% alteration in hip migration index was reported as being statistically significant, and the GDG questioned whether this was clinically meaningful given the method of measurement. The GDG's view was, therefore, that caution should be used when considering CITB in children and young people with scoliosis.

Together the case series described a high incidence of complications associated with the infusion pump for CITB, including surgical complications in 59%, mechanical complications in 39%, and pump failure in 2%. The GDG noted that since the introduction of CITB treatment there have been technical advances and refinements in surgical techniques and in pump and catheter design, such that the risks described in the published case series included in the guideline review are unlikely to reflect current experience. The group also noted the high level of satisfaction reported by parents even in the historical studies.

While recognising the limitations of the available evidence, the GDG concluded that CITB treatment had the potential to alleviate spasticity and to produce clinically important changes. Evidence from the RCT included in the guideline review, supported by the reports from the prospective case series, indicated that CITB treatment could reduce muscle tone and produce clinical benefits with respect to various clinical problems and goals.

The GDG's experience of using ITB was also that, in properly selected patients, it could produce important benefits.

The GDG recognised, based on the evidence and their clinical consensus that there were potential risks associated with the CITB treatment and these included all the general risks associated with surgery, such as the need for general anaesthetic. However, the group concluded that the benefit that could be derived from treatment had the potential to render these risks acceptable.

The GDG also agreed that effectiveness of CITB treatment in any child or young person could not be assured without an appropriate form of concomitant physical therapy.

The group therefore recommended that consideration be given to using CITB treatment if, despite the use of appropriate non-invasive treatments, spasticity or dystonia were continuing to cause difficulties with pain or muscle spasms, posture or function, and/or self-care (or ease of care by parents or carers).

The GDG considered CITB treatment to be a major intervention that would not be justified in the absence of clinically important difficulties. The group noted that the strongest evidence for improvement in quality of life was in severely limited children and young people (GMFCS level V). This observation, in the opinion of the GDG, was not sufficient to preclude more functional children (GMFCS level III, IV or V) from pump implantation where clinical judgement indicates benefits are likely to outweigh possible harms, and where ITB testing has been undertaken and a positive response to such testing has been obtained. Therefore, based on the available evidence and the knowledge and experience of the GDG, the group chose to highlight in the recommendations that children and young people who are likely to benefit from CITB treatment are those with bilateral spasticity, typically affecting both upper and lower limbs, and moderate or severe motor functional problems (GMFCS level III, IV or V).

The GDG agreed, based on clinical opinion, that there were circumstances in which CITB treatment would not be appropriate and that this should be highlighted in the recommendations. The group noted that the reduction in spasticity that CITB treatment is likely to achieve would not be helpful if the child or young person depended on this increased tone to compensate for muscle weakness and to support function. In order to receive CITB treatment, a child would need to be physically big enough so that the CITB infusion pump could be comfortably accommodated. As individual development varies greatly in children with spasticity, the GDG did not think it would be helpful or possible to give a precise age at which an infusion pump could first be implanted. Instead, the recommendation simply states that the child should not be too small, and in this regard the recommendation is likely to be compatible with the SPCs for those baclofen preparations that are suitable for delivery by injection or infusion (these preparations do not have not have UK marketing authorisation for children younger than 4 years). Local or systemic intercurrent infection would also be a contraindication. In addition the GDG noted, based on clinical experience, that CITB would also generally be contraindicated in children and young people:

- with co-existing medical conditions (for example, uncontrolled epilepsy or coagulation disorders)
- with malnutrition (because risk of infection and delayed wound healing is increased when surgery is performed in poorly nourished patients)
- with respiratory disorders associated with a risk of respiratory failure
- who had undergone a spinal fusion procedure (where it is considered that the technical challenges of pump implantation predispose the child or young person to greater post-operative morbidity, including infection and leaking of the CSF).

Due to the invasive nature of the intervention and associated risks, the GDG decided that was essential to monitor the response to CITB treatment accurately to determine whether it was effective and should be continued. The GDG concluded that this monitoring should reflect the pre-implantation assessments (that is, it should take account of intended goals and the criteria for a satisfactory response to ITB as outlined above). As before, the GDG concluded that the accuracy of monitoring would be improved if there was continuity in the healthcare professionals conducting the assessments and so the group recommended that assessments should preferably be done by the same professionals who had been involved in the pre-implantation assessments. The group also noted that following pump implantation it may be necessary to titrate the dose of baclofen to optimise effectiveness. If an unsatisfactory response is observed, the GDG’s view was that this should be queried in the first instance to ensure that the conclusions of the monitoring process were not inaccurate and that the treatment itself really had failed. Firstly the group considered that it would be important to check that there were no technical faults in the delivery system and that the catheter was correctly placed to deliver the drug to the intrathecal space. If no such problems were identified, the group considered that the next logical step would be to consider reducing the dose of ITB gradually to determine whether spasticity and associated symptoms increased. However, if after such investigation, the response was confirmed to be unsatisfactory, the specialist neurosurgical centre and other members of the network team should discuss removal of the pump and alternative management options with the child or young person and their parents or carers. Finally once the lifespan of the pump is nearing completion, a gradual reduction in dose should be considered to allow the child or young person to decide whether to continue treatment with a new pump based on their own goals and perceived quality of life.

The GDG recognised that successful CITB treatment was dependent on the support of parents or carers. When considering CITB treatment it is essential that careful consideration be given to family resources for safely supporting a child or young person receiving CITB treatment. The group concluded that when CITB treatment is first considered, children and young people and their parents or carers should be informed verbally and in writing about: the surgical procedure used to implant the pump; the need for regular hospital follow-up visits; the requirements for pump maintenance and the risks associated with pump implantation; pump-related complications and adverse effects that might be associated with ITB infusion. All aspects of this information provision should facilitate decision making on the part of the child or young person and their parents or carers about whether ITB is an appropriate treatment option.

The GDG agreed that after making a decision to proceed to CITB treatment, but before implantation of the pump, appropriate further information should be given verbally and in writing about CITB treatment and its safe and effective management. This information should emphasise that it is dangerous to stop CITB treatment suddenly and that the treatment should not be stopped without seeking advice from a healthcare professional. Children and young people and their parents or carers should understand the intended effects of ITB, the important potential adverse effects, and the need to return to hospital for follow-up appointments. They should be made aware of the symptoms and signs to be expected if the dose of baclofen is inadequate or excessive. They should also be made aware of the symptoms and signs that might suggest pump-related complications. Throughout ITB treatment, children and young people and their parents or carers need to receive support, regular follow-up and a consistent point of contact with the specialist neurosurgical centre, and this emphasized in the recommendations.

Trade-off between net health benefits and resource use

The GDG concluded that cost effectiveness evidence is uncertain due to limited evidence of clinical effectiveness, including improved quality of life. The group questioned whether this may largely be a reflection of the difficulties in capturing meaningful changes in children and young people with moderate or severe spasticity that has not responded to other interventions. The group noted the high degree of satisfaction with the procedure among children and young people and their caregivers and evidence of reduced pain following CITB pump implantation.

The GDG considered whether successful CITB treatment would lead to a reduction in orthopaedic interventions. Orthopaedic intervention is expensive and any reduction in its use should be taken into account when considering the overall cost effectiveness of CITB. The need for an orthopaedic intervention could also be an indirect measure of quality of life.

Although the evidence for clinical effectiveness was limited the GDG's view was that in appropriately selected children and young people CITB treatment could produce clinically important changes that would have a considerable impact on the child or young person's quality of life. CITB treatment can relieve pain from severe muscle spasms and significantly improve posture or function, and these effects would, in turn, allow the child or young person to participate more in daily activities. Therefore, in appropriately selected patients in whom other treatments have not worked, the GDG concluded that the benefits of CITB treatment are likely to justify the costs of implanting the infusion pump. Moreover, the GDG noted that ITB is already used in clinical practice in carefully selected patients, and the absence of unequivocal evidence of cost effectiveness was not sufficient to direct a change in practice away from such use of this treatment.

Other considerations

The GDG's view was that CITB treatment should start within 3 months of satisfactory results being obtained using ITB testing. Delays or refusal of funding for pump insertion after a positive outcome from ITB testing are likely to result in further deterioration in the child or young person's condition, and this would be distressing for them and their parents or carers.

The group noted that, in light of the potential contraindications for CITB (see above), if CITB treatment is indicated in a child or young person with scoliosis and in whom a spinal fusion procedure is likely to be necessary, the infusion pump should be implanted before performing the spinal fusion.

Recommendations

Number | **Recommendation**

Intrathecal baclofen

General principles

83 Consider treatment with continuous pump-administered intrathecal baclofen[††††] 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).

84 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.

85 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.

86 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.

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

88 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.

89 When considering continuous pump-administered intrathecal baclofen, inform children and young people and their parents or carers verbally and in writing about continuous pump-administered intrathecal baclofen. Give information about the following:

- 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.

[††††] At the time of publication (June 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.

Number	Recommendation
	Intrathecal baclofen testing
90	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.

91	Before intrathecal baclofen testing, inform children and young people and their parents or carers verbally and in writing 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.

92	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.
93	The test dose or doses of intrathecal baclofen should be administered using a catheter inserted under general anaesthesia.
94	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.
95	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).
96	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.
97	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.
98	Initial and post-test assessments should be performed by the same healthcare professionals in the specialist neurosurgical centre.

Number	Recommendation
	Continuous pump-administered intrathecal baclofen
99	Before implanting the intrathecal baclofen pump, inform children and young people and their parents or carers, verbally and in writing, 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.
100	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 96).
101	Support children and young people receiving treatment with continuous pump-administered intrathecal baclofen and their parents or carers by offering regular follow-up and a consistent point of contact with the specialist neurosurgical centre.
102	Monitor the response to continuous pump-administered intrathecal baclofen. This monitoring should preferably be performed by the healthcare professionals in the regional specialist centre who performed the pre-implantation assessments.
103	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).
104	Titrate the dose of intrathecal baclofen after pump implantation, if necessary, to optimise effectiveness.
105	If treatment with continuous pump-administered intrathecal baclofen does not result in a satisfactory response (see recommendation 104), 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.
106	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.
107	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.

Number	Research recommendation
19	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?
20	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?
21	What is the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared to usual care in children and young people who are at GMFCS level IV or V? **Why this is important** The GDG's recommendation to consider offering continuous pump-administered intrathecal baclofen focused on children and young people in whom the use of appropriate non-invasive treatments did not relieve difficulties associated with spasticity (specifically pain or muscle spasms, posture or function, or ease of care). Such children and young people will typically be at GMFCS level IV or V. Further research is needed to evaluate the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared with usual care in these children and young people. Relevant research designs include randomised controlled trials, prospective cohort studies and qualitative studies. The outcomes to be investigated as part of the research include: quality of life; reduction of pain; reduction of tone; acceptability and tolerability; participation or inclusion; and adverse effects and their association with any potential predisposing factors.
22	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?

9 Orthopaedic surgery

Introduction

The clinical manifestations of non-progressive brain disorders that cause spasticity may change over time and result in deformities of the limbs or spine. These effects may be due to a combination of abnormal muscle tone resulting in muscle imbalance, joint contractures or bony deformity. Management options include non-operative and operative treatments. Examples of non-operative management include tone reduction with BoNT and lengthening of muscles by applying a plaster cast. The musculotendinous unit can also be lengthened surgically, bony torsions can be treated by osteotomy (bone division), joints can be stabilised by fusion (arthrodesis), displaced hips can be relocated surgically, and spinal deformity can be corrected surgically and stabilised.

Appropriate surgical management procedures will vary between one child or young person and another. Functional goals for the marginal walker (GMFCS level III or IV) will include maintaining existing mobility skills, possibly obtaining independent transfer skills, ensuring comfortable, stable sitting and lying down, and optimising upper and lower limb posture and function. In the non-walker functional aims will include stable, pain-free sitting and lying down, and optimisation of upper and lower limb posture and function. For children and young people in GMFCS level V there is a high risk of developing a spinal deformity and a 90% risk of hip displacement (defined as a migration percentage of greater than 30%). Spinal deformity and hip displacement are potentially amenable to orthopaedic surgery. A child or young person in GMFCS level V may have a 20-degree knee contracture that does not require surgery, but correction of the same knee deformity in a GMFCS level II child or young person may be a key factor in improving that individual's gait pattern.

Functional goals involving the upper limb will include optimisation of upper limb posture and function, but cosmetic aspects are also important. The hand is the most publicly visible part of the body other than the face. Surgery to the upper limb may also benefit function and daily care (for example, lengthening the elbow flexors in a child or young person in GMFCS level V may improve hygiene in the elbow crease and a wrist fusion in a child or young person with hemiplegia may improve hand function). Improvement in hand and wrist posture may child or young person to use a powered wheelchair or communication device.

Children and young people who are able to walk may receive surgery to improve their walking efficiency and also to relieve pain. Historically such gait-improvement surgery occurred as a series of operations over succeeding years (the so-called 'birthday syndrome'). Currently there is a trend to deliver surgery in one procedure, or 'event'. This requires a thorough pre-operative assessment that is often informed by gait analysis to ensure that the optimal combination of surgical procedures is chosen. The surgery is performed on one or both lower limbs and often at different anatomical levels (for example, the hip, thigh, knee, leg or foot). The procedures may include osteotomy of the femur or tibia, bony stabilisation of the foot, and surgery to lengthen or transfer muscles and tendons. Single-event multilevel surgery (SEMLS) is the term used to describe different operations at different anatomical levels that are performed in a single procedure. Rehabilitation after SEMLS may be prolonged and it can take up to 24 months to gain the maximum benefit from this type of surgery. Patients evaluated pre-operatively by gait analysis will usually undergo a similar post-operative evaluation.

The impact of major orthopaedic surgery or SEMLS on the child or young person and their family should not be underestimated. It may take 1 year or more for a child or young person to gain the maximum benefit from the procedure.

A key question is whether or not the SEMLS approach is advantageous for the child or young person when compared with staged surgery.

One difficulty in evaluating surgical results in children and young people with non-progressive brain disorders that cause spasticity is being able to distinguish between post-surgical effects on function and the natural history of the condition and concomitant changes in stature as the child or young person grows. The indication for surgery may coincide with a time in the child or young person's development when function is deteriorating.

No related NICE guidance was identified for the review questions considered in this chapter.

Review questions

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

What is the effectiveness of SEMLS in managing musculoskeletal deformity in children with spasticity caused by a non-progressive brain disorder?

Description of included studies

Four studies were identified for inclusion for this review question (Gorton 2009; Molenaers 2001; Thomason 2011; Yang 2008). The studies addressed the following five comparisons.

- Hip adductor lengthening surgery versus no intervention in children under 6 years of age with bilateral spastic cerebral palsy followed for at least 18 months was evaluated in one retrospective review of case notes (Yang 2008).
- Hip adductor lengthening surgery versus injection of BoNT-A treatment in children under 6 years of age with bilateral spastic cerebral palsy followed for at least 18 months was evaluated in the same retrospective review of case notes (Yang 2008).
- Lower extremity bony or soft tissue surgery versus standard care (no surgery) in ambulatory children (mean age 11.3 years) with hemiplegia, diplegia and quadriplegia was evaluated in one prospective cohort study (Gorton 2009).
- Lower extremity SEMLS and intensive physical therapy versus multilevel BoNT treatment and casting in children and young people aged 4-21 years with hemiplegia or diplegia with generalised joint impairments was evaluated in one retrospective comparative study (Molenaers 2001).
- SEMLS and physical therapy versus physical therapy alone in children and young people aged 6-12 years with cerebral palsy who were in GMFCS level II or III was evaluated in one parallel RCT (Thomason 2011). In this study SEMLS was defined as at least one surgical procedure performed at two different anatomical levels (the hip, knee or ankle) on both sides of the body and was tailored to the child or young person's needs (mean 8 interventions, SD 4 interventions).

Evidence profiles

Orthopaedic surgery

Tendon lengthening versus no intervention

The retrospective study that examined case notes (Yang 2008) did not report optimisation of movement and function. The study evaluated prevention of deterioration.

Table 9.1 Evidence profile for hip adductor lengthening surgery compared with no intervention in children under 6 years of age with bilateral spasticity; hip displacement assessment

Number of studies	Number of participants		Effect		Quality
	Soft tissue surgery	No intervention	Relative (95% CI)	Absolute (95% CI)	
Mean change hip migration percentage over at least 18months (better indicated by lower values)					
1 study (Yang 2008)	60[a]	69[b]	-	MD 8.00 lower (10.88 lower to 5.12 lower)*[c]	LOW
Mean change hip migration percentage per year (better indicated by lower values)					
1 study (Yang 2008)	60[d]	69[e]	-	MD 6 lower (8.89 to 3.11 lower)*[c]	LOW

CI confidence interval, MD mean difference, SD standard deviation
a Change from baseline Mean (SD) = -3.3 (6.1)
b Change from baseline Mean (SD) = 4.7 (10.3) p<0.05 from baseline
c p<0.05 reported by authors
d Mean change (SD) -1.6 (4.4)
e Mean change (SD) 4.4 (11.3)

Table 9.2 Evidence profile for high functional ability (GMFCS I and II) compared with low functional ability (GMFCS III and IV) in children under 6 years of age with bilateral spasticity following hip adductor lengthening surgery; hip displacement assessment

Number of studies	Number of participants		Effect		Quality
	Soft tissue surgery GMFCS level I or II	Soft tissue surgery GMFCS level III or IV	Relative (95% CI)	Absolute (95% CI)	
Mean change hip migration percentage per year, subgroup analysis by functional ability (better indicated by lower values)					
1 study (Yang 2008)	28 legs	72 legs	-	MD 2.4 lower	VERY LOW

CI confidence interval, GMFCS Gross Motor Function Classification System, MD mean difference

The study did not report reduction of pain, quality of life, acceptability and tolerability or adverse effects.

Early bony and soft tissue surgery versus no intervention

The prospective cohort study (Gorton 2009) evaluated optimisation of movement and function. One of the outcomes reported was the Gillette Gait Index (GGI).

Table 9.3 Evidence profile for lower extremity bony or soft tissue surgery compared with standard care (no surgery) in ambulatory children; functioning assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Bony and/or soft tissue surgery	**Standard care**	**Relative (95% CI)**	**Absolute (95% CI)**	
Velocity at 1 year (m/second, better indicated by higher values)					
1 study (Gorton 2009)	75[a]	75[b]	-	MD 1. 6 higher*[c]	VERY LOW
GMFM-D score (standing, GMFM version not reported) at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[d]	75[e]	-	MD 2.4 lower* [c]	VERY LOW
GMFM-E score (walking, running and jumping, GMFM version not reported) at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[f]	75[g]	-	MD 2.8 lower*[c]	VERY LOW
GMFM-66 score at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[h]	75[i]	-	MD 1.8 lower*[c]	VERY LOW

ANCOVA analysis of covariance, CI confidence interval, GGI Gillette Gait Index, GMFM-66 Gross Motor Function Measure 66-item version, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference, PODCI Parent Pediatric Outcomes Data Collection Instrument

* Calculated by the NCC-WCH

a Mean change from baseline at 1 year = 1.3

b Mean change from baseline at 1 year = - 0.3

c No statistically significant difference (p > 0.05) by ANCOVA with baseline means adjusted for PODCI transfers and Basic Mobility, GGI, velocity< earlier BoNT injection, earlier surgical procedure and study site (as a proxy for surgeon)

d Mean change from baseline at 1 year = 0.0

e Mean change from baseline at 1 year = 2.4

f Mean change from baseline at 1 year = -0.7

g Mean change from baseline at 1 year = 2.1

h Mean change from baseline at 1 year = 0.0

i Mean change from baseline at 1 year = 1.8

The study did not report prevention of deterioration but it did report quality of life assessment.

Table 9.4 Evidence profile for lower extremity bony or soft tissue surgery compared with standard care (no surgery); quality of life assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Early bony and/or soft tissue surgery	**No intervention**	**Relative (95% CI)**	**Absolute (95% CI)**	
PedsQL physical functioning scale score at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[a]	75[b]	-	MD 9 higher*[c]	VERY LOW
PedsQL emotional functioning scale score at 1 year (better indicated by higher values)					
1 study	75[d]	75[e]	-	MD 3.4 higher*[f]	VERY LOW

(Gorton 2009)					
PedsQL social functioning scale score at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[g]	75[h]	-	MD 5.4 higher*[f]	VERY LOW
PedsQL school functioning scale score at 1 year (better indicated by higher values)					
1 study (Gorton 2009)	75[i]	75[j]	-	MD 0.6 lower*[f]	VERY LOW

ANCOVA analysis of covariance, CI confidence interval, GGI Gillette Gait Index, MD mean difference, PedsQL Pediatric Quality of Life Inventory, PODCI Parent Pediatric Outcomes Data Collection Instrument
a Mean change from baseline at 1 year = 4.7
b Mean change from baseline at 1 year = -4.3
c P= 0.039 by ANCOVA
d Mean change from baseline at 1 year = 1.2
e Mean change from baseline at 1 year = -2.2
f No statistically significant difference (p>0.05) by ANCOVA with baseline means adjusted for PODCI transfers and Basic Mobility, GGI, velocity< earlier BoNT injection, earlier surgical procedure and study site (as a proxy for surgeon)
g Mean change from baseline = 4.3
h Mean change from baseline = -1.1
i Mean change from baseline = 2.2
j Mean change from baseline = 2.8

The study did not report acceptability and tolerability or adverse effects.

Orthopaedic surgery (any procedure) versus botulinum toxin

The retrospective study that examined case notes (Yang 2008) did not report optimisation of movement and function. The study evaluated prevention of deterioration.

Table 9.5 Evidence profile for lower extremity SEMLS and intensive physical therapy versus multilevel botulinum toxin injections and casting in children and young people with unilateral or bilateral spasticity and generalised joint impairments

Number of studies	Number of participants		Effect		Quality
	Soft tissue surgery	Botulinum toxin	Relative (95% CI)	Absolute (95% CI)	
Mean change hip migration percentage at least at 18 months (better indicated by lower values)					
1 study (Yang 2008)	60[a]	65[b]	-	MD 1.7 lower (4.26 lower to 0.86 higher)*[c]	VERY LOW
Mean change hip migration percentage per year, all children (better indicated by lower values)					
1 study (Yang 2008)	60[d]	65[e]	-	MD 0.9 lower (2.83 lower to 1.03 higher)*[c]	VERY LOW
Mean change hip migration percentage per year, high-functioning children (GMFCS level I or II, better indicated by lower values)					
1 study (Yang 2008)	28 legs[f]	40 legs[g]	-	MD 1 lower (3.4 lower to 1.4 higher)*[h]	VERY LOW
Mean change hip migration percentage per year, low functioning children (GMFCS level III or IV, better indicated by lower values)					

1 study (Yang 2008)	72 legs[i]	90 legs[j]	-	MD 1 lower (2.71 lower to 0.71 higher)*[h]	VERY LOW

CI confidence interval, GMFCS Gross Motor Function Classification System, MD mean difference, NS not (statistically) significant, SD standard deviation
* Calculated by the NCC-WCH
a Change from baseline Mean (SD) = -3.3 (6.1)
b Change from baseline Mean (SD) = -1.6 (8.4)
c p=NS reported
d Change from baseline Mean (SD) = -1.6 (4.4)
e Change from baseline Mean (SD) = -0.7 (6.5)
f Change from baseline Mean (SD) = -3.4 (4.8)
g Change from baseline Mean (SD) = -2.4 (5.2)
h Significance test not reported
i Change from baseline Mean (SD) = -1.0 (4.1)
j Change from baseline Mean (SD) = 0.0 (6.9)

Single-event multilevel surgery

Single-event multilevel surgery versus physical therapy

The RCT (Thomason 2011) evaluated range of movement, optimisation of function and quality of life outcomes.

Table 9.6 Evidence profile for hip adductor lengthening surgery compared with injection of botulinum toxin type A in children under 6 years of age with bilateral spasticity; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Single event multi-level surgery and physical therapy	Physical therapy only	Relative (95% CI)	Absolute (95% CI)	
GMFM-66 at 12 months (better indicated by higher values)					
1 study (Thomason 2011)	11[a]	8[b]	-	MD 1.3 higher*	LOW
GMFM-66 at 24 months(better indicated by higher values)					
1 study (Thomason 2011)	11[c]	-	-	MD 4.9 higher (0.98 higher to 8.7 higher)*	VERY LOW
GGI at 12 months (better indicated by lower values)					
1 study (Thomason 2011)	11[d]	8[e]	-	MD 211 lower*	LOW
GGI at 24 months (better indicated by lower values)					
1 study (Thomason 2011)	11[f]	-	-	MD 213 lower (327 lower to 100 lower)*	LOW

CI confidence interval, GGI Gillette Gait Index, GMFM-66 Gross Motor Function Measure 66-item score, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Baseline mean (SD) = 65.3 (11.1), Score at 12 months mean (SD) = 66.1 (8.9)

b Baseline mean (SD) = 70.3 (11.3), Score at 12 months mean (SD) = 69.8 (11.4)
c Baseline mean (SD) = 65.3 (11.1), Score at 24 months mean (SD) = 70.2 (10.1) Difference from baseline reported as p<0.05
d Baseline mean (SD) = 353 (211), Score at 12 months mean (SD) = 153 (81)
e Baseline mean (SD) = 370 (194), Score at 12 months mean (SD) = 381 (196)
f Baseline mean (SD) = 353 (211), Score at 24 months mean (SD) = 139 (80) Difference from baseline reported as p<0.05

Table 9.7 Evidence profile for hip adductor lengthening surgery compared with injection of botulinum toxin type A in children under 6 years of age with bilateral spasticity; quality of life (parental report)

Number of studies	**Number of participants**		**Effect**		**Quality**
	Single event multi-level surgery and physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
CHQ-PF50 physical functioning domain score at 12 months (better indicated by higher values)					
1 study (Thomason 2011)	11[a]	8[b]	-	MD 3 lower	LOW
CHQ-PF50 physical functioning domain score at 24 months (better indicated by higher values)					
1 study (Thomason 2011)	11[c]	-	-	MD 22 higher (from 4 higher to 39 higher)	VERY LOW
CHQ-PF50 social/emotional function domain score at 12 months (better indicated by higher values)					
1 study (Thomason 2011)	11[d]	8[e]	-	MD 12 lower	LOW
CHQ-PF50 family cohesion domain score at 12 months (better indicated by higher values)					
1 study (Thomason 2011)	11[f]	8[g]	-	MD 11 higher	LOW

CHQ-PF50 Child Health Questionnaire - Parent Form 50, CI confidence interval, MD mean difference, SD standard deviation
* Calculated by the NCC-WCH
a Baseline mean (SD) = 47 (26), Score at 12 months mean (SD) = 58 (26)
b Baseline mean (SD) = 62 (35), Score at 12 months mean (SD) = 76 (25)
c Baseline mean (SD) = 47 (26), Score at 24 months mean (SD) = 69 (18) Difference (95% CI): reported as p<0.05
d Baseline mean (SD) = 69 (34), Score at 12 months mean (SD) = 65 (36)
e Baseline mean (SD) = 89 (21) Score at 12 months mean (SD) = 97 (8)
f Baseline mean (SD) = 72 (20), Score at 12 months mean (SD) =83 (13)
g Baseline mean (SD) = 69 (20), Score at 12 months mean (SD) = 69 (20)

Single-event multilevel surgery versus botulinum toxin

The retrospective study (Molenaers 2001) evaluated optimisation of movement and function.

Table 9.8 Evidence profile for single-event multilevel surgery compared with physical therapy; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Single event multi-level surgery	Botulinum toxin	Relative (95% CI)	Absolute (95% CI)	
Walking velocity (m/second, better indicated by higher values)					
1 study (Molenaers 2001)	43 limbs[a]	43 limbs[b]	-	MD 0.07 lower*[c]	VERY LOW

CI confidence interval, MD mean difference, NS not (statistically) significant
* Calculated by the NCC-WCH
a Mean change from baseline -0.1, p = NS reported
b Mean change from baseline -0.03, p = NS reported
c No comparison across treatment groups given

The study did not report prevention of deterioration, reduction of pain, quality of life, acceptability and tolerability or adverse effects.

Evidence statement

Orthopaedic surgery

Tendon lengthening versus no intervention

No evidence was identified relating to optimisation of movement and function.

With regard to prevention of deterioration, one retrospective review of case notes reported that compared to baseline there was a statistically significant decrease in hip migration percentage (at 18 months or more) and in hip migration percentage per year in children with diplegia and quadriplegia who received hip adductor lengthening surgery compared to those who received no surgical intervention. (LOW) A subgroup analysis that compared the results of high- and low-functioning children with diplegia and quadriplegia (high-functioning, GMFCS level I or II; low-functioning, GMFCS level III or IV) within the group receiving hip adductor lengthening surgery provided evidence that compared to baseline there was a greater reduction in hip migration percentage per year in high-functioning children although the statistical significance of this finding could not be determined. (VERY LOW)

No evidence was identified relating to reduction of pain, quality of life, acceptability and tolerability or adverse effects.

Early bony and soft tissue surgery versus no intervention

With regard to optimisation of movement and function, one prospective cohort study of ambulatory children with hemiplegia, diplegia or quadriplegia provided evidence that compared to baseline there was an improvement in velocity, but a reduction in functioning (GMFM-D, GMFM-E and GMFM-66 across treatment groups) at 12 months after lower extremity orthopaedic surgery was performed compared to standard non-surgical care, although the statistical significance of the findings could not be determined. The study authors reported that there were no statistically significant differences in adjusted mean final score comparisons between treatment groups for these outcomes. (VERY LOW)

No evidence was identified relating to prevention of deterioration.

With regard to quality of life, one prospective cohort study of ambulatory children with hemiplegia, diplegia or quadriplegia provided evidence that compared to baseline there was an improvement in PedsQL physical, emotional and social functioning scale scores, but a reduction in school functioning scale scores at 1 year after lower extremity orthopaedic surgery compared to standard non-surgical care, although the statistical significance of these findings could not be determined. The study authors reported that there was a statistically significant improvement in adjusted mean final score comparisons between treatment groups for physical functioning scale scores after lower extremity orthopaedic surgery compared to standard non-surgical care, but that there were no statistically significant differences in adjusted mean final score comparisons between treatment groups for emotional, social or school functioning scale scores. (VERY LOW)

No evidence was identified relating to acceptability and tolerability or adverse effects.

Orthopaedic surgery (any procedure) versus botulinum toxin

No evidence was identified relating to optimisation of movement and function.

With regard to prevention of deterioration, one retrospective review of case notes of children with diplegia or quadriplegia reported no statistically significant difference in hip migration percentage per year when hip adductor lengthening surgery was compared to BoNT treatment. (VERY LOW)

With regard to prevention of deterioration, one retrospective review of case notes provided evidence that compared to baseline there was a decrease that was not statistically significant in hip migration percentage (at 18 months or more) and in hip migration percentage per year in children with diplegia and quadriplegia who received hip adductor lengthening surgery compared to those who received BoNT treatment. (VERY LOW)

A subgroup analysis of high-functioning (GMFCS level I or II) children with diplegia and quadriplegia within each treatment group provided evidence that compared to baseline there was reduction in hip migration percentage per year that was not statistically significant in those who received hip adductor lengthening surgery compared to those who received BoNT treatment. (VERY LOW)

A subgroup analysis of low-functioning (GMFCS level III or IV) children with diplegia and quadriplegia within each treatment group provided evidence that compared to baseline there was reduction in hip migration percentage per year that was not statistically significant in those who received hip adductor lengthening surgery compared to those who received BoNT treatment. (VERY LOW)

No evidence was identified relating to reduction of pain, quality of life, acceptability and tolerability or adverse effects.

Single-event multilevel surgery

Single-event multilevel surgery versus physical therapy

With regard to optimisation of function, one RCT in children and young people with cerebral palsy who were in GMFCS level II or III provided evidence that compared to baseline there were improvements in overall function (GMFM-66 scores) and walking (GGI scores) at 12 months in those who received SEMLS and physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (LOW) The same RCT provided evidence that compared to baseline there were statistically significant improvements in overall function (GMFM-66 scores) and walking (GGI scores) at 24 months in the group that received SEMLS and physical therapy.

With regard to quality of life, one RCT in children and young people with cerebral palsy who were in GMFCS level II or III provided evidence that compared to baseline there were reductions in CHQ-PF50 physical and social or emotional function domain scores at 12 months, but an improvement in CHQ-PF50 family cohesion domain scores at 12 months in those who received SEMLS and physical therapy compared to children who received physical therapy alone, although the statistical significance of these findings could not be determined. (LOW) The same RCT provided evidence that compared to baseline there was a statistically significant increase in CHQ-PF50 physical function at 24 months in the group that received SEMLS and physical therapy. (VERY LOW)

Single-event multilevel surgery versus botulinum toxin

One retrospective study of children and young people with hemiplegia or diplegia with generalised joint impairments (this term was not defined by the study authors) provided evidence that compared to baseline there was a greater reduction in walking velocity at 12 months in children and young people who received SEMLS and intensive rehabilitation physical therapy compared to those who received BoNT, although the statistical significance of this finding could not be determined. (VERY LOW)

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion:

- tendon transfer versus no intervention
- osteotomy versus no intervention
- joint fusion or arthrodesis versus no intervention
- early bony and soft tissue surgery versus soft tissue surgery alone
- orthopaedic surgery (any procedure) versus physical therapy
- orthopaedic surgery (any procedure) versus orthoses
- early orthopaedic surgery versus delayed orthopaedic surgery
- SEMLS versus interval surgery
- SEMLS versus orthoses.

Health economics

No economic evaluations for orthopaedic surgery were identified in the literature search conducted for the guideline. There was limited clinical evidence available to answer the review questions considered in this chapter and the evidence identified was of poor quality and involved short-term follow-up. The GDG's experience was that surgery could be beneficial in improving function, including mobility, reducing pain and increasing comfort, cosmetic improvements, and preventing deterioration. Improvements in these areas can have a significant impact on a child or young person's health-related quality of life.

Surgery is an expensive treatment option requiring time in hospital and rehabilitation afterwards. Reference costs relating to orthopaedic surgery are reported in Chapter 11. Surgery is also an invasive treatment option; there are risks associated with any surgery, and there can be adverse events related specifically to the types of orthopaedic surgery considered here.

There was not enough clinical evidence available from the literature to develop a health economic analysis that could aid the GDG's decision making. Since a number of different surgical procedures were considered here, using the NICE threshold for cost effectiveness to determine the level of effectiveness needed did not seem suitable for these review questions. Further research is needed to investigate effectiveness of surgery in terms of function, pain reduction, and impact on quality of life. Long-term outcomes should be recorded as part of future research to aid understanding of how orthopaedic surgery affects different groups of children and young people according to limb involvement and the severity of their spasticity.

Evidence to recommendations

Relative value placed on the outcomes considered

The aims of orthopaedic surgery include improving function, correcting deformity and alleviating pain, as well as improving ease of care and cosmesis. Outcomes concerning optimisation of movement and function selected by the GDG included domains likely to be relevant to outcomes of orthopaedic surgery. The GDG recognised that more complex studies of gait are often undertaken, for example, in the setting of a 'gait laboratory'; such approaches can assess a range of potentially informative measures that may be useful in determining an appropriate treatment plan for individual patients. Many research studies present detailed and varied outcomes based on these sophisticated approaches to assessing gait, but the GDG did not choose to include all of these in their examination of the evidence, preferring to restrict their search to studies reporting velocity and distance because these outcomes are important to patients.

Hip migration percentage is the orthopaedic standard used to evaluate hip displacement in children and young people who have spasticity as a result of a non-progressive brain disorder. The reduction or relief of pain is also a relevant surgical outcome measure. Quality of life, acceptability and tolerability and complications are also key surgical outcome measures. Long-term follow-up is desirable, but there is a difficulty in separating the effects of an intervention from those relating to the natural progression of the condition over time.

Trade-off between clinical benefits and harms

The evidence identified in the review was very limited. It showed that there may be some benefit to some children or young people of specific orthopaedic procedures (for example, hip abductor lengthening surgery), but the evidence was not sufficiently robust for the GDG to reach any meaningful conclusions (see 'Quality of the evidence' below). The GDG therefore used their own judgement and clinical experience to consider the likely benefits and harms of orthopaedic interventions.

Despite the lack of research evidence the GDG considered that orthopaedic surgery can be effective in correcting deformity and improving function in children and young people who have spasticity as a reult of a non-progressive brain disorder. Orthopaedic surgery is based on rational principles of altering the structure of muscles and bones to alleviate deformity and pain and to improve function. The use of surgery is based on extensive experience gained over many years and the GDG agreed that expert surgical intervention in appropriately selected patients would lead to worthwhile clinical improvements.

In their deliberations about the recommendations the GDG noted the following risks associated with orthopaedic surgery. In the first place they noted that the risks of orthopaedic surgery for the management of spasticity included all the general risks of any surgical procedure, for example, the need for general anaesthesia. The group also noted that it might take 1-2 years for patients to recover fully and gain the full benefit from SEMLS. Even if surgery might be beneficial in principle, the tendency for spasticity and its complications to progress over time might hide such benefits. Orthopaedic surgery may be a major procedure with attendant risks of pain, haemorrhage and infection, but immediate post-operative pain after surgery in the lower limbs could be managed effectively with epidural analgesia. The risks of haemorrhage requiring blood transfusion would vary, but become greater with more extensive surgery. For example, a mean blood loss of 15.4 ml/kg for a hip reconstruction has been reported (McNerney 2000) as has an average total blood loss of 2.8 l during posterior spinal surgery for scoliosis (Tsirikos 2008). In operations that require division and stabilisation of bone with metallic internal fixation devices there is a risk of non-union of bone. This is unlikely after limb or pelvic surgery, but it is seen after surgery to correct or improve a spinal deformity. For example, in 5% (5/93) of patients in a case series required further surgery to repair a pseudarthosis (non-union) of the spine (Lonstein 2011).

While the risks of surgery were considered to be significant, the GDG agreed that it was also likely that orthopaedic surgery would result in significant benefits to the child or young person in specific circumstances.

Orthopaedic surgery can be used for fixed bony deformity (a common complication of spasticity), which cannot be corrected with non-surgical treatments. There are also limits to non-operative improvement or correction of fixed shortening of a musculotendinous unit or a contracture. The choice for children and young people and their families and carers may be between accepting a fixed deformity with its associated disadvantages or the child or young person undergoing an orthopaedic procedure to improve or correct the deformity.

It is well recognised that the likelihood of hip displacement (hip migration percentage greater than 30%) increases with GMFCS level, and children and young people in level IV or V are at particular risk (Soo 2006; Hägglund 2007). Hip displacement can cause pain, decreased ability to tolerate sitting or standing, and increased difficulty with perineal care and hygiene. It may also cause shortening of the thigh on the affected side and increased tone in the hip musculature and possible muscle shortening as a result of the displacement. These problems can have a significant adverse effect on a child or young person's comfort during sitting and daily activities. The GDG recognised that in every child or young person with spasticity consideration should be given to the possibility of hip displacement because this is a complication of major importance, it being common and having a major impact on the child or young person and forming a significant workload for orthopaedic surgeons.

The GDG also highlighted spinal deformity (such as scoliosis or kyphosis) as common complication of spasticity that can affect a child or young person's ability to sit and, in some, can limit use of their upper limbs; when severe it can also have an adverse effect on cardio-pulmonary function. Spinal deformity can have a significant impact on comfort of the child or young person and their ability to function. In severe instances, impingement of the ribs against the pelvis may be painful. The GDG was aware that if surgery is undertaken early it can improve the spinal deformity and provide the secondary benefits of stable and comfortable seating and potential improvement in upper limb function. While the GDG acknowledged that the management of these specific conditions was outside of the scope of the guideline (meaning that specific recommendations to this effect could not be included in the guideline) the group agreed that clinical recognition of spinal deformity before it becomes severe is an important aspect of the management of spasticity which should prompt an orthopaedic assessment.

Problems with the posture of the shoulder girdle and upper limb caused by spasticity can limit function and reduce a child or young person's independence and ability to participate in activities. Additionally, upper limb contractures can cause difficulties with skin hygiene, particularly in the axilla, wrist creases and hand. Adverse posture, loss of range of movement, fixed muscle shortening and skeletal deformities of the lower limbs can often affect walking adversely. This may result in pain, loss of walking efficiency and can, for some patients, eventually threaten independent walking. There are limits to the extent to which non-operative management can help in these circumstances and orthopaedic surgery may be indicated to correct fixed deformities and improve walking efficiency. The GDG agreed, therefore, that an assessment by an orthopaedic surgeon should be considered for children and young people with any of the following:

- upper limb function (for example, putting on or taking off clothing) is limited by muscle shortening due to spasticity, contractures or bony deformities resulting in an unfavourable limb posture, or pain
- lower limb function (for example, walking) is limited by muscle shortening due to spasticity, contractures or bony deformities resulting in an unfavourable limb posture, or pain
- 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.

Given the risks involved, the GDG concluded that it was important to carefully select patients likely to benefit from surgery (for example, those who are at high risk of hip dislocation and who might benefit from surgery to prevent such an outcome). If non-surgical management is a possibility, then due consideration should be given to less invasive treatment options. However, on balance, the potential benefits to the child or young person from judicious surgery would outweigh potential adverse effects. The group also noted that effectiveness could only be assured if the child or young person was receiving an appropriately adapted programme of physical therapy.

The GDG agreed that the key aspects of mitigating risks and maximising benefit for this intervention included monitoring leading to timely access to surgical service, patient selection, the expertise of those performing the surgery, information sharing, the setting in which surgery takes place, rehabilitation including any adjunctive treatment and assessment.

The GDG agreed that specific expertise was necessary to ensure appropriate patient selection as the indications for surgery are extremely varied and the decision would be effected by many specific factors, for example, comorbitites, family circumstances, or the child or young person's individual preferences. For this reason the GDG did not think it was helpful to list specific indications for particular surgical interventions, but instead recommended that children and young people who were likely to benefit should undergo a surgical assessment with the implication that suitable candidates would then proceed to surgery.

Given the complexity of the decision making process the GDG consensus was that orthopaedic surgery should be undertaken by surgeons who are expert in the concepts and techniques involved in surgery for this group of patients. The group also considered that the decision should not take place in isolation, but be considered as part of a wider management programme for the child or young person and in collaboration with other experts who might have a better understanding of the child or young person's individual circumstances or needs, or would be involved in delivering post-operative care, for example, a paediatrician or paediatric neurologist, and a physiotherapist or occupational therapist. Many children and young people in GMFCS level IV or V have significant comorbidities, including nutritional and respiratory problems. Those undergoing surgery to relocate the hip or for scoliosis are at risk of post-operative chest infection and weight loss. Many patients are below the 25th centile for weight and poor pre-operative nutritional status is a risk factor for wound infection after scoliosis surgery (Jevsevar 1993); such effects may occur in up to 10% of patients (Szoke 1998; Sponseller 2000). The group were aware, however, that such multidisciplinary working does not always occur in current practice. For this reason that GDG agreed that, although surgery is not appropriate for every child or young person, it should not be isolated from the network of care. Instead the group recommended that surgical expertise should be included in the network team so that these services are covered by the same stipulations regarding use of agreed care pathways, effective communication and integrated team working outlined in the recommendations about principles of care (see Chapter 4 for further details of the rationale for these recommendations). The GDG noted that the success of surgery is contingent on a high level of commitment on behalf of the child or young person and their family, includes a significant rehabilitation period and often the use of other adjunctive treatments. The group therefore recommended that 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 and any specific risks associated with the surgery; details of the rehabilitation programme, including how and where it will be delivered, and what the components will be (for example, a programme of adapted physical therapy, the use of orthoses, or treatment with oral drugs or BoNT-A).

In addition the GDG felt it was necessary to specify that orthopaedic surgery should take place in a paediatric setting to allow the use of appropriate perioperative pain relief, paediatric anaesthesia and access to paediatric nursing skills and therapies. Many children and young people with spasticity will have comorbidities (for example, feeding difficulties, epilepsy, and communication or learning difficulties). Surgery in a child or young person with potentially complex needs carries a higher risk of perioperative complications than usual. The GDG considered that SEMLS offers potential advantages over interval surgery for children and young people undergoing surgery to improve gait because, typically, the surgery would require one hospital admission and one period of rehabilitation. Patients undergoing SEMLS to improve gait would require a thorough pre-operative assessment. Gait analysis is considered to be the pre-operative 'gold standard' when evaluating children and young people with complex motor disorders who are likely to benefit from multilevel lower limb surgery to improve their gait and function (Thomason 2011). Identifying gait pathologies pre-operatively informs the surgical team of procedures such as tendon and muscle surgery, osteotomies and foot stabilisation from which the child or young person is likely to benefit.

The GDG considered that it was essential to assess the outcomes of surgical procedures, but the group did not think it would be helpful or possible to list specific assessment techniques, as these would depend on the specific intervention and treatment goals, which, for the reasons outlined above, would be extremely variable. Generally the group did not make any specific recommendations in this regard, therefore, but considered that this would be implicit in their recommendation that surgeons carrying out the procedure should be expert in the concepts and techniques involved in surgery for this group of patients. The GDG made one exception to this, which was to specify that assessment following surgery to improve gait should take place 1-2 years later because this would take account of the normal recovery period and therefore ensure that the outcome of the procedure is accurately determined.

The GDG considered that delaying surgery until function has deteriorated could reduce the effectiveness of the surgery. The group considered, therefore, that surgery should not be considered a last resort, but an adjunct to other management techniques. This should be reinforced through the early involvement of an orthopaedic surgeon even if this does not result in the child or young person undergoing a surgical procedure. The GDG considered that this was particularly relevant to preventing hip displacement and that the best way to ensure timely referral was to recommend that monitoring is undertaken from the point at which the child or young person is first referred to the network of care. As this monitoring would take place before referral to the surgeon it would be the joint responsibility of the network team. Thus, although the rationale for these recommendations is based on the GDG's experience regarding the effectiveness of orthopaedic surgery, the corresponding recommendations are presented as principles of care (see Chapter 4).

The GDG made a recommendation that network care pathways should include a pathway to ensure that children and young people at increased risk of hip displacement are appropriately monitored. The group also drew up a list of clinical indications of possible hip displacement, based on their clinical expertise. The group noted that when a hip is displaced, it is common for there to be reduction in hip mobility often associated with deterioration in hip abduction and in some cases by increased difficulty with sitting or standing and with perineal care or hygiene. There may be an increase in hip muscle tone. In some cases dislocation of the hip may be associated with a difference in the length of the legs. Some children and young people will experience pain in these circumstances.

The GDG considered that in addition to clinical monitoring and surveillance for hip problems, based on current practice and their clinical experience, radiological monitoring was also important. The GDG was aware of the adverse effects associated with X-rays and therefore thought it was important to strike a balance between the benefit of identifying hip displacement and unnecessarily exposing children and young people to radiation. While the group was aware of the existence of published international practice guidance and/or consensus statements on this topic, these did not meet the inclusion criteria for the guideline review. Ultimately the group concluded that a hip X-ray should be performed in children and young people in whom, based on clinical judgement, there are concerns about possible hip displacement. The group also agreed that a hip X-ray should be performed at 24 months in children and young people with bilateral cerebral palsy. For children and young people who are in GMFCS level III, IV or V, the group decided that repeating the X-ray annually should be considered on an individual basis. Repeating the X-ray every 6 months and/or orthopaedic assessment should be considered on an individual basis for children and young people with a hip migration percentage that is greater than 15% or is increasing by more than 10% per year. The GDG did not consider it was necessary to recommend radiological monitoring for any other groups of children or young people on the premise that they were not at sufficient risk to justify the adverse effects of the X-ray and because they would already be covered by the overarching recommendations about clinical monitoring and indications for assessment.

The GDG considered that the recommendation that the network team should monitor the child or young person's condition for worsening of spasticity and the development of secondary consequences of spasticity (this is presented under principles of care; see Chapter 4) would be sufficient to ensure that relevant children and young people receive timely surgical assessment for the indications listed above to do with limitations with upper or lower limb function, contractures causing problems with skin hygiene and cosmetic concerns.

Trade-off between net health benefits and resource use

Orthopaedic surgery is an expensive treatment option requiring time in hospital and rehabilitation afterwards. The GDG's experience is that such surgery can be beneficial in improving function including mobility, reducing pain and increasing comfort, improving cosmesis, and also preventing deterioration. The GDG considered that orthopaedic surgery is likely to be a good use of resources for appropriately selected children and young people.

Appropriate monitoring of a child or young person who has spasticity as a result of a non-progressive neurological condition will result in better outcomes of future surgery because this will enable timely identification of any problems.

Quality of evidence

One study suggested a clinical benefit from orthopaedic surgery in the prevention of hip migration (Yang 2008). It showed that hip adductor lengthening surgery significantly decreased hip migration compared with no treatment. This was based on evidence of low quality. The same study found a greater reduction in hip migration percentage per year in high-functioning children, but the statistical significance of this finding could not be determined.

Another low quality study reported a statistically significant increase in functioning 1 year after lower extremity orthopaedic surgery compared to standard non-surgical care. However, this finding was based on evidence of very low quality.

No studies that compared SEMLS with staged surgery were identified for inclusion. One RCT was identified that compared SEMLS to physical therapy alone (Thomason 2011) and reported a statistically significant improvement in the GGI at 12 months in children and young people undergoing additional surgery. One study comparing SEMLS and rehabilitation of children and young people with unilateral spasticity affecting an arm and a leg or bilateral spasticity affecting the legs, but no statistically significant difference outcome was reported (Molenaers 2001).

All of the available studies had important limitations. Two studies (Yang 2008; Gorton 2009) included children with unilateral spasticity affecting an arm and a leg, bilateral spasticity affecting the legs only, or bilateral spasticity affecting both arms and legs; these studies reported results from all patterns of spasticity together. It would have been more informative to have results reported separately for each of these very different clinical subgroups. One study (Yang 2008) was a retrospective cohort study based on review of case notes and radiological records children in South Korea. There might have been important differences compared to clinical practice in the UK. Two further studies (Gorton 2009; Molenaers 2001) had follow-up periods of only 12 months, and the RCT (Thomason 2011) only provided pre-post treatment data for the children and young people who had received SEMLS to 24 months. The GDG's experience was that it might take longer for patients to gain the maximum benefit from orthopaedic surgery. Only a limited number of the outcomes identified as important by the GDG were reported in the literature.

Recommendations

Number	Recommendation
	Orthopaedic surgery
108	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.
109	An assessment should be performed by an orthopaedic surgeon within the network team if: • based on clinical findings (see recommendation 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.
110	Consider an assessment by an orthopaedic surgeon in the network team for children and young people with: • hip migration greater than 15% **or** • hip migration percentage increasing by more than 10 percentage points per year.
111	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

Number	Recommendation
	the child or young person.

112	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.

113	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.
114	The decision to perform orthopaedic surgery to improve gait should be informed by a thorough pre-operative functional assessment, preferably including gait analysis.
115	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.
116	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.

Number	Research recommendation
23	What is the clinical and cost effectiveness of soft tissue surgery in terms of preventing hip dislocation?
24	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?

10 Selective dorsal rhizotomy

Introduction

SDR is a neurosurgical operation on nerves entering the spinal cord. The aim of SDR is to improve gross motor function, particularly the ability to walk, by reducing muscle spasticity. The operation was first performed in 1908 and developed further in the 1980s by Peacock who was responsible for introducing SDR into the USA. SDR is currently available in a number of centres in the USA and Canada, but only one centre in England and Wales has performed the operation on a regular basis and published results.

SDR involves identifying nerve roots coming into the spinal cord from leg muscles and severing some of them. One of two approaches may be used to access the nerve roots: the first involves removing six to eight lamina (multilevel approach); the second (less invasive) approach is to remove and replace just one or two lamina (single level approach). Resection of the nerve roots interrupts the abnormal circuit of nerve impulses that keeps muscle tone high. The nerve roots must be identified correctly during the operation using electrical stimulation. If nerve roots coming into the spinal cord from the skin, bladder or bowel are cut then the patient may develop numbness or bladder or bowel incontinence.

SDR is irreversible and selecting appropriate children and young people to undergo the procedure is very important. The surgical technique requires good exposure of nerve roots and meticulous attention to identification of roots that will be cut. In the literature, the percentage of nerve roots cut varies from 14-50%. Nerve roots to be cut are from lumbar 1 (L1) level to sacral 2 (S2) level, although some surgeons avoid cutting S2 roots to reduce the risk of incontinence.

Potential complications of SDR may be temporary or permanent, and kyphoscoliosis (curvature of the spine) or spondylolisthesis (slipped vertebrae) may occur afterwards. As with any other irreversible operation, the benefits should outweigh the potential complications before proceeding.

Most children and young people who have undergone SDR have had spastic diplegic cerebral palsy and, since the aim of the operation is to improve the child or young person's ability to walk, most were in GMFCS level II or III.

After SDR, most children and young people are weak, and they may initially lose motor ability. An intensive period of rehabilitation is required after the surgery, and the setting (inpatient or outpatient care during the rehabilitation period) will be a consideration. The full benefits of SDR might not be realised for up to 1 year after the surgery, and the ongoing need for physical therapy is a major commitment for the child or young person and their family.

'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) contains the following recommendations.

- Evidence relating to SDR for spasticity in cerebral palsy highlights a risk of serious but well-recognised complications. The evidence on efficacy (that is, how well the procedure works in the studies in which it has been evaluated) is adequate and the procedure may be used provided that normal arrangements for clinical governance and audit are in place.
- As part of the consent process parents and carers should be informed that the procedure is irreversible, and that SDR sometimes leads to deterioration in walking ability or bladder function, or later complications including spinal deformity. Parents and carers should

understand that prolonged physical therapy (specifically physiotherapy) and aftercare will be required and that additional surgery may be required.

- Selection of patients and their treatment should be carried out by a multidisciplinary team with specialist training and expertise in the care of spasticity in patients with cerebral palsy, and with access to the full range of treatment options. The team would normally include a physiotherapist, a paediatrician and surgeons, all with specific training and expertise.
- NICE encourages further research into SDR, especially in relation to long-term outcomes. Outcome measures should include the incidence of neurological impairment and spinal deformity, the need for additional operations, and assessment of disability, social inclusion, and quality of life.

Although 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) makes recommendations on the safety and efficacy of SDR, it does not address whether or not the NHS in England and Wales should fund SDR. The remit of this clinical guideline includes evaluation of the clinical and cost effectiveness of SDR. The GDG prioritised consideration of SDR combined with physical therapy as compared to physical therapy and no SDR (with or without other interventions) in children and young people who have spasticity, with or without other motor disorders (dystonia, muscle weakness or choreoathetosis) as a result of a non-progressive brain disorder.

The search strategy used for this question was the same as the search strategy used during development of 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373). Thus, the GDG considered all the evidence identified for inclusion in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373), plus evidence published more recently. In accordance with the NICE guideline development process, a specific review protocol was developed for the guideline. The guideline review protocol identified specific populations, interventions (combinations of SDR with other interventions such as physical therapy), comparators, and outcomes on which to base decisions regarding clinical and cost effectiveness of SDR. The guideline review process differed further from the process used in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) in that the GRADE approach was used to grade the quality of the evidence included in the guideline review, and the GDG's interpretation of the evidence and formulation of recommendations was explicitly linked to the graded evidence. In particular, the guideline review focused on the best quality evidence, and so it included only prospective comparative studies and case series involving more than 200 children or young people. 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373), in contrast, included evidence from small non-comparative studies and retrospective comparative studies. Compared to 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373), the GDG prioritised additional outcomes for consideration, including AROM. The GDG also considered outcomes measured at different follow-up points (for example, 6 months, 9 months, 12 months and 24 months) separately, rather than pooled outcomes over all time points. This approach has the potential to distinguish between temporary and sustained (or immediate and delayed) outcomes.

Review question

What is the clinical effectiveness of SDR in children and young people with spasticity caused by a non-progressive brain disorder?

Description of included studies

Seven studies were identified for inclusion for this review question (Abbott 1992; Buckon 2004b; Engsberg 2006; Kim 2001; McLaughlin 1998; Steinbok 1997; Wright 1998). The studies addressed two comparisons (SDR plus physical therapy versus physical therapy alone, and SDR plus physical therapy versus orthopaedic (soft tissue) surgery plus physical therapy), although two of the studies were non-comparative (see below).

Three parallel RCTs (McLaughlin 1998; Steinbok 1997; Wright 1998) and one non-randomised prospective study (Engsberg 2006) compared SDR plus physical therapy to physical therapy alone. A total of 90 children and young people, all of whom had diplegia, were included in the three RCTs. One RCT included children aged 3-7 years (Steinbok 1997), another included children and young people aged 3-18 years (McLaughlin 1998), and the remaining study did not specify the age range of the participants (although the mean age was 4 years 10 months; Wright 1998). The non-randomised prospective study (Engsberg 2006) presented outcomes for 84% (65/77) of the children and young people with spastic diplegic cerebral palsy (GMFCS level I, II or III) and 40 children and young people with no disability who were included in the study. The mean ages (SDs) of the children and young people were 9.0 (5.3) years in the SDR plus physical therapy group and 9.7 (4.5) years in the physical therapy alone group.

Two of the RCTs reported that all SDR operations were performed by the same surgeon (McLaughlin 1998; Wright 1998). Two trials conducted rhizotomies from L2 to S2 (Steinbok 1997; Wright 1998), and the other trial conducted rhizotomies from L1 to S2 (McLaughlin 1998). The percentages of dorsal roots transected were 58% for L2 to S1 and 40% for S2 (Steinbok 1997), 50% on average of each dorsal root (Wright 1998), and 26% (range 14% to 50%) from L1 to S2 (McLaughlin 1998). The non-randomised prospective study conducted rhizotomies from L1 to S2 transecting approximately 65% of rootlets (Engsberg 2006).

Similar quantities and types of physical therapy (specifically physiotherapy) were received by both groups in one RCT (Steinbok 1997). The techniques used included passive movements, strengthening and NDT. Weight-bearing exercises were emphasised in both treatment groups. Measures were taken to maintain blinding of physiotherapists. In another RCT (Wright 1998) all participants received similar types of physical therapy, but those who underwent SDR plus physical therapy had higher treatment intensity during their 6-week post-operative stay to improve strength in the trunk and lower extremities. The physical therapy techniques used in both treatment groups in this RCT included range of movement, strengthening through functional activities, facilitation of normal movement patterns and postural control, standing and gait-related activities, and work on fine motor skills and functional abilities. In the third RCT (McLaughlin 1998), the techniques used were described in less detail, but they were reported to be tailored to the individual child or young person's needs. The emphasis and techniques used were reported to be appropriate for children and young people undergoing SDR, and 20 different categories of treatment were documented by the treating community physical therapists. In the non-randomised prospective study, the SDR plus physical therapy group received physical therapy sessions in their home towns four times per week for 8 months after discharge. Treatments were then reduced to three times per week for an additional 12 months. The physical therapy alone group received the same number of physical therapy sessions. Treatment in both treatment groups concentrated on the trunk and lower extremities, on strengthening, and on functional activities. Billing data were used to confirm that both groups received similar amounts of physical therapy (Engsberg 2006).

Caregivers were masked to treatment allocation in two RCTs (Steinbok 1997; Wright 1998), but not in the other (McLaughlin 1998). Outcome assessors were masked to treatment allocation in all three studies. One RCT (Wright 1998) reported that assessors were able to distinguish between treatment groups, but they were not involved in providing care for the participants. Children and young people in both groups in the non-randomised prospective study were similar at baseline for age, sex, weight, GMFCS level and gait status, and all were judged to be suitable candidates for SDR. Details of the recruitment process, inclusion and exclusion criteria and baseline clinical assessments were reported in the article (Engsberg 2006).

Outcomes were reported at 6 months in one RCT, 9 months in one RCT, 12 months in two RCTs, and 24 months in one RCT. All three RCTs used MAS scores to assess tone and reported the GMFM scores. One RCT reported range of movement, and one reported walking. No evidence was identified for GAS, PEDI, acceptability and tolerability (as reported by the child or young person or their parent or carer) or the CHQ for quality of life. None of the RCTs reported mortality rates. In one RCT (McLaughlin 1998), back and lower extremity pain and urinary problems were reported via an adverse effects questionnaire administered by the investigators every 3 months over the 24-month follow-up period. Outcomes were reported at 8 months and 20 months in the non-randomised prospective study (Engsberg 2006).

One non-randomised prospective study (Buckon 2004b) compared SDR plus physical therapy to orthopaedic (soft tissue) surgery plus physical therapy. Twenty-five children with spastic diplegia (age range 4-10 years; mean age 71.3 months) and their parents were invited to choose between SDR and soft tissue surgery after receiving information about both procedures. The orthopaedic surgeon and neurosurgeon who performed the procedures were reported to be in clinical equipoise in relation to their judgements about the effectiveness of the treatments. The selection criteria for SDR were: age 4-10 years; predominantly spastic disorder; good trunk control; lower extremity contractures < 10 degrees; able to isolate lower-extremity movements; follow-up physical therapy available (three or four times per week); history of prematurity; no significant ataxia, athetosis or scoliosis; good lower-extremity antigravity strength; ambulatory with or without assistive devices; and co-operative. The inclusion criteria for soft tissue surgery were kinematic dysfunction and evidence of dynamic limitation of movement and spasticity on static examination that would benefit from muscle and tendon lengthening, release or transfer. Parents were given a booklet, counselling from both surgeons, the opportunity to talk to physical therapists and other physicians, and were assisted in finding published articles to inform their decisions. Parents returned 1 month after the initial assessment to have any remaining questions answered, and to inform the clinical staff of the family's decision.

Eighteen families chose SDR, and the other seven chose soft tissue surgery. The children in the SDR group had a mean age of 71.3 months; 17 were community ambulators (11 without and six with assistive devices), and one was a household ambulator (GMFCS level I, n = 3; level II, n = 8; level III, n = 7). The children in the soft tissue surgery group had a mean age of 78.6 months; six were community ambulators (three without and three with assistive devices), and one was a household ambulator (GMFCS level I, n = 2; level II, n = 2; level III, n = 4). The majority of orthopaedic procedures performed were releases and lengthenings, although two children also had osteotomies. The participants received post-surgical physical therapy that was standard for the intervention that they received. Functional outcomes were assessed using the Gross Motor Performance Measure (GMPM), GMFM and PEDI at baseline and at 6 months, 12 months and 24 months after surgery.

Two case series (Abbott 1992; Kim 2001) reported non-comparative evidence on post-operative and long-term urinary problems, post-operative ileus, scoliosis and hip subluxation in children and young people who underwent SDR. One case series included children and young people aged 2-13 years (Kim 2001), and the other did report not the age range of the participants (Abbott 1992).

Evidence profiles

Selective dorsal rhizotomy plus physical therapy versus physical therapy alone

Reduction of spasticity and optimisation of movement

All three RCTs identified for inclusion used MAS scores to assess tone at the elbow, hip, knee, ankle, and overall tone. Outcomes were assessed at 6 and 12 months (Wright 1998), at 9 months (Steinbok 1997), and at 12 and 24 months (McLaughlin 1998). Range of movement was measured at 9 months (Steinbok 1997), while AROM and PROM were measured at 6 months and 12 months (Wright 1998) and AROM was measured at 8 months and 20 months in the non-randomised prospective study (Engsberg 2006).

Table 10.1 Evidence profile for selective dorsal rhizotomy and physical therapy compared with physical therapy only in children with diplegia; tone and joint movement assessment

Number of studies	**Number of participants**		**Effect**		**Quality**
	Selective dorsal rhizotomy and physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
Mean change in AROM, trunk rotation at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[a]	36[b]	-	MD = 4 lower*	VERY LOW

Mean change in AROM, trunk rotation at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[c]	36[d]	-	MD = 3 lower*	VERY LOW
Mean change in AROM, pelvis rotation at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[e]	36[f]	-	MD = 1 lower*	VERY LOW
Mean change in AROM, pelvis rotation at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[g]	36[h]	-	MD = 2 lower*	VERY LOW
Mean change in AROM, pelvic tilt at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[i]	36[j]	-	MD = 2 lower*	VERY LOW
Mean change in AROM, pelvic tilt at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[k]	36[l]	-	MD = 2 lower*	VERY LOW
Mean change MAS score, hip adductors at 9 months (better indicated by lower values)					
1 study (Steinbok 1997)	14	14	-	MD 1.1 lower (1.54 to 0.66 lower)*	MODERATE
Mean change in AROM, hip extension at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[m]	12[n]	-	MD = 19.6 lower*	MODERATE
Mean change in AROM, hip flexion/extension at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[o]	36[p]	-	MD = 3 higher*	VERY LOW
Mean change in AROM, hip extension at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD 19.1 higher (11.95 to 26.25 higher)*	HIGH
Mean change in AROM, hip extension at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[q]	12[r]	-	MD = 3.7 lower*	MODERATE
Mean change in AROM, hip flexion/extension at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[s]	36[t]	-	MD = 3 higher*	VERY LOW
Mean change in PROM hip extension at 6 months (better indicated by higher values)					
1 study (Wright	12[u]	12[v]	-	MD = 5.5	MODERATE

1998)				higher*	
Mean change in PROM, hip extension at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[w]	12[x]	-	MD = 0*	MODERATE
Mean change MAS score, knee at 6 months (better indicated by lower values)					
1 study (Wright 1998)	12[y]	12[z]	-	MD = 1 lower*	MODERATE
Mean change MAS score, knee at 9 months (better indicated by lower values)					
1 study (Steinbok 1997)	14	14	-	MD 1 lower (1.45 to 0.55 lower)*	MODERATE
Mean MAS score, knee at 12 months (better indicated by lower values)					
1 study (Wright 1998)	12[y]	12[z]	-	MD = 1 lower*	MODERATE
Mean change in AROM, knee extension at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[A]	12[B]	-	MD = 12.6 higher*	MODERATE
Mean change in AROM, knee flexion/extension at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[c]	36[D]	-	MD = 4 higher*	VERY LOW
Mean change in range of movement, knee at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD 17.7 higher (7.73 to 27.67 higher)*	HIGH
Mean change in AROM, knee extension at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[E]	12[F]	-	MD = 7.2 higher*	MODERATE
Mean change in AROM, knee flexion/extension at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[G]	36[H]	-	MD = 4 higher*	VERY LOW
Mean change in AROM, knee flexion at initial contact at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[I]	36[J]	-	MD = 3 lower*	VERY LOW
Mean change in AROM, knee flexion at initial contact at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[K]	36[L]	-	MD = 5 lower*	VERY LOW
Mean change in PROM, knee extension at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[M]	12[N]	-	MD = 7.5 lower*	MODERATE

Mean change in PROM, knee extension at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[O]	12[P]	-	MD = 3 higher*	MODERATE
Mean change in PROM, popliteal angle at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[Q]	12[R]	-	MD = 8.4 lower*	MODERATE
Mean change in PROM, popliteal angle at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[S]	12[T]	-	MD = 4.7 lower*	MODERATE
Mean MAS score, ankle at 6 months (better indicated by lower values)					
1 study (Wright 1998)	12[U]	12[V]	-	MD = 1 lower*	MODERATE
Mean change in MAS score, ankle at 9 months (better indicated by lower values)					
1 study (Steinbok 1997)	14	14	-	MD 1.5 lower (2.02 to 0.98 lower)*	HIGH
Mean change in MAS score, ankle at 12 months (better indicated by lower values)					
1 study (Wright 1998)	12[W]	12[X]	-	MD = 0.5 lower*	MODERATE
Mean change in AROM, ankle dorsiflexion at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[Y]	12[Z]	-	MD = 17.6 higher*	MODERATE
Mean change in AROM, ankle dorsiflexion/plantarflexion at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[aa]	36[bb]	-	MD = 1 higher*	VERY LOW
Mean change in AROM, ankle at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD 0.5 higher (7.51 lower to 8.51 higher)*	MODERATE
Mean change in AROM, ankle dorsiflexion 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[cc]	12[dd]	-	MD = 27 higher*	MODERATE
Mean change in AROM, ankle dorsiflexion/plantarflexion at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[ee]	36[ff]	-	MD = 1 lower*	VERY LOW
Mean change in AROM, ankle dorsiflexion/plantarflexion at initial contact at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[gg]	36[hh]	-	MD = 1 higher*	VERY LOW
Mean change in AROM, dorsiflexion/plantarflexion at initial contact at 20 months (better indicated by					

higher values)					
1 study (Engsberg 2006)	29[ii]	36[jj]	-	MD = 0*	VERY LOW
Mean change in extension, foot progression angle at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[kk]	36[ll]	-	MD = 3 lower*	VERY LOW
Mean change in extension, foot progression angle at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[mm]	36[nn]	-	MD = 8 lower*	VERY LOW
Mean change in PROM, ankle dorsiflexion with knee extended at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[oo]	12[pp]	-	MD = 9.7 higher*	MODERATE
Mean change in PROM, ankle dorsiflexion with knee extended at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[qq]	12[rr]	-	MD = 11.2 higher*	MODERATE
Mean change in MAS total score at 6 months (read from graph, better indicated by lower values)					
1 study (McLaughlin 1998)	21[ss]	17[tt]	-	MD = 0.85 lower*	MODERATE
Mean change in MAS total score at 12 months (better indicated by lower values)					
1 study (McLaughlin 1998)	21[uu]	17[vv]	-	MD = 0.55 lower*	LOW
Mean change in MAS total score at 24 months (better indicated by lower values)					
1 study (McLaughlin 1998)	21[ww]	Mean change = 0 n=17[xx]	-	MD = 0.88 lower*	MODERATE

AROM active range of movement, CI confidence interval, MAS Modified Ashworth Scale, MD mean difference, PROM passive range of movement, SD standard deviation

* Calculated by the NCC-WCH

a Baseline mean (SD) = 15 ± 9, Score at 8 months mean (SD) = 11 ± 5

b Baseline mean (SD) = 12 ± 6, Score at 8 months mean (SD) = 12 ± 6

c Baseline mean (SD) = 15 ± 9, Score at 20 months mean (SD) = 12 ± 7

d Baseline mean (SD) = 12 ± 6, Score at 20 months mean (SD) = 12 ± 6

e Baseline mean (SD) = 19 ± 7, Score at 8 months mean (SD) = 17 ± 6

f Baseline mean (SD) = 17 ± 7, Score at 8 months mean (SD) = 18 ± 7

g Baseline mean (SD) = 19 ± 7,, Score at 20 months mean (SD) = 18 ± 4 reported as significant difference to baseline

h Baseline mean (SD) = 17 ± 7, Score at 20 months mean (SD) = 18 ± 7

i Baseline mean (SD) = 8 ± 3, Score at 8 months mean (SD) = 7 ± 3

j Baseline mean (SD) = 7 ± 3, Score at 8 months mean (SD) = 8 ± 3

k Baseline mean (SD) = 8 ± 3, Score at 20 months mean (SD) = 6 ± 3

l Baseline mean (SD) = 7 ± 3, Score at 20 months mean (SD) = 7 ± 3

m Mean change from baseline =-4

n Mean change from baseline =15.6
o Baseline mean (SD) = 43 ± 7, Score at 8 months mean (SD) = 46 ± 7
p Baseline mean (SD) = 43 ± 7, Score at 8 months mean (SD) = 43 ± 7
q Mean change from baseline =2.2
r Mean change from baseline =5.9
s Baseline mean (SD) = 43 ± 7, Score at 8 months mean (SD) = 46 ± 8
t Baseline mean (SD) = 43 ± 7, Score at 8 months mean (SD) = 43 ± 7
u Mean change from baseline =7.3
v Mean change from baseline=1.8
w Mean change from baseline =7.5
x Mean change from baseline= = 7.5
y Mean change from baseline = -1
z Mean change from baseline = 0
A Mean change from baseline = 16.5
B Mean change from baseline = -3.9
C Baseline mean (SD) = 44 ± 13, Score at 8 months mean (SD) = 49 ± 12
D Baseline mean (SD) = 45 ± 12, Score at 8 months mean (SD) = 46 ± 13
E Mean change from baseline = 15.4
F Mean change from baseline = 8.2
G Baseline mean (SD) = 44 ± 13, Score at 20 months mean (SD) = 52 ± 13 reported as significant difference compared to baseline
H Baseline mean (SD) = 45 ± 12, Score at 20 months mean (SD) = 47 ± 13
I Baseline mean (SD) = 32 ± 12, Score at 8 months mean (SD) = 28 ± 11
J Baseline mean (SD) = 29 ± 8, Score at 8 months mean (SD) = 28 ± 9
K Baseline mean (SD) = 32 ± 12, Score at 20 months mean (SD) = 28 ± 12
L Baseline mean (SD) = 29 ± 8, Score at 20 months mean (SD) = 30 ± 8
M Mean change from baseline = 4.5
N Mean change from baseline = 12
O Mean change from baseline = 6.4
P Mean change from baseline = 3.4
Q Mean change from baseline = -4.6
R Mean change from baseline = 3.8
S Mean change from baseline = -4.6
T Mean change from baseline = 0.1
U Mean change from baseline = -1
V Mean change from baseline = 0
W Mean change from baseline =-0.5
X Mean change from baseline = 0
Y Mean change from baseline = 12.8
Z Mean change from baseline = -4.8
aa Baseline mean (SD) = 15 ± 8, Score at 8 months mean (SD) = 16 ± 6
bb Baseline mean (SD) = 17 ± 7, Score at 8 months mean (SD) = 17 ± 6
cc Mean change from baseline = 19.5
dd Mean change from baseline = -7.5
ee Baseline mean (SD) = 15 ± 8, Score at 20 months mean (SD) = 16 ± 4
ff Baseline mean (SD) = 17 ± 7, Score at 20 months mean (SD) = 19 ± 7
gg Baseline mean (SD) = −5 ± 7, Score at 8 months mean (SD) = −4 ± 6
hh Baseline mean (SD) = −3 ± 7, Score at 8 months mean (SD) = - 3 ± 7
ii Baseline mean (SD) = −5 ± 7, Score at 20 months mean (SD) = −4 ± 6
jj Baseline mean (SD) = −3 ± 7, Score at 20 months mean (SD) = −2 ± 6
kk Baseline mean (SD) = −3 ± 18, Score at 8 months mean (SD) = −7 ± 15
ll Baseline mean (SD) = −7 ± 13, Score at 8 months mean (SD) = −8 ± 12
mm Baseline mean (SD) = −3 ± 18, Score at 20 months mean (SD) = −9 ± 15
nn Baseline mean (SD) = −7 ± 13, Score at 20 months mean (SD) = −5 ± 11
oo Mean change from baseline = 11.9
pp Mean change from baseline = 2.2
qq Mean change from baseline = 8.8

rr Mean change from baseline = -2.4
ss Mean change from baseline = -1
tt Mean change from baseline = -0.15
uu Mean change from baseline = -0.88
vv Mean change from baseline = -0.13
ww Mean change from baseline = -0.88
xx Mean change from baseline = 0

Optimisation of function

All three RCTs (McLaughlin 1998; Steinbok 1997; Wright 1998) reported GMFM outcomes for each dimension and total scores. Outcomes were assessed at 6 months, 9 months, 12 months or 24 months, depending on the study. The non-randomised prospective study reported GMFM percentage scores at 8 months and 20 months. A timed walk and gait analysis was conducted at 12 months in one RCT (Wright 1998) and at 8 months and 20 months in the non-randomised prospective study (Engsberg 2006).

Table 10.2 Evidence profile for selective dorsal rhizotomy and physical therapy compared with physical therapy only in children with diplegia; functioning assessment

Number of studies	Number of participants		Effect		Quality
	Selective dorsal rhizotomy and physical therapy	Physical therapy only	Relative (95% CI)	Absolute (95% CI)	
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[a]	12[b]	-	MD = 3.1 lower*	MODERATE
Mean change in GMFM-A score (lying and rolling, GMFM version not reported) at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14[c]	14[d]	-	MD = 0.2 lower*	MODERATE
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 12 months (better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	21	17	-	MD 0.84 lower (3.14 lower to 1.46 higher)*	LOW
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 0.1 lower (2.25 lower to 2.05 higher)*	MODERATE
Mean change in GMFM-B score (sitting, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[e]	12[f]	-	MD = 11.7 higher*	MODERATE
Mean change in GMFM-B score (sitting, GMFM version not reported) at 9 months (better indicated by					

higher values)					
1 study (Steinbok 1997)	14[g]	14[h]	-	MD = 15 higher*	MODERATE
Mean change in GMFM-B score (sitting, using GMFM-88) at 12 months (better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	21	17	-	MD 1.2 higher (5.58 lower to 7.98 higher)*	LOW
Mean change in GMFM-B score (sitting, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 1.6 lower (8.63 lower to 5.43 higher)*	MODERATE
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[i]	12[j]	-	MD = 0.3 higher*	MODERATE
Mean change in GMFM-C score (crawling and kneeling, GMFM version not reported) at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14[k]	14[l]	-	MD = 7.7 higher*	MODERATE
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 12 months (better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	21	17	-	MD 0.1 lower (6.61 lower to 6.41 higher)*	LOW
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 0.3 lower (6.57 lower to 5.97 higher)*	MODERATE
Mean change in GMFM-D score (standing, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 4.2 higher*	HIGH
Mean change in GMFM-D score (standing, GMFM version not reported) at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14[m]	14[n]	-	MD = 2.3 higher*	MODERATE
Mean change in GMFM-D score (standing, using GMFM-88) at 12 months (better indicated by higher values)					
2 studies	21[o]	17[p]	-	MD 2.6 higher	LOW

(McLaughlin 1998; Wright 1998)				(8.02 lower to 13.22 higher)*	
Mean change in GMFM-D score (standing, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 3.4 lower (15.14 lower to 8.34 higher)*	MODERATE
Mean change in GMFM-E score (walking, running and jumping, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[q]	12[r]	-	MD = 2.9 higher*	MODERATE
Mean change in GMFM-E score (walking, running and jumping, GMFM version not reported) at 9 months (better indicated by higher values)					
1 study (Steinbok 1997)	14[s]	14[t]	-	MD = 6.0 higher*	MODERATE
Mean change in GMFM-E score (walking, running and jumping, using GMFM-88) at 12 months (better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	21	17	-	MD 0.5 higher (5.74 lower to 6.74 higher)*	LOW
Mean change in GMFM-E score (walking, running and jumping, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 1.6 higher (7.92 lower to 11.12 higher)*	MODERATE
Mean change in GMFM-88 total score at 6 months (better indicated by higher values)					
1 study (Wright 1998)	12[u]	12[v]	-	MD = 4.8 higher*	MODERATE
Mean change in GMFM total score at 9 months (GMFM version not reported, better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD 6.2 higher (2.26 to 10.14 higher)*	MODERATE
Mean change in GMFM-88 total score at 12 months (better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	33	29	-	MD 3.21 higher (0.09 lower to 6.5 higher)*	VERY LOW
Mean change in GMFM-88 total score at 24 months (better indicated by higher values)					
1 study (McLaughlin 1998)	21	17	-	MD 0.2 lower (7.28 lower to 6.88 higher)*	MODERATE
Mean change in GMFM percentage score at 8 months (better indicated by higher values)					

1 study (Engsberg 2006)	29[w]	36[x]	-	MD = 0*	VERY LOW
Mean change in GMFM percentage score at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[y]	36[z]	-	MD = 3 higher*	VERY LOW
Mean change in timed walk at 6 months (m/minute, better indicated by higher values)					
1 study (Wright 1998)	12[A]	12[B]	-	MD = 3.1 lower*	MODERATE
Mean change in timed walk at 12 months (m/minute, better indicated by higher values)					
1 study (Wright 1998)	12[C]	12[D]	-	MD = 19.4 higher*	MODERATE
Mean change in gait speed (cm/second) at 8 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[E]	36[F]	-	MD = 11 higher*	VERY LOW
Mean change in velocity (m/second) gait analysis at 12 months (better indicated by higher values)					
1 study (Wright 1998)	12[G]	12[H]	-	MD = 0.04 lower*	MODERATE
Mean change in gait speed (cm/second) at 20 months (better indicated by higher values)					
1 study (Engsberg 2006)	29[I]	36[J]	-	MD = 18 higher*	VERY LOW
Mean change in use of assistive device gait analysis at 12 months (better indicated by lower values)					
1 study (Wright 1998)	12[K]	12[L]	-	MD = 0.25 higher*	MODERATE

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-88 Gross Motor Function Measure 88-item score, GMFM-A Gross Motor Function Measure dimension A, GMFM-B Gross Motor Function Measure dimension B, GMFM-C Gross Motor Function Measure dimension C, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MAS Modified Ashworth Scale, MD mean difference, SD standard deviation

* Calculated by the NCC-WCH

a Mean change from baseline = 1.6
b Mean change from baseline = 4.7
c Mean change from baseline = 4.1
d Mean change from baseline = 4.3
e Mean change from baseline = 13.6
f Mean change from baseline = 1.9
g Mean change from baseline = 17.8
h Mean change from baseline = 2.8
i Mean change from baseline = 5.5
j Mean change from baseline =5,2
k Mean change from baseline =12.1
l Mean change from baseline = 4.4
m Mean change from baseline = 8.3
n Mean change from baseline = 4.1
o Mean change from baseline = 12.1
p Mean change from baseline = 9.8
q Mean change from baseline = 4.2

r Mean change from baseline =1.3
s Mean change from baseline = 10.4
t Mean change from baseline = 4.4
u Mean change from baseline = 6.8
v Mean change from baseline = 2
w Baseline mean (SD) = 87 ± 10, Score at 8 months mean (SD) = 88 ± 9
x Baseline mean (SD) = 89 ± 7, Score at 8 months mean (SD) = 90 ± 7
y Baseline mean (SD) = 87 ± 10, Score at 20 months mean (SD) = 92 ± 8 reported as significantly different from baseline
z Baseline mean (SD) = 89 ± 7, Score at 20 months mean (SD) = 91 ± 7 reported as significantly different from baseline
A Mean change from baseline = 5
B Mean change from baseline = 8.1
C Mean change from baseline = 15.9
D Mean change from baseline = -3.5
E Baseline mean (SD) = 81 ± 22, Score at 8 months mean (SD) = 91 ± 25
F Baseline mean (SD) = 91 ± 26, Score at 8 months mean (SD) = 90 ± 22
G Mean change from baseline = 0.16
H Mean change from baseline = 0.2
I Baseline mean (SD) = 81 ± 22, Score at 20 months mean (SD) = 101 ± 24
J Baseline mean (SD) = 91 ± 26, Score at 20 months mean (SD) = 93 ± 22
K Mean change from baseline = 0.25 Four children in the SDR + therapy group changed to a less supportive device during 12 L follow up. Two children using walkers at baseline used two canes at 12m, one child who did not walk at baseline used a walker at 12m and one child using a walker at baseline walked independently at 12m
L Mean change from baseline = 0

Quality of life

None of the studies identified for inclusion reported quality of life.

Adverse effects

Two of the RCTs (McLaughlin 1998; Steinbok 1997) and both case series (Abbott 1992; Kim 2001) reported adverse effects. One RCT (McLaughlin 1998) used a structured adverse event questionnaire administered to the parents by the investigators in person or by telephone at 3-month intervals. The case series comprised retrospective reviews of children and young people who had undergone SDR in hospitals in New York from 1986 to 1992 (Abbott 1992) or in Korea for the 10 years leading up to 2000 (Kim 2001).

None of the studies identified for inclusion reported mortality rates.

Outcomes assessing pain were reported in one RCT (McLaughlin 1998) and in one case series (Kim 2001). The RCT reported that six of the 21 children and young people in the SDR plus physical therapy group experienced a total of 14 incidents of back pain during the 24-month follow-up period, compared to no incidents at all among the 17 children and young people in the physical therapy group. (MODERATE) Lower extremity pain was reported by ten of the 21 children and young people (a total of 11 incidents) in the SDR plus physical therapy group during the same follow-up period, compared to 16 out of the 17 children and young people (19 incidents) in the physical therapy group. (MODERATE) The case series (Kim 2001) reported that all 208 patients experienced post-operative back pain, which was controlled well using an intravenous fentanyl drip for 3 days post-operatively. The incidence of long-term back pain among children and young people who underwent SDR plus physical therapy was 3.4% (7/208). (VERY LOW)

Both case series reported outcomes related to urinary problems (bladder dysfunction), although the precise outcomes evaluated varied from study to study. Across both case series (Abbott 1992; Kim 2001), 7.2% (33/458) children who underwent SDR plus physical therapy experienced post-operative urinary retention. (VERY LOW) One RCT (Steinbok 1997) reported transient urinary retention in one of 14 children who underwent SDR plus physical therapy, and this resolved by the fourth post-operative day; no cases were reported in the physical therapy group. (MODERATE) One case series (Abbott 1992) reported that 0.4% of children (1/250) who underwent SDR plus physical therapy required catheterisation 18 months after surgery. (VERY LOW) The other case series (Kim 2001) reported that 1% (2/208) of children who underwent SDR plus physical therapy experienced long-term urinary incontinence (no further details reported). (VERY LOW) One RCT (McLaughlin 1998) recorded urinary adverse effects as part of the questionnaire administered to parents. Three of the 21 children and young people in the SDR plus physical therapy group reported one urinary adverse event each during the 24-month follow-up period, compared to no events among the 17 children and young people in the physical therapy group. (MODERATE)

One case series (Abbott 1992) reported an incidence rate of 1.2% (3/250) for post-operative ileus following SDR plus physical therapy. (VERY LOW)

One case series (Kim 2001) reported scoliosis rates in children following SDR surgery using laminectomy or laminoplasty; 8.6% (5/58) of children and young people developed scoliosis after laminectomy and 1.3% (2/150) developed scoliosis after laminoplasty. (VERY LOW)

Both case series examined outcomes relating to hip dislocation. In one study (Abbott 1992), 2.4% (6/250) of children and young people developed hip dislocation requiring a varus derotation osteotomy. In the other study (Kim 2001), 1% (2/208) of children and young people developed progressive hip migration requiring orthopaedic surgery.

Acceptability and tolerability

None of the studies identified for inclusion reported outcomes related to acceptability and tolerability.

Reduction of pain

The evidence relating to pain is presented under adverse effects (see above).

Selective dorsal rhizotomy plus physical therapy versus orthopaedic (soft tissue) surgery

Reduction of spasticity and optimisation of movement

The only study identified for inclusion (Buckon 2004b) did not report reduction of spasticity and optimisation of movement.

Optimisation of function

Pediatric evaluation of disability inventory

Table 10.3 Evidence profile for selective dorsal rhizotomy and physical therapy compared with orthopaedic surgery in children with diplegia; functioning assessment (PEDI)

Number of studies	**Number of participants**		**Effect**		**Quality**
	Selective dorsal rhizotomy and physical therapy	**Orthopaedic surgery**	**Relative (95% CI)**	**Absolute (95% CI)**	
Mean change in PEDI functional skills scale, self-care domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[a]	7[b]	-	MD 2.17 higher (1.93 lower to 6.27 higher)*	VERY LOW
Mean change in PEDI functional skills scale, self-care domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[c]	7[d]	-	MD 0.68 higher (4.36 lower to 5.72 higher)*	VERY LOW
Mean change in PEDI functional skills scale, self-care domain score at 24 months (better indicated by higher values)					

1 study (Buckon 2004b)	18[e]	7[f]	-	MD 3.72 higher (1.90 lower to 9.34 higher)*	VERY LOW
Mean change in PEDI functional skills scale, mobility domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[g]	7[h]	-	MD 2.91 higher (2.05 lower to 7.87 higher)*	VERY LOW
Mean change in PEDI functional skills scale, mobility domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[i]	7[j]	-	MD 1.89 higher (3.75 lower to 7.53 higher)*	VERY LOW
Mean change in PEDI functional skills scale, mobility domain score at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[k]	7[l]	-	MD 0.17 higher (6.30 lower to 6.64 higher)*	VERY LOW
Mean change in PEDI functional skills scale, social function domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[m]	7[n]	-	MD 0.10 higher (10.31 lower to 10.51 higher)*	VERY LOW
Mean change in PEDI functional skills scale, social function domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[o]	7[p]	-	MD 0.12 higher (8.16 lower to 8.40 higher)*	VERY LOW
Mean change in PEDI functional skills scale, social function domain score at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[q]	7[r]	-	MD 0.82 higher (7.41 lower to 9.05 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, self-care domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[s]	7[t]	-	MD 1.72 higher (4.04 lower to 7.48 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, self-care domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[u]	7[v]	-	MD 2.44 lower (8.75 lower to 3.87 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, self-care domain score at 24 months (better indicated by higher values)					
1 study (Buckon	18[w]	7[x]	-	MD 2.36 higher (3.68 lower to	VERY LOW

2004b)				8.40 higher)*	
Mean change in PEDI caregiver assistance scale, mobility domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[y]	7[z]	-	MD 2.28 higher (2.93 lower to 7.49 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, mobility domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[A]	7[30]	-	MD 6.17 higher (0.83 lower to 13.17 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, mobility domain score at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[C]	7[D]	-	MD 7.75 higher (1.81 lower to 17.31 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, social function domain score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[E]	7[F]	-	MD 0.32 lower (12.86 lower to 12.22 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, social function domain score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[G]	7[H]	-	MD 6.21 higher (1.94 lower to 14.36 higher)*	VERY LOW
Mean change in PEDI caregiver assistance scale, social function domain score at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[I]	7[J]	-	MD 4.47 higher (7.34 lower to 16.28 higher)*	VERY LOW

CI confidence interval, MD mean difference, PEDI Paediatric Evaluation of Disability Inventory, SD standard deviation
* Calculated by the NCC-WCH
a Mean change (SD) from baseline = 3.27 (4.37)
b Mean change (SD) from baseline = 1.1 (4.82)
c Mean change (SD) from baseline = 6.18 (6.91)
d Mean change (SD) from baseline = 5.5 (5.27)
e Mean change (SD) from baseline = 11.89 (6.81)
f Mean change (SD) from baseline = 8.17 (6.29)
g Mean change (SD) from baseline = 1.41 (3.8)
h Mean change (SD) from baseline = -1.5 (6.26)
i Mean change (SD) from baseline = 3.73 (7.94)
j Mean change (SD) from baseline = 1.84 (5.79)
k Mean change (SD) from baseline = 7.51 (7.11)
l Mean change (SD) from baseline = 7.34 (7.52)
m Mean change (SD) from baseline = 1.22 (5.95)
n Mean change (SD) from baseline = 1.12 (13.56)
o Mean change (SD) from baseline = 3.19 (6.56)
p Mean change (SD) from baseline = 3.07 (10.4)
q Mean change (SD) from baseline = 7.82 (6.63)

r Mean change (SD) from baseline = 7.0 (10.31)
s Mean change (SD) from baseline = 2.82 (9.77)
t Mean change (SD) from baseline = 1.1 (4.82)
u Mean change (SD) from baseline = 3.06 (10.73)
v Mean change (SD) from baseline = 5.5 (5.27)
w Mean change (SD) from baseline = 10.53 (8.33)
x Mean change (SD) from baseline = 8.17 (6.29)
y Mean change (SD) from baseline = 0.78 (5.15)
z Mean change (SD) from baseline = -1.5 (6.26)
A Mean change (SD) from baseline = 8.01 (11.97)
B Mean change (SD) from baseline = 1.84 (5.79)
C Mean change (SD) from baseline = 13.58 (13.76)
D Mean change (SD) from baseline = 5.83 (9.64)
E Mean change (SD) from baseline = 1.12 (13.56)
F Mean change (SD) from baseline = 1.44 (14.67)
G Mean change (SD) from baseline = 3.07 (10.4)
H Mean change (SD) from baseline = -3.14 (8.89)
I Mean change (SD) from baseline = 7.0 (10.31)
J Mean change (SD) from baseline = 2.53 (14.59)

Gross motor function measure

Table 10.4 Evidence profile for selective dorsal rhizotomy and physical therapy compared with orthopaedic surgery in children with diplegia; functioning assessment (GMFM)

Number of studies	**Number of participants**		**Effect**		**Quality**
	Selective dorsal rhizotomy and physical therapy	**Orthopaedic surgery**	**Relative (95% CI)**	**Absolute (95% CI)**	
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[a]	7[a]	-	MD = 0	VERY LOW
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[a]	7[a]	-	MD = 0	VERY LOW
Mean change in GMFM-A score (lying and rolling, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[a]	7[a]	-	MD = 0	VERY LOW
Mean change in GMFM-B score (sitting, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[b]	7[c]	-	MD 0.57 higher (1.86 lower to 3.00 higher)*	VERY LOW
Mean change in GMFM-B score (sitting, using GMFM-88) at 12 months (better indicated by higher					

values)					
1 study (Buckon 2004b)	18[d]	7[e]	-	MD 1.10 higher (1.55 lower to 3.75 higher)*	VERY LOW
Mean change in GMFM-B score (sitting, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[f]	7[g]	-	MD 0.72 higher (2.21 lower to 3.65 higher)*	VERY LOW
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[h]	7[i]	-	MD 4.29 higher (0.15 lower to 8.73 higher)*	VERY LOW
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[j]	7[k]	-	MD 2.68 higher (1.99 lower to 7.35 higher)*	VERY LOW
Mean change in GMFM-C score (crawling and kneeling, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[l]	7[m]	-	MD 2.99 higher (0.52 lower to 6.50 higher)*	VERY LOW
Mean change in GMFM-D score (standing, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[n]	7[o]	-	MD 4.87 lower (15.15 lower to 5.41 higher)*	VERY LOW
Mean change in GMFM-D score (standing, using GMFM-88) at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[p]	7[q]	-	MD 14.38 lower (29.07 lower to 0.31 higher)*	VERY LOW
Mean change in GMFM-D score (standing, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[r]	7[s]	-	MD 12.40 lower (30.68 lower to 5.88 higher)*	VERY LOW
Mean change in GMFM-E score (walking, running and jumping standing, using GMFM-88) at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[t]	7[u]	-	MD 5.10 higher (4.33 lower to 14.53 higher)*	VERY LOW
Mean change in GMFM-E score (walking, running and jumping standing, using GMFM-88) at 12 months (better indicated by higher values)					
1 study	18[v]	7[w]	-	MD 1.69 lower	VERY LOW

(Buckon 2004b)				(10.50 lower to 7.12 higher)*	
Mean change in GMFM-E score (walking, running and jumping standing, using GMFM-88) at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[x]	7[y]	-	MD 2.73 higher (13.30 lower to 18.76 higher)*	VERY LOW
Mean change in GMFM-88 total score at 6 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[z]	7[A]	-	MD 1.02 higher (3.06 lower to 5.10 higher)*	VERY LOW
Mean change in GMFM-88 total score at 12 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[B]	7[C]	-	MD 2.51 lower (7.63 lower to 2.61 higher)*	VERY LOW
Mean change in GMFM-88 total score at 24 months (better indicated by higher values)					
1 study (Buckon 2004b)	18[D]	7[E]	-	MD 1.19 lower (8.29 lower to 5.91 higher)*	VERY LOW

CI confidence interval, GMFM Gross Motor Function Measure, GMFM-88 Gross Motor Function Measure 88-item score, GMFM-A Gross Motor Function Measure dimension A, GMFM-B Gross Motor Function Measure dimension B, GMFM-C Gross Motor Function Measure dimension C, GMFM-D Gross Motor Function Measure dimension D, GMFM-E Gross Motor Function Measure dimension E, MD mean difference

* Calculated by the NCC-WCH

a Mean change from baseline = 0 All children could perform lying and rolling task
b Mean change from baseline = 1.76 (4.06)
c Mean change from baseline = 1.19 (2.09)
d Mean change from baseline = 2.24 (4.97)
e Mean change from baseline = 1.14 (1.78)
f Mean change from baseline = 1.67 (4.63)
g Mean change from baseline = 0.95 (2.7)
h Mean change from baseline = 2.25 (5.63)
i Mean change from baseline = -2.04 (4.85)
j Mean change from baseline = 3.7 (9.39)
k Mean change from baseline = 1.02 (2.32)
l Mean change from baseline = 3.33 (6.41)
m Mean change from baseline = 0.34 (2.55)
n Mean change from baseline = 3.56 (13.88)
o Mean change from baseline = 8.43 (10.85)
p Mean change from baseline = 6.13 (17.68)
q Mean change from baseline = 20.51 (16.49)
r Mean change from baseline = 12.14 (18.38)
s Mean change from baseline = 24.54 (21.85)
t Mean change from baseline = 2.32 (7.91)
u Mean change from baseline = 2.78 (11.73)
v Mean change from baseline = 4.86 (12.8)
w Mean change from baseline = 6.55 (8.81)
x Mean change from baseline = 14.44 (16.38)
y Mean change from baseline = 11.71 (19.08)
z Mean change from baseline = 1.98 (5.22)
A Mean change from baseline = 0.96 (4.45)
B Mean change from baseline = 3.39 (7.82)
C Mean change from baseline = 5.9 (4.89)

D Mean change from baseline = 6.32 (8.38)
E Mean change from baseline = 7.51 (8.04)

Quality of life

The study did not report quality of life.

Acceptability and tolerability

The study did not report outcomes related to acceptability and tolerability.

Reduction of pain

The study did not report reduction of pain.

Adverse effects

The study did not report adverse effects.

Evidence statement

Selective dorsal rhizotomy plus physical therapy versus physical therapy alone

Reduction of spasticity and optimisation of movement

With regard to trunk rotation and pelvic rotation, one non-randomised prospective study provided evidence that, compared to baseline, there was a reduction in AROM at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that differences in mean final scores across treatment groups were not statistically significant but that the reduction in AROM in pelvic rotation at 20 months from baseline was statistically significant in children who received SDR plus physical therapy.

With regard to pelvic tilt, one non-randomised prospective study provided evidence that compared to baseline there was a reduction in AROM at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the reduction in AROM in children who received SDR plus physical therapy compared to those who received physical therapy alone was statistically significant at 20 months, but not at 8 months (mean final score comparison across groups).

With regard to hip joints, one RCT reported that compared to baseline, there was a statistically significant reduction in tone (evaluated using MAS scores) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (MODERATE) One RCT provided evidence that compared to baseline, there was a reduction in AROM in hip extension at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One non-randomised prospective study provided evidence that compared to baseline, there was an improvement in AROM in hip flexion or extension at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the increase in AROM in children who received SDR plus physical therapy compared to those who received physical therapy alone was statistically significant at 20 months, but not at 8 months (mean final score comparison across groups). One RCT reported that compared to baseline, there was a statistically significant improvement in range of movement at the hip joint at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (HIGH) One non-randomised prospective study provided evidence that compared to baseline, there was an improvement in PROM in hip extension at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, but no difference between treatment groups at 12 months, although the statistical significance of this finding could not be determined.

(MODERATE) The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

With regard to knee joints, one RCT provided evidence that, compared to baseline, there was a reduction in tone at the knee joint (evaluated using MAS scores) at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the reduction in tone in children who received SDR plus physical therapy compared to children who received physical therapy alone differences were statistically significant at 6 months and 12 months (mean final score comparison across groups). One RCT reported that, compared to baseline, there was a statistically significant reduction in tone (evaluated using MAS scores) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (MODERATE)

One RCT provided evidence that, compared to baseline, there was an improvement in AROM in knee extension at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One non-randomised prospective study provided evidence that, compared to baseline, there was an improvement in AROM in knee flexion or extension at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One RCT reported that compared to baseline, there was a statistically significant improvement in range of movement at the knee joint at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (HIGH) One non-randomised prospective study provided evidence that compared to baseline, there was a reduction in AROM in knee flexion at initial contact at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

One RCT provided evidence that compared to baseline, there was a reduction in PROM in knee extension at 6 months, but an improvement at 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One RCT provided evidence that compared to baseline, there was a reduction in PROM of the popliteal angle at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) No further details relating to the popliteal angle were reported. The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

With regard to the ankle joint, one RCT provided evidence that, compared to baseline, there was a reduction in tone at the ankle joint (evaluated using MAS scores) at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the reduction in tone in children who received SDR plus physical therapy compared to those who received physical therapy alone differences were statistically significant at 6 months and 12 months (mean final score comparison across groups). One RCT reported that, compared to baseline, there was a statistically significant reduction in tone (evaluated using MAS scores) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (HIGH) One RCT provided evidence that, compared to baseline, there was an improvement in AROM in ankle dorsiflexion at 6 months and 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were statistically significant. One non-randomised prospective study provided evidence that, compared to baseline, there was an improvement in AROM in ankle dorsiflexion or plantarflexion at 8 months, but a deterioration at 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One RCT reported that, compared to baseline, there was an improvement in range of movement at the knee joint at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE) One non-randomised prospective study provided evidence that compared to baseline, there was an improvement in AROM in ankle dorsiflexion or plantarflexion at initial contact at 8 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, but no difference between treatment groups at 20 months, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. One non-randomised prospective study provided evidence that, compared to baseline, there was an improvement in AROM in ankle dorsiflexion or plantarflexion at initial contact at 8 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, but no difference between treatment groups at 20 months. The statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant. The same study provided evidence that, compared to baseline, there was a reduction in extension foot progression angle at 8 months and 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant at 8 months, but they were statistically significantly different at 20 months. One RCT provided evidence that compared to baseline, there was an improvement in PROM in ankle dorsiflexion with knee extended at 6 months and 12 months in children who received SDR plus physical therapy compared to children who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were statistically significant at 6 and 12 months. With regard to total MAS scores, one RCT provided evidence that, compared to baseline, there was an improvement at 6 months (MODERATE), 12 months (LOW) and 24 months (MODERATE) in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. The authors reported that the differences in mean final scores across treatment groups were not statistically significant at 6 months but were statistically significant at 12 and 24 months.

Optimisation of function

With regard to GMFM-A (lying and rolling), one RCT provided evidence that compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT provided evidence that compared to baseline, there was a reduction in GMFM-A at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors did not report the statistical significance of the difference in mean final scores across treatment groups or of the difference in mean change from baseline scores across treatment groups. Two RCTs reported results for GMFM-A (evaluated using GMFM-88) at 12 months. One RCT reported that, compared to baseline, there was a reduction in function in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (LOW) The second RCT provided evidence that, compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The authors of the second RCT reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT reported that, compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE)

With regard to GMFM-B (sitting), one RCT provided evidence that, compared to baseline, there was an improvement in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT provided evidence that, compared to baseline, there was an improvement in function (evaluated using GMFM, version not reported) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors did not report the statistical significance of the difference in mean final scores across treatment groups or of the difference in mean change from baseline scores across treatment groups. Two RCTs reported results for function (evaluated using GMFM-88) at 12 months. One RCT reported that compared to baseline, there was an improvement in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (LOW) The second RCT provided evidence that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The authors of the second RCT reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT reported that, compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE)

With regard to GMFM-C (crawling and kneeling), one RCT provided evidence that compared to baseline, there was an improvement in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT provided evidence that compared to baseline, there was an improvement in function (evaluated using GMFM, version not reported) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors did not report the statistical significance of the difference in mean final scores across treatment groups or of the difference in mean change from baseline scores across treatment groups. Two RCTs reported results for function (evaluated using GMFM-88) at 12 months. One RCT reported that compared to baseline, there was a reduction in function in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (LOW) The second RCT provided evidence that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The authors of the second RCT reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT reported that compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to children who received physical therapy alone that was not statistically significant. (MODERATE)

With regard to GMFM-D, one RCT provided evidence that, compared to baseline, there was an improvement in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was statistically significant. One RCT provided evidence that, compared to baseline, there was an improvement in function (evaluated using GMFM, version not reported) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors did not report the statistical significance of the difference in mean final scores across treatment groups or of the difference in mean change from baseline scores across treatment groups. Two RCTs reported results for function (evaluated using GMFM-88) at 12 months. One RCT reported that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (LOW) The second RCT provided evidence that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The authors of the second RCT reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT reported that, compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE)

With regard to GMFM-E, one RCT provided evidence that compared to baseline, there was an improvement in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT provided evidence that compared to baseline, there was an improvement in function (evaluated using GMFM, version not reported) at 9 months in children who received SDR plus physical therapy compared to children who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors did not report the statistical significance of the difference in mean final scores across treatment groups or of the difference in mean change from baseline scores across treatment groups. Two RCTs reported results for function (evaluated using GMFM-88) at 12 months. One RCT reported that, compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (LOW) The second RCT provided evidence that, compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (LOW) The authors of the second RCT reported that the improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone was statistically significant (mean final score comparison across groups). One RCT reported that compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE)

With regard to total GMFM scores, one RCT provided evidence that, compared to baseline, there was an improvement in function (evaluated using GMFM-88) at 6 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant. One RCT provided evidence that compared to baseline, there was a statistically significant improvement in function (evaluated using GMFM, version not reported) at 9 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. (MODERATE) Two RCTs reported results for function (evaluated using GMFM-88) at 12 months. One RCT reported that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (VERY LOW) The second RCT provided evidence that compared to baseline, there was an improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of this finding could not be determined. (VERY LOW) The authors of the second RCT reported that the improvement in function in children who received SDR plus physical therapy compared to those who received physical therapy alone was statistically significant (mean final score comparison across groups). One RCT reported that compared to baseline, there was a reduction in function (evaluated using GMFM-88) at 24 months in children who received SDR plus physical therapy compared to those who received physical therapy alone that was not statistically significant. (MODERATE)

One non-randomised prospective study provided evidence that, compared to baseline, there was no difference between treatment groups in GMFM percent scores at 8 months, but an improvement at 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone. The statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

With regard to walking, one RCT provided evidence, that compared to baseline, there was a reduction at 6 months, and an increase at 12 months, in the distance children who received SDR plus physical therapy were able to walk in 60 seconds compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

One non-randomised prospective study provided evidence that, compared to baseline, there was an increase in gait speed at 8 months and a reduction in gait speed at 20 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (VERY LOW) The authors reported that the differences in mean final scores across treatment groups were not statistically significant.

One RCT reported that, compared to baseline, there was a reduction in walking velocity at 12 months in children who received SDR plus physical therapy compared to those who received physical therapy alone, although the statistical significance of these findings could not be determined. (MODERATE) The authors reported that the difference in mean final scores across treatment groups was not statistically significant.

Quality of life

No studies reported quality of life.

Adverse effects

No studies reported mortality rates.

Although one RCT and one case series evaluated back pain as an outcome, the clinical importance of the results was unclear because the studies did not report whether the results excluded back pain experienced routinely in the first few days or weeks after any type of back surgery. (MODERATE) Lower extremity pain was reported in fewer children and young people in the SDR plus physical therapy group compared to the physical therapy-only group during a 24-month follow-up period. (MODERATE) A case series reported that all 208 patients experienced short-term post-operative back pain that was controlled well using intravenous fentanyl for 3 days. The incidence of long-term back pain was 3.4% (7/208) among children and young people who underwent SDR plus physical therapy. (VERY LOW)

Two case series reported outcomes related to urinary problems (bladder dysfunction). Across both case series 7.2% (33/458) of children who underwent SDR plus physical therapy experienced post-operative urinary retention. (VERY LOW) An RCT reported transient urinary retention in one of 14 children who underwent SDR plus physical therapy, and this resolved by the fourth post-operative day; no cases were reported in the physical therapy-only group. (MODERATE) One case series reported that 0.4% of children (1/250) who underwent SDR plus physical therapy required catheterisation 18 months after surgery. (VERY LOW) Another case series reported that 1% (2/208) of children who underwent SDR plus physical therapy experienced long-term urinary incontinence. (VERY LOW) One RCT reported that three of the 21 children and young people in the SDR plus physical therapy group experienced one urinary adverse event each during the 24-month follow-up period, compared to no events among the 17 children and young people in the physical therapy-only group. (MODERATE)

One case series reported an incidence rate of 1.2% (3/250) for post-operative transient ileus following SDR plus physical therapy. (VERY LOW)

One case series reported scoliosis rates in children following SDR surgery using laminectomy (L1 to S1) or laminoplasty (L1 to L5) and subsequent upper sacral laminectomy; 8.6% (5/58) of children and young people developed scoliosis after laminectomy and 1.3% (2/150) developed scoliosis after laminoplasty. (VERY LOW)

Both case series examined outcomes relating to hip dislocation. One study reported that 2.4% (6/250) of children and young people developed hip dislocation requiring a varus derotation osteotomy. In the other study, 1% (2/208) of children and young people developed progressive hip migration requiring orthopaedic surgery.

Acceptability and tolerability

No studies reported acceptability and tolerability.

Reduction of pain

The evidence relating to pain is presented above (under adverse effects).

Selective dorsal rhizotomy plus physical therapy versus orthopaedic (soft tissue) surgery

Reduction of spasticity and optimisation of movement

No studies reported reduction of spasticity and optimisation of movement.

Optimisation of function

One non-randomised comparative study compared the effects of SDR and orthopaedic (soft tissue) surgery at 6, 12 and 24 months using PEDI self-care, mobility and social function domains within the functional skills and caregiver assistance scales. Compared to baseline, there was evidence that there were improvements that were not statistically significant in children who received SDR and physical therapy compared to those who received orthopaedic surgery for all assessments of function at 6, 12 and 28 months, except for the self-care domain score, caregiver assistance scale at 12 months and the social function domain score, caregiver assistance scale at 6 months, where there was a comparative reduction in function that was not statistically significant. (VERY LOW)

The same study also compared the effects of SDR and orthopaedic (soft tissue) surgery at 6 months, 12 months and 24 months using the GMFM-88 assessment tool. With regard to GMFM-A scores, there were no changes from baseline for children who received SDR and physical therapy or for those who received orthopaedic surgery because all children could perform the lying and rolling task at baseline. (VERY LOW) With regard to GMFM-B and GMFM-C scores there was evidence that compared to baseline there were improvements in sitting and crawling and kneeling that were not statistically significant at 6, 12 and 28 months in children who received SDR and physical therapy compared to those who received orthopaedic surgery. (VERY LOW) With regard to GMFM-D scores there was evidence that compared to baseline there were reductions in standing function that were not statistically significant at 6, 12 and 28 months in children who received SDR and physical therapy compared to those who received orthopaedic surgery. (VERY LOW) With regard to GMFM-E scores there was evidence that compared to baseline there were improvements in walking, running and jumping at 6 and 28 months, but a reduction in function at 12 months in children who received SDR and physical therapy compared to those who received orthopaedic surgery. None of these findings as statistically significant (VERY LOW) (VERY LOW) With regard to total GMFM-88 scores there was evidence that compared to baseline there was an improvement in overall function at 6 months, but a reduction in function at 12 and 28 months in children who received SDR and physical therapy compared to those who received orthopaedic surgery. None of these findings was statistically significant. (VERY LOW)

Quality of life

No studies reported quality of life.

Acceptability and tolerability

No studies reported acceptability and tolerability.

Reduction of pain

No studies reported reduction of pain.

Adverse effects

No studies reported adverse effects.

Other comparisons of interest

The GDG also prioritised evaluation of the following interventions and comparators, but no studies were identified for inclusion:

- SDR plus physical therapy versus BoNT plus physical therapy
- SDR plus physical therapy versus ITB plus physical therapy.

Health economics

No economic evaluations for SDR were identified in the literature search conducted for the guideline this review question. The NICE Interventional Procedures Advisory Committee (IPAC) which developed 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) had access to an unpublished dissertation presenting a pilot economic analysis of SDR in the UK (Edwards 2010). The cost analysis from the dissertation is outlined here (further details are presented in Chapter 11).

The clinical evidence identified in relation to SDR included short- and medium-term outcomes (that is, outcomes measured at up to 24 months) for two treatment comparisons: SDR plus physical therapy versus physical therapy alone; and SDR plus physical therapy versus orthopaedic surgery (soft tissue surgery). In the comparison of SDR plus physical therapy versus physical therapy alone a statistically significant reduction in tone in lower extremity joints was reported, whereas no statistically significant difference was reported for timed walking, gait analysis, optimisation of function, individual dimensions of the GMFM, or total GMFM scores. In the comparison of SDR plus physical therapy versus soft tissue surgery no evidence was identified in relation to reduction of spasticity or optimisation of movement (that this is not the same as identifying evidence of no difference). For optimisation of function, however, the evidence identified reported no statistically significant differences in individual domains of PEDI, in individual dimensions of the GMFM, or total GMFM scores.

The cost of SDR is approximately £25,362, and this includes the cost associated with 7 weeks of hospital inpatient rehabilitation (Edwards 2010). Further details of the resource use related to SDR are presented in Chapter 11. Since no good-quality long-term outcome data (that is, outcomes measured after 24 months and, preferably, into adult life) are available it is not possible to determine whether the initial reduction in tone reported in the clinical evidence would lead to clinically important long-term benefits. Conducting a cost effectiveness analysis requires estimates of long-term outcomes, such as improvements in quality of life. The only statistically significant benefit reported in the clinical evidence reviewed for the guideline was a reduction in tone in lower extremity joints. However, the GDG was unable to extrapolate this to a clinically important long-term improvement in function that would represent an increase in quality of life. Based only on the available short- and medium-term clinical outcomes SDR cannot be said to be cost effective.

Evidence to recommendations

Relative value placed on the outcomes considered

SDR is a procedure intended to reduce muscle spasticity, and so outcome measures should focus on changes in tone in relevant muscles. In particular the GDG wished to know if reduced tone resulted in improvements in function, including the child or young person's abilities in terms of self-care and walking (such as speed of walking). Independence in the tasks of daily living that required walking and standing were considered important. Measures of stamina (distance walked in a given time) were not reported in the evidence identified for inclusion.

Much of the evidence reported findings in terms of scores intended to measure changes in muscle tone (for example, Ashworth scores) or range of movement for a particular joint. The GDG considered these findings far less valuable than those relating to function, independence or quality of life as they found it difficult to interpret the reported scores in a clinically or socially meaningful way.

Pain is a symptom of spasticity and presence of pain affects quality of life. The GDG considered reduction in pain to be an important outcome measure.

As SDR is an irreversible procedure, the risks of complications of the surgery, including non-specific risks (such as infection) associated with other types of surgery, and the specific complications of cutting dorsal nerve roots and performing laminectomy, are critical in decision making where the benefits for the child or young person may be marginal over time.

The GDG considered that the ideal long-term outcome would be the ability to maintain independent walking into adult life, but the evidence identified for inclusion did not report that length of follow-up.

Consideration of clinical benefits and harms

Some short- and medium-term improvements in motor function as measured by individual dimensions of the GMFM or GMFM total scores were statistically significant. However, even for those dimensions where such effects were demonstrated (for example, GMFM-D (standing) or GMFM total score) the effects were not consistent or sustained across all durations of follow-up considered in the evidence (6-24 months). The GDG considered that if the observed improvements could be maintained through to adult life then the outcomes of SDR would be clinically important. The improvements take time to appear, however, and the GDG believed that in the first 6-12 months after the procedure, quality of life for the child or young person and their family may decrease temporarily because of post-operative adverse effects of the surgery itself, the need for a period of inpatient physical therapy, and the prolonged rehabilitation period that follows.

The short- and medium-term reductions in spasticity and optimisation of movement demonstrated by improvements in muscle tone or range of movement in hip, knee and ankle joints were not consistent or sustained across all durations of follow-up considered in the evidence (6-24 months).

Although the risks of permanent morbidity following surgery are low, the potential consequences are serious. Children and young people, and their parents and carers, should be informed about the risks to facilitate informed decision making. The GDG noted differences in techniques for exposing dorsal nerve roots (laminectomy) and considered whether better exposure reduced the risks of damage to roots from the skin, bladder or bowel. The GDG noted that in one published study laminectomy of L1 to S1 was associated with a greater incidence of post-operative scoliosis than laminoplasty of L1 to L5 followed by upper sacral laminectomy.

The GDG concluded that a strong recommendation to offer SDR (or even a weak recommendation to consider SDR) could not be supported in the absence of high-quality evidence of a consistent and sustained (long-term) improvement (more than 2 years, for example sustained into adult life) in motor function or pain control. Anecdotal evidence from an unpublished dissertation (Edwards 2010) suggests that in appropriately selected children and young people SDR may achieve such outcomes, but further research, preferably conducted using RCTs or comparative observational studies, is needed to evaluate the clinical and cost effectiveness of the procedure in terms of long-term outcomes.

Pre-existing muscle shortening and bony deformity may interfere with post-operative rehabilitation and limit improvement in motor function. If surgery is postponed the child or young person will need to undergo a further period of post-operative recovery. It may take a child or young person up to 2 years to recover fully from major orthopaedic surgery, and so it may be appropriate to consider performing orthopaedic surgery before or at the same time as SDR.

The non-randomised study that compared SDR and orthopaedic (soft tissue) surgery showed no significant differences between the two treatment groups in relation to any of the outcomes reported. The GDG noted, however, that the evidence from this study was of very low quality and concluded that it did not support a recommendation to offer soft tissue surgery instead of SDR, although the GDG recognised that SDR and orthopaedic surgery might be performed sequentially for some children and young people.

SDR does not avoid the need for orthopaedic surgery in the longer term. The onset of muscle shortening, bone or joint deformity, or scoliosis may cause pain or impair function and it is important, therefore, that the child or young person is offered regular reviews until they are fully grown (when the risk of new orthopaedic complications is much lower). Once a child or young person has undergone SDR, the epidural space is obliterated and epidural anaesthesia during subsequent orthopaedic surgery, or during childbirth, will not be possible.

The GDG considered that rehabilitation after SDR is a process that would continue until the child or young person was fully grown and it requires, therefore, a long-term commitment from the child or young person and their family. There might be a need for further periods of intensive inpatient rehabilitation involving physiotherapy and use of additional or different orthoses compared to before surgery. Post-operative weakness in leg muscles is common, and targeted strength training will be an important component of post-surgery physical therapy. Orthoses and other supportive devices (such as walking frames) may be required to allow the child or young person to practice new skills and gain strength and balance. The GDG recognised that children and young people may gain weight after SDR and this may affect rehabilitation and motor function adversely.

The GDG considered that it would be important to ensure that the commitment required to follow a rehabilitation programme after SDR did not adversely affect other aspects of the child or young person’s life (such as education).

The GDG concluded that while long-term reduction in spasticity might be expected after SDR, evidence for a long-term improvement in gross motor function was lacking.

Consideration of net health benefits and resource use

The GDG considered that the high initial cost of SDR would be justified only if improvements in motor function were maintained into adult life (for example, if the child or young person were to progress through one or more levels of the GMFCS). Alternatively, if a clinically important improvement in quality of life following SDR could be demonstrated then the procedure might be shown to be cost effective even in the absence of progression in terms of GMFCS levels.

The GDG also considered that a sustained reduction in spasticity might reduce the long-term requirement for targeted resources, such as physical therapy, orthoses and mobility equipment, and this could result in significant cost savings to the NHS.

Quality of evidence

The quality of the evidence for reductions in spasticity and optimisation of movement ranged from very low to high. The quality of the evidence for improvement in function also ranged from very low to high. None of the evidence addressed long-term outcomes (that is, more than 24 months after surgery, and preferably through to adult life). The interventions and comparators evaluated in the included studies varied in relation to:

- the numbers of nerve roots divided and spinal segment levels involved (for example, in one RCT a mean of only 26% of sensory nerve rootlets were divided, which does not reflect the procedure as it is undertaken currently)
- the content of the physical therapy components of the interventions and comparators (in one study the children and young people who underwent SDR received a more intensive initial physical therapy programme than did the physical therapy-only group).

The numbers of children and young people involved in the studies were small and no subgroup analyses were undertaken to try to identify clinical characteristics that might be associated with better outcomes after SDR.

Other considerations

The GDG considered that children and young people undergoing SDR should be followed up according to a standardised framework until they reached adulthood. Given the lack of good quality outcome data, the GDG further considered that anonymised data should be collected through a national audit of outcomes of SDR procedures that have already been undertaken, including long-term outcomes and adverse effects. Since any one centre offering SDR is likely to perform the procedure on only a small number of children or young people each year, a national audit would allow more rapid collection of robust data, with the potential for comparing different centres in the long term, provided the same validated outcome measures are recorded in each centre. Collating and publishing data on adverse effects would provide information about the benefits and risks associated with SDR, and this would be of importance to children and young people considering SDR and their parents and carers. Such data might also allow comparisons to be made between outcomes of different practices or techniques used during SDR, such as the extent of bone removal and the number of rootlets cut.

In formulating their recommendations the GDG considered existing guidance contained in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373). In particular, the GDG noted the importance of care being delivered by a multidisciplinary team with specialist training and expertise in the care of spasticity and with access to the full range of treatment options. 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373) emphasises that the SDR team would normally include a physiotherapist, a paediatrician and surgeons, all with specific training and expertise. The GDG recognised that current practice is to coordinate all aspects of clinical care for children and young people who have spasticity and co-existing motor disorders and their early musculoskeletal complications as a result of a non-progressive brain disorder through multidisciplinary teams comprising similar groups of healthcare professionals to those recommended in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373). The group recommended that care be delivered by a network that incorporates integrated team working as a general principle in the provision of care for these children and young people with spasticity (see Chapter 4).

Key conclusions

In the experience of the GDG, many children and young people have serious difficulties with walking because of the degree of spasticity that is present, as well as weakness and poor selective motor, control etc. The GDG recognised the longstanding knowledge of neurophysiological processes that result in spasticity, including the theoretical basis for expecting SDR to reduce muscle tone. The limited evidence available demonstrated that SDR does indeed reduce tone, and the GDG recognised that there was no reason to suspect that tone would increase subsequently (over a period of years) because the procedure is irreversible. There was, however, a lack of evidence supporting a clinical benefit of SDR in relation to optimisation of function. The GDG highlighted the evidence suggestive of benefit in this area, particularly the improvements in the GMFM-D (standing) at 6 months and the GMFM total score at 9 months (although these effects were not consistently observed across all studies nor sustained across all periods of follow-up, and most of the evidence was of low or moderate quality). No evidence at all was identified in relation to quality of life.

The GDG considered that the available evidence supported further evaluation through clinical research of SDR as a treatment to improve walking ability. The GDG discussed and agreed six clinical criteria for identifying children and young people to whom SDR could be offered as part of research. The criteria were:

- abnormal tone (pure spasticity)
- good leg muscle strength
- straight legs and minimal muscle shortening
- good selective motor control in the legs
- good cognitive skills
- not overweight.

The GDG considered that the clinical pattern represented by the combination of the six criteria was most likely to be present in children and young people with cerebral palsy who have bilateral spasticity affecting the leg and who are in GMFCS level I, II or III. The GDG considered that the possible functional gain in children and young people in GMFCS level I was not sufficient to outweigh the risks of complications, and so they would not recommend offering SDR to children and young people in this group. Children and young people in GMFCS level II or III were, however, thought likely to be able to derive the clinical benefit of improved walking ability through undergoing SDR. Thus the GDG prioritised further research into the effectiveness and safety of SDR in children and young people in GMFCS level II or III. The GDG also highlighted in their research recommendations the importance of physical therapy (particularly physiotherapy) as an adjunctive treatment to improve the chances of a successful outcome after SDR, since this reflected the evidence available currently.

In the GDG's view, SDR is more likely to be effective if spasticity is judged to be the major factor impairing movement. If weakness, dystonia, poor motor control or musculoskeletal deformities are the main causes of motor impairment, then SDR is much less likely to be effective. Poor selective motor control and dystonia will not be improved by SDR and will significantly affect the child or young person's ability to benefit from physical therapy during rehabilitation. Muscle weakness may become apparent immediately after SDR and the child or young person will require intensive strengthening physiotherapy.

No evidence was identified to support the use of SDR in more severely affected children, in children with unilateral spasticity affecting the leg, or in children and young people who have spasticity as the result of a head injury. The GDG acknowledged that in more severely affected children and young people, pain from spasticity affects quality of life and using SDR to reduce spasticity even when there is no likelihood of improved function might be justified once other treatments have been considered or used. The available evidence was, however, considered to be insufficient to recommend SDR in this context without further research.

The GDG noted that severe scoliosis might make SDR more difficult to perform, and the GDG concluded that SDR should not be offered to children and young people with this condition.

The GDG also noted that hip dislocation, unless surgically corrected before SDR, would reduce the effectiveness of the procedure and make post-operative rehabilitation difficult (because the child or young person might be in pain, and sitting and standing might be difficult).

The post-operative rehabilitation period places significant demands on the child or young person and their family. Providing physical therapy regularly for up to 2 years after performing SDR may present difficulties for children and young people living in geographically remote areas. Physical therapists may need to rely heavily on the child or young person's parents and other family members to supervise exercises, and this could have an impact on family life, including quality of life for parents and siblings. Children and young people with spasticity and co-existing learning difficulties or sensory impairments might have difficulty coping with rehabilitation programmes, and this would need to be considered carefully by parents or carers before consenting to treatment. Further research should, therefore, consider the practicalities of life for children and young people who have undergone SDR and their parents or carers, and how healthcare services can be developed to support families in a variety of circumstances.

The GDG recognised that SDR is one of a number of treatment options for children and young people and stressed that healthcare professionals might prefer to consider treatments with lower risks of adverse effects. Alternative treatments might include BoNT-A injections or ITB. However, ITB has mainly been considered for children and young people with more severe disability than those undergoing SDR and no evidence was identified to allow comparison of the clinical benefits and harms between SDR and ITB. Nevertheless, SDR is irreversible, and so everyone involved in making decisions about whether to choose SDR should first ensure that the procedure is appropriate for the individual child or young person.

The GDG recognised that children and young people or their parents or carers may wish to explore all available treatment options. Despite SDR being used in USA since the 1980s, and more than 1,000 children and young people having undergone the procedure in one centre, there is no good quality evidence that the procedure results in clinically important improvements in motor function that are sustained over several years. The GDG was aware that SDR has been performed in several other countries during the past 30 years (including Australia, Canada, Japan and South Africa). Children who can walk with walking aids before the age of 10 years may lose the ability in their teenage years because of weight gain or further muscle shortening or weakness. The available evidence does not identify whether the loss of walking ability can be prevented by SDR. It is important that children and young people considering SDR, and their parents or carers, are aware of the shortcomings of the evidence. In formulating aspects of their research recommendations relating to information for children and young people and their parents or carers the GDG mirrored existing guidance in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373).

Recommendations

Number	Recommendation
	Selective dorsal rhizotomy
117	Offer selective dorsal rhizotomy to improve walking ability in children and young people with spasticity only as part of a national research programme designed to collect data on standardised long-term outcomes.

Number	Research recommendation
25	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? Why this is important The available evidence relating to selective dorsal rhizotomy suggests that the procedure results in some short- and medium-term improvements in motor function. The effects reported were not consistent across all studies nor sustained across all durations of follow-up investigated (6–24 months). The GDG considered that if the observed improvements could be maintained through to adult life then the outcomes of selective dorsal rhizotomy would be clinically important and this would be a cost effective treatment option. Further research is urgently needed to evaluate long-term outcomes (including adverse effects) of selective dorsal rhizotomy followed by an intensive rehabilitation programme involving physical therapy (and prioritising targeted strength training) compared with physical therapy alone. The research could be conducted using a range of designs, including randomised controlled trials and audits of outcomes from procedures already performed. The research should focus on selective dorsal rhizotomy performed: between the ages of 3 and 9 years in children with spasticity who are at GMFCS level II or III (because these children are likely to benefit most from selective dorsal rhizotomy) and before the development of significant contractures at the ankles, knees and hips. The following criteria should help to identify children who could be included in the research: abnormal tone (pure spasticity), good leg muscle strength, straight legs and minimal muscle shortening, good selective motor control in the legs, good cognitive skills, and not being overweight. Abnormal tone that is predominantly dystonia, and severe scoliosis or hip dislocation, should form part of the exclusion criteria. The research should be coordinated through a multicentre research programme; use nationally agreed outcome measures (such as incidence of neurological impairment and spinal deformity, the need for additional operations, and assessment of disability, social inclusion, and quality of life) and follow-up periods to facilitate national audit; and include assessment of the child's clinical condition before and after selective dorsal rhizotomy using the same formally validated assessment techniques; consider the timing of selective dorsal rhizotomy in relation to orthopaedic surgery if the child has muscle shortening or torsional abnormalities; consider the involvement of the child, their parents, carers or other family members, and members of the local multidisciplinary child development team in the rehabilitation programme after discharge from hospital; monitor the child's clinical condition regularly until they are fully grown (to detect and manage weight gain and orthopaedic and spinal complications). The following information should be given to children and their parents or carers to facilitate informed

	decision making about participation in research: selective dorsal rhizotomy is irreversible; there is a risk of serious temporary or permanent postoperative complications (such as deterioration in walking ability or bladder function) and later complications such as spinal deformity; prolonged physiotherapy and aftercare will be needed; additional surgery may be needed; subsequent to selective dorsal rhizotomy epidural anaesthesia will not be possible (for example, during additional surgery or childbirth); the evidence already available in relation to selective dorsal rhizotomy is based on studies involving small numbers of children, and there is currently no evidence from which to assess long-term outcomes (those experienced more than 24 months after performing selective dorsal rhizotomy, and preferably into adult life); confounding factors for long-term outcomes could include the natural history of the condition (for example, the child’s condition might deteriorate over time regardless of whether or not selective dorsal rhizotomy is performed).
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?

11 Health economics

11.1 Introduction

Health economic analysis allows decision makers to consider resource use alongside the benefits of a treatment in order to decide if it is good value compared to the next best alternative. Cost effectiveness analysis (with the units of effectiveness expressed in QALYs) is widely recognised as a useful approach for measuring and comparing different health interventions. Using the QALY as the final outcome allows one to measure the impact of health care in terms of how it extends life as well as how it affects health-related quality of life. Using this generic outcome allows different treatments to be compared using the same threshold for decision making.

In this guideline good quality published clinical evidence has been limited and therefore the benefits of treatment have been based on GDG consensus. Where possible economic analysis has been developed by working backwards from the NICE cost effectiveness threshold to find what level of effectiveness would be necessary in order to find an intervention cost effective. This type of analysis does not give cost effectiveness results, but provides a framework to decide whether a treatment is likely to be good value of NHS resources.

The NICE threshold is £20-£30,000 per QALY. For the treatment of spasticity it is the quality adjustment which is most important. Health related quality of life can be measured in terms of effect on domains of functioning and psychological wellbeing which focus on how well a person is able to carry out a full and meaningful life, such as mobility, self-care, ability to perform usual activities, pain/discomfort, and anxiety/depression. The purpose of the treatments for spasticity considered in this guideline is to reduce pain, improve function and mobility, provide cosmetic improvements, and prevent deterioration which may have resulted in loss of function. The view of the GDG was that improvements in these dimensions of health differ for different children and young people, depending on the extent of their impairment, their age and social context. Using this approach, whether a treatment ‘works’ for a particular child or young person can be determined by considerations other than the effectiveness of that treatment. For example, an orthosis may not have improved a child or young person’s health-related quality of life, but it may have given them sufficient limb support to sit unaided. Where the goal of an intervention is not a measurable improvement in health-related quality of life alone, evaluating the cost effectiveness of specific treatments is a particular challenge.

For almost all the interventions considered in the guideline, published evidence of cost effectiveness was completely lacking. In the following areas, further analysis was undertaken to support the GDG’s decision making:

- physical therapy versus no active treatment
- AFOs versus no active treatment
- BoNT versus oral drugs in combination with other interventions
- CITB, including ITB testing before CITB versus no ITB testing, and CITB versus oral drugs in combination with other interventions
- orthopaedic surgery versus no active treatment
- SDR versus no active treatment.

None of the analyses presented in this chapter follow NICE’s reference case for health economic analysis because of the lack of evidence for effectiveness and because the GDG was not able to quantify the benefits of treatment in a way that could be used in an economic analysis using consensus values for unknown parameters. In all the topics considered for economic evaluation resource use and costs were quantified. Details of the methods used in relation to each review question are presented in this chapter. For each question the following are reported; review of published economic literature; description of resource use and costs; and conclusions of the analysis. A discussion of results was also included for questions in relation to which a full health economic analysis was undertaken.

For many of the treatments considered in this guideline the GDG felt that the benefits to health-related quality of life outweighed the potential harms. Patient selection is important, particularly for the ITB pump, orthopaedic surgery and SDR, as only certain groups of patients are likely to benefit and treatment will not be appropriate for other groups. Patient choice is also important as their active participation, such as in physical therapy programmes and use of orthoses, is key to the success of several treatments.

Given the lack of published evidence, further comparative research is necessary to capture benefits in terms of function, pain, adverse events and quality of life. This further research should ideally be conducted using the EuroQol Group's EQ-5D instrument (a child-friendly version is available) or the Health Utilities Index (which was developed for children). Long-term outcomes are needed for the ITB pump, SDR and surgery as these are expensive and invasive treatments with associated risks. Also the studies should be designed to allow subgroup analysis by severity of spasticity in terms of the gross motor function classification system (GMFCS), and also limb involvement (hemiplegia, diplegia, and quadriplegia). Studies should be designed to allow data on resource use to be collected to allow cost analysis. Cost effectiveness analysis comparing treatments for each subgroup would provide better information for decision making.

For each review question considered in the guideline, this document includes a health economic summary based on evidence and GDG opinion.

11.2 Physical therapy (physiotherapy and/or occupational therapy)

Health economic question

What is the cost effectiveness of physical therapy (physiotherapy and/or occupational therapy) in children with spasticity with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder compared to no physical therapy?

Literature review

No published health economic evaluations were identified in the literature search conducted for this review question.

Further analysis

Introduction

The clinical evidence presented in this guideline was limited and could not be used to develop an economic evaluation for this review question. A 'what-if' analysis was considered. After much discussion the GDG came to the view that it would not be possible to quantify the mean benefits of physical therapy for the following reasons:

- the guideline covers children and young people with considerable variation in impairment from those with spasticity affecting how a single joint works to those with severe spasticity affecting all their limbs
- therapeutic goals are individualised to the child or young person within the family and will change over time and in different contexts
- no research study was identified that quantified the mean benefit of physical therapy in a way that would be clinically meaningful
- the GDG was not able to come to a consensus view on what a single measurable health outcome would be for this group.

Given the factors described above it was not possible to see how an evaluation could be undertaken that would provide meaningful results in which the GDG would have confidence. Therefore no economic evaluation could be undertaken. However the resource implications of providing therapy were discussed by the GDG.

Methods

A cost description of the service was undertaken for the GDG using staff costs from the Personal Social Services Research Unit (PSSRU) Costs of health and social care 2010. This shows the costs of therapists providing care in different settings and for hourly sessions once, twice or three times a week. This was presented to the GDG to aid consideration of the costs related to providing physical therapy.

Resource use and costs

Table 11.1 shows the comparative costs for physiotherapy and occupational therapy across different NHS settings where only staff costs are taken into account. Client cost per hour includes the costs of overheads across the different settings but does not take into account the travel time required by community physiotherapists. The costs are very similar in all settings for both physiotherapy and occupational therapy.

Table 11.1 Cost description for physical therapy (PSSRU Unity costs of health and social care 2010)

	Cost per hour of client contact	Intensity (hours per week)		
		3x week	2x week	1x week
Community physiotherapy	£42	£6,048	£4,032	£2,016
Hospital physiotherapy	£40	£5,760	£3,840	£1,920
Mean physical therapy		£5,904	£3,936	£1,968
Community occupational therapy	£42	£6,048	£4,032	£2,016
Hospital occupational therapy	£43	£6,192	£4,128	£2,064
Mean occupational therapy		£6,120	£4,080	£2,040

Conclusion

Cost data for physical therapy have limited use without associated benefits. The cost of increasing physical therapy for children with spasticity could be significant but without knowing the benefits of increasing physical therapy we cannot know if it will be cost effective. From GDG discussions the therapist plays a key role not only in providing treatment, but also in assessing the patient, and providing information to the parents about, and ways to improve a child’s daily tasks and activities.

11.3 Orthoses

Health economic question

What is the cost effectiveness of AFOs as compared to no orthosis in children with spasticity and with or without other motor disorders caused by a non-progressive brain disorder?

Literature review

No published health economic evaluations were identified in the literature search conducted for this review question.

Further analysis

Introduction

As with physical therapy, there was limited good quality effectiveness evidence for the effectiveness of using an orthosis compared to not using an orthosis. The outcomes of importance vary depending on the specific goal. The outcomes were reported for intermediate effects which over time could result in improvement in function and health-related quality of life. For example, the GDG considered that improved gait efficiency would contribute to subtle improvements in energy expenditure which could lead to increased activity and therefore allow more participation. As with physical therapy no research study has quantified the mean benefit of orthoses in a way that would be clinically meaningful. Also orthoses are used in conjunction with other interventions, such as physical therapy and BoNT. It would be difficult to estimate the benefits of orthoses over and above these interventions. Again, as with physical therapy, it was not possible to undertake an evaluation that would provide meaningful results in which the GDG would have confidence.

Initially a service description was developed with the assistance of Exeter University and the Royal Berkshire NHS Foundation Trust to potentially inform an economic evaluation.

Methods

Two orthotists were contacted who gave descriptions of the process for having an orthosis supplied and fitted. Costs were then applied to staff time for appointments, and the cost of the orthosis. Data were presented to the GDG to allow the consideration of resource use and costs when making recommendations for orthoses.

Resource use and costs

Three appointments are required:

- an initial assessment which takes between 20-30 minutes with a physiotherapist or occupational therapist, this includes taking measurements
- a follow-up appointment to fit the orthosis takes 20-30 minutes and takes place about 2 weeks after the assessment
- a follow-up appointment to check everything is correct (this is usually offered only for a child or young person who has not had an orthosis before).

Orthotists start at band 5 and can work up to band 7 as a senior orthotist. Only a third of orthotists are employed by the NHS with the rest working for private companies. Using the cost per hour of client contact with a physiotherapist[‡‡‡‡] (band 5 median) to represent the cost of an orthotist then the appointments will cost about £27 (40 minutes) to £62 (1.5 hours) to supply and fit an orthosis if the orthotist is employed in the NHS.

The cost of an AFO is about £120 to £300 each (estimates from Exeter University and the Royal Berkshire NHS Foundation Trust). Lower limb orthoses are usually custom made, whereas upper limb orthoses can be products supplied from stock.

[‡‡‡‡] £42 per hour of client contact with a community physio, £40 with a hospital physio – the mean was used. Unit costs of health and social care 2010, PSSRU.

The orthosis needs to be replaced every 10-12 months or less depending on the child's rate of growth. The straps on the orthosis usually wear out after about 12 months. If the orthosis does not fit well and is uncomfortable then the child will not wear it.

Conclusion

As with physical therapy, the cost data for orthoses have limited use without associated benefits. Orthoses are used in conjunction with other treatments and it would be useful to understand the additional benefits of using an orthosis with each of the other interventions.

11.4 Botulinum toxin

Health economic question

What is the cost effectiveness of intramuscular BoNT-A in combination with other interventions (physical therapy) as compared to continuing on oral drugs with other interventions, in children with spasticity and with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder where there is no longer a beneficial effect from the oral drugs?

Literature review

No UK-based economic evaluations were identified from the literature search. A cost consequence analysis was identified for Australia (Houltram 2001), a cost minimisation analysis for Germany (Ruiz 2004), and a cost impact analysis from the USA (Balkrishnan 2002). Not enough detail was reported to adapt these analyses to the UK setting and, therefore, these studies are not discussed further here.

The clinical literature review identified that the evidence for the effectiveness of BoNT was equivocal. Cost effectiveness analysis was developed to consider what level of effect would be needed to find BoNT injections cost effective at the NICE threshold for cost effectiveness (£20,000 per QALY) compared to continuing on oral drugs.

Further analysis

Methods

The time horizon for the analysis was 1 year. The pharmacological activity of BoNT-A was assumed to last 3-4 months. There was limited evidence that showed no significant prolonged effect with repeated injections. The analysis considers one, two or three sets of injections over a year. Only costs relevant to the NHS are included in the analysis.

It is assumed that patients are referred to BoNT treatment when oral drugs stop working, therefore the comparator will be continuing on oral drugs. All patients continue with physical therapy.

Resource use and costs

A cost description was developed based on service descriptions from Leeds and Great Ormond Street Hospital. The BoNT service team comprises:

- two consultants
- a physiotherapist
- an occupational therapist
- a nurse
- a registrar.

A new patient will have a detailed assessment to determine their suitability for BoNT treatment which will be performed by a consultant.

The assessment includes:

- clinical examination

- video gait analysis
- goniometry
- measurement of gross motor function (not conducted for every child or young person)
- treatment goals are agreed and documented
- integrated care pathway paperwork completed
- patients are weighed, consent obtained, and the BoNT prescribed.

The administration of BoNT involves a day-case admission unless it is an inpatient referral.

All admissions require:

- general examination to ensure fitness for sedation or general anaesthetic
- parental consent for sedation or general anaesthetic and for injection

The majority of injections are performed under sedation in the treatment room. Muscles to be injected are identified by a member of the BoNT team and marked, and a local anaesthetic is administered (AMETOP). A sedative is administered (oral midazolam at a dose of 0.5mg/kg, maximum dose 15mg). Patients who are old enough to cooperate, and are in agreement, will be offered entonox analgesia (nitrous oxide). This is usually combined with ethyl chloride spray anaesthesia. Entonox is administered by trained nurses.

A member of the BoNT service team performs the injections, using ultrasound guidance to locate the muscles. Once the child has woken and recovered they are discharged home. A handwritten discharge summary is completed, and a dictated summary is produced afterwards by team members.

Follow-up appointments use the same assessments as pre-injection. At Great Ormond Street Hospital there are two appointments at 3 and 17 weeks post injection; at Leeds the follow-up appointment is at 6 weeks.

For the first appointment for the pre-assessment, the reference cost for a consultant-led face-to-face appointment was used, with the corresponding reference cost of follow-up appointments for any subsequent appointments (see Table 11.2).

Table 11.2 Costs of pre-assessment and follow-up assessment (NHS reference costs 2010-11)

Reference cost description	Unit Cost	Lower quartile	Upper quartile
Consultant led: first attendance non-admitted face to face – paediatric neurodisability	£481	£286	£600
Consultant led: follow-up attendance non-admitted face to face – paediatric neurodisability	£277	£206	*

*The upper quartile was reported as £270 and so will not be used in the analysis.

The appointment for the injection of BoNT has a reference cost assigned, 'Torsion dystonia and other involuntary movements drugs band 1' (XD09Z), as it is a high cost drug (NHS 2006). The unit cost for 2010-11 was £321 (lower quartile £175, upper quartile £418). There is also a specialist uplift to tariffs for children of 60% (Department of Health 2011), if this is applied then the cost increases to £514. This reference cost will include all costs related to the procedure, the day case admission, drug costs, and staff.

Standard care will be taken as continuing oral drugs, assumed to be baclofen (Table 11.3) (physiotherapy and occupational therapy costs are assumed to be the same for both treatment arms and so not included in the analysis).

Table 11.3 Cost of standard care, oral baclofen, for one year

	Cost for one year	reference
Oral baclofen 30mg per day	£20.73	Children's BNF 2010-2011 £1.59 per 84 tablets 10mg Doses range from 10-60mg daily depending on the child's age and weight

Costs to treat adverse events which are not transient are shown in Table 11.4. The GDG thought serious adverse events were very unlikely for patients receiving BoNT and so the baseline analysis was conducted without adverse events.

Table 11.4 Costs for adverse effects (NHS reference costs 2010-11)

Non-elective inpatient	Unit cost	Lower quartile	Upper quartile
Epilepsy syndrome without CC (PA02B)	£508	£361	£565
Acute upper respiratory tract infection and common cold (PA11Z)	£456	£315	£558

Outcomes

The clinical evidence from the trials was variable for reducing spasticity and optimising movement and function. The quality of life evidence only reported a significant benefit in the emotional role estimation. However, 66% to 81% of parents in one cross-over RCT rated BoNT treatment as good, very good or excellent.

The adverse events reported in the literature review for this question were; incontinence, short term muscle weakness (Reddihough 2002), one child with a history of epilepsy being admitted to hospital for seizure management shortly after injection (Russo 2007), In four studies grip weakness was reported (Boyd 2004, Fehlings 2000, Olesch 2010, Russo 2007). Other reports included nausea, vomiting, flu symptoms, coughing, soreness at injection site, respiratory infections, headache, fainting episodes, anxiety, depression, alopecia and fatigue.

Given the lack of clinical effectiveness evidence for BoNT the benefits of treatment were estimated by the GDG. Using an EQ-5D UK time trade off value set, descriptions of potential benefits were developed to help guide the GDG decision making. GDG discussion identified the dimensions of the EQ-5D that would most likely be affected by BoNT treatment from mobility, self-care, ability to perform usual activities, pain/discomfort, and anxiety/depression.

The conservative assumption for this analysis is that patients do not deteriorate if they continue on oral drugs.

Synthesis of costs and outcomes

Using the data from the clinical evidence and the costs above a simple analysis shows the mean cost per person having 2 sets of BoNT injections in 1 year is approximately £2,000. This assumes injections are given in a day case setting and only one follow-up appointment is needed. The cost of the next best alternative (standard care for this analysis) is approximately £21 per year.

If two follow-up appointments are needed at three and 17 weeks after the first set of injections then the average cost rises to around £2,600. If BoNT is given three times in a year then the costs increase to £2,800 per person per year.

Table 11.5 Mean cost per child or young person for two sets of injections of botulinum toxin in 1 year

	unit cost	total cost
Pre-assessment	£481	£481
Injection as day case	£514	£1028
Follow-up	£277	£544
TOTAL		£2,062

Effectiveness threshold analysis

Given the lack of effectiveness evidence, the NICE threshold for cost effectiveness of £20,000 was used to calculate the minimum change in effectiveness that would be needed to find BoNT-A cost effective. The incremental cost of BoNT-A involving two sets of injections in 1 year compared to oral baclofen:

£2,062 - £21 = £2,041.

Cost ÷ QALYs = ICER

£2,041 ÷ QALYs = £20,000 per QALY

£2,041 ÷ £20,000 = 0.1

In order for two sets of BoNT-A injections to be considered cost effective compared to oral baclofen then a QALY gain of 0.1 would need to be achieved over the year.

The following descriptions were developed from the EuroQol Group's EQ-5D instrument to demonstrate what outcomes would be needed for the threshold for effectiveness to be reached. For patients who have moderate pain or discomfort approximately 80% would have to experience no pain or discomfort if given 2 sets of BoNT injections during a year. For patients with extreme pain or discomfort approximately 25% would have to experience only moderate pain or discomfort if given 3 sets of BoNT injections during a year.

For patients who have some problems with self care, and some problems performing their usual activities, 80% would have to improve so they had no problems with self-care or performing their usual activities if they have 2 sets of BoNT injections in a year.

The other way to consider the effectiveness of BoNT is as a prevention of deterioration; 80% of patients who have no pain are prevented from experiencing moderate pain if they are treated with BoNT after oral drugs fail; or 25% of patients who have moderate pain would be prevented from experiencing extreme pain; or 80% of patients who have no problems with self-care and performing usual activities are prevented from deteriorating so they have some problems with self-care and performing usual activities.

Conclusion

There is uncertainty in this analysis as the clinical effectiveness evidence is variable. Only a small increase in quality of life is needed for this to be considered cost effective at the NICE threshold, and so even with uncertain clinical effectiveness it is likely that BoNT will be found cost effective to use. It seems from the clinical evidence that what is reported in the trials is not what the clinicians are looking for from BoNT in practice. Data on how BoNT treatment benefits children and young people in terms of mobility, self-care, usual activities, pain and discomfort, and anxiety and depression would be needed for further economic evaluation.

11.5 Intrathecal baclofen

Health economic questions

What is the cost-effectiveness of an ITB test before receiving CITB compared to no test in children and young people with spasticity due to a non-progressive brain disorder?

What is the cost-effectiveness of CITB in combination with other interventions (physiotherapy, occupational therapy) compared to oral drugs with other interventions?

Literature review

An economic evaluation set in the UK was identified in the literature search (Sampson 2002). The evaluation was clear and it was easy to identify the sources for the costs and effectiveness. It did not have a comparator intervention because the effectiveness evidence was based on case studies with no control groups. The model compared the costs of testing, implanting the pump and follow-up visits for 5 years (life of the battery for the pump), with the estimated benefits to quality of life.

The clinical effectiveness evidence used in the evaluation was taken from published studies identified in a literature search. Trials were included if they had more than one patient, an average follow-up of at least 6 months, and included the following outcomes:

- bedbound patients becoming able to sit in a wheelchair
- patients who had severe difficulty sitting in a wheelchair being able to sit comfortably
- wheelchair users improving their wheelchair mobility
- wheelchair users improving their ability to transfer
- wheelchair-bound patients becoming ambulatory
- ambulatory patients improving their ability to walk
- improved ability to perform activities of daily living
- improved ease of nursing care
- patients with skin integrity problems who showed improvements in these symptoms
- reduction in spasm-related pain.

All the studies included patients with severe disabling spasticity no longer responding to oral medications and where the patients had already had a positive response to a bolus dose of ITB. Studies included both children and adults with different causes of spasticity, but the results were reported for all patients together. The studies used a wide variety of outcomes. Functional and quality of life outcomes were generally not measured using standard scores.

The proportion of patients responding to treatment is an intermediate outcome. The authors translated intermediate outcomes into QALYs using EQ-5D scores based on the evidence identified in the review and supported by clinical opinion (Table 11.6). The EuroQol Group's EQ-5D instrument measures health-related quality of life using five dimensions: mobility; self-care; usual activities; pain/discomfort; and anxiety/depression. Each dimension has three levels: no problems; some problems; and extreme problems. The patients were divided into the following categories to estimate EQ-5D scores: Three populations of patients were divided into the following categories:

- category 1: bedbound patients experiencing severe spasm-related pain
- category 2: bedbound patients who were not in pain
- category 3: wheelchair users with moderate spasm-related pain.

The proportion of patients who would be expected to have no change in quality of life or changes in pain, depression, ability to sit in wheelchairs, ability to care for themselves, and participation in activities of daily living, are shown in column 2 of Table 11.6. These are based on combinations of the following specified outcomes from the literature search:

- bedbound patients becoming able to sit in a wheelchair (66% of patients in the included studies responded)
- improved ability to perform activities of daily living (73% of patients responded)
- reduction in spasm-related pain (89% of patients responded).

Table 11.6 Estimated improvement in quality of life based on proportion who experience changes in specified outcomes for three categories of severity of spasticity for adults and children (source: Sampson 2002)

Category of patients	Changes in health-related quality of life measured by EQ-5D (proportion of patients who experience change with CITB)	Baseline quality of life value (EQ-5D score) estimated by authors	Estimated adjusted quality of life improvement each year with CITB
1 bedbound patients experiencing severe spasm-related pain	No change 11% Reduction in pain 23% Reduction in pain, able to sit in wheelchair, reduction in anxiety and depression scores 66%	-0.594	0.50
2 bedbound patients who were not in pain	No change 34% Able to sit in wheelchair, reduction in anxiety and depression scores 66%	-0.208	0.27
3 wheelchair users with moderate spasm-related pain	No change with CITB 11% Reduction in pain only 16% Reduction in pain, improved ability to care for self and perform activities of daily living 73%	0.079	0.43

CITB continuous pump-administered intrathecal baclofen

Cost estimates published in the study were derived from three centres within the UK where the procedure was being performed. Benefits of the ITB pump were assumed to last 5 years as this is the lifetime of the pump's battery. Table 11.7 shows the costs reported from 1999.

Table 11.7 Change in mean cost of intrathecal baclofen testing and continuous pump-administered intrathecal baclofen over a 5-year period (Sampson 2002)

	1999 Cost	2010/11 Cost		
		Min	**max**	**mean**
Pre-screening assessment costs (30 minutes neurosurgeon time and outpatient clinic visit)	£330 - £556	£483	£814	£648
Test dose (Lumbar puncture, lumbar catheter, injection of a therapeutic substance, 2 days hospitalisation, drug costs, physiotherapist, and nursing time for patient observation)	£940 - £1570	£1,376	£2,298	£1,837
Cost of implantation procedure (cost of pump, catheter, procedure, drugs, 5-day inpatient stay)	£8730 - £10,260	£12,776	£15,0152	£13,895
Other costs (tests, pathology, radiology, microbiology), excluding potential transport	£550			£805

costs				
Cost of follow-up (refill kit, drug costs, physiotherapist assessment, and outpatient visit) average of 4 to 8 refills per year	£140 - £150	£205	£220	£212
Procedure	£11,743			£17,185
Follow-up 1 year	£870			£1,273
TOTAL	£15,420			£23,135

The cost per QALY for each category of patients was:

- category 1, £6,900
- category 2, £12,790
- category 3, £8,030.

There was no comparator treatment in this study therefore the results do not represent ICERs. The conclusion of the study was that if the QALY gain was less than approximately 0.15 or if the cost of CITB was above £19,000 over the 5 year period then the cost per QALY would be greater than the NICE £20,000 threshold for willingness to pay for a QALY gain.

The published economic evaluation Sampson 2002 was used as the basis for developing a new model which looked at the cost effectiveness of both testing and implanting the ITB pump.

Further analysis

Methods

The costs of testing, implanting the pump and follow-up visits over 5 years have been taken from Sampson 2002 (Table 11.7) and converted to 2010/11 costs (using the hospital and community health services pay and prices index uplift (Curtis 2011)).

As the model runs over 5 years, costs and benefits accrued after the first year are discounted by 3.5% for costs and 3.5% for benefits (1.5% tested for benefits)**Error! Bookmark not defined.**. The perspective of this evaluation is from the NHS, therefore only includes costs and benefits relevant to the NHS.

A treatment pathway was developed with the help of the GDG in which additional elements of treatment were identified that were not included in the previous study (Sampson 2002). The main change to the published model structure was the inclusion of a comparator treatment. It was assumed that all patients would receive physiotherapy and so this was not included in the model.

In the model the following three comparisons were considered.

- Children and young people considered suitable candidates have a pre-screening assessment and are tested before the pump is implanted. Patients who have a positive test will go on to have the pump implanted. Patients who have a negative test will have standard treatment.
- Children and young people considered suitable candidates by their clinicians have a pre-screening assessment, and get the pump implanted without a test dose.
- ITB testing and pump is not available for any patients. Children and young people considered suitable candidates by their clinicians will continue to receive standard treatment.

The results of three small studies (reported in six publications) from the review of clinical evidence were combined to populate the baseline model parameters, including a total of 117 patients. The studies were:

- Awaad study (Awaad 2003)
- Gilmartin-Krach study (Gilmartin 2000; Krach 2004)
- Hoving study (Hoving 2007; Hoving 2009a; Hoving 2009b)

(see Appendix L for further details). Seven patients have been excluded from the clinical evidence who had a positive test result but did not have the pump implanted. Of these, six patients were excluded as they were ineligible to have a pump implanted, and there was one death unrelated to treatment.

Three of the children who had a positive test chose not to have the pump implanted. Although the exact reasons for these decisions are not clear from the studies all three have been included in the economic analysis to reflect that some patients may choose not to have the pump implanted after the test (see Table 11.8).

Therefore, 110 of the 117 patients included in the studies from the clinical review were used to determine the risks for this analysis (see Table 11.8).

Table 11.8 Clinical values and corresponding inputs for the test and no test arms of the model (% values rounded)

Model parameter	Values from clinical evidence	Inputs into model (%) test arm	Inputs into model (%) no test arm
Patients undergoing the test	110		
Negative test result	7	6%	-
Positive test result	110	94%	-
Pump implanted	100	97% (of positive tests)	100%
Positive test result but pump not implanted	3	3%	-

The GDG was asked to identify which adverse events reported in the clinical review for CITB should be included in the analysis. Adverse events related to baclofen are considered to be transient with low cost implications and minimal impact on quality of life.

The combined studies reported that 7 pumps were removed and 3 patients required second operations to correct problems with the pump or catheter. One pump was removed due to lack of effect of ITB after a positive test. Table 11.9 reports the inputs for the model taken from the 110 patients included from the clinical review.

Table 11.9 Clinical values from 110 patients included from the clinical review and corresponding inputs for the CITB arms of the model (% values rounded)

Model parameter	Values from clinical evidence (N)	Inputs into model (%) test arm before pump implanted	Inputs into model (%) no test arm before pump implanted
Major infection due to test	1	0.9%	-
Minor infection due to test	1	0.9%	-
Pump removed due to major infection	6	6%	6%
Pump removed due to lack of clinical improvement	1 for testing arm 8 for no-test arm*	1%	9.4%
Second operation required	3	6%	6%

*includes the 7 children and young people who would have had a negative test result

The following scenarios were included in the initial treatment pathway to be modelled, but no evidence was identified in the clinical review and so they have been removed from the final model:

- technical failure of the pump requiring it to be removed
- where no effect is seen or the effect is too small then the dose is increased resulting in an additional follow-up visit
- orthopaedic surgery (a possible outcome of using the ITB pump was thought to be delayed or prevented surgery).

Resource use and costs

Standard therapy was the continuation of physiotherapy and oral drugs (baclofen) for 5 years (Table 11.10). It is assumed that patients with the ITB pump also continued with physiotherapy and so this cost was not included in either arm of the model. The updated 2010/11 costs for the ITB pump are reported in Table 11.7. Where the ITB treatment is unsuccessful and the patient has the pump removed they will go back to taking oral baclofen.

Table 11.10 Cost of standard therapy for one year

		Cost per year	reference
Standard therapy	Oral baclofen – 30mg per day (to represent an average dose)	£20.65	84 tablets 10mg = £1.59 Children's BNF 2010-2011 /

The review of the clinical literature for the guideline found evidence of adverse effects related to both the test and implanting the pump and so these have been included in the model. Both procedures require a hospital stay and involve injections or a catheter inserted into the spinal cord. There is a risk of infection which can be minor and easily treated, or a major infection such as meningitis. The costs of treating these infections are shown in Table 11.11. The costs are assumed to be the same whether the infection is due to the test procedure or the pump implant procedure. Meningitis is a major adverse event which can cause death or serious disability, with high associated costs. It is assumed that if a patient has a major infection the pump will not be implanted.

Table 11.11 Costs of treating infections due to test or implant procedures

		Cost	Additional length of stay	reference
Minor infection	course of flucloxacillin oral solution (125mg/5mL 100ml)	£3.67	0 days	BNFc 2010-11
Major infection	Non-elective inpatient stay for major infection without complications (PA16B)	£2,623	4.61 days	NHS reference costs 2010/11

In the model if a patient develops a major infection during the surgery the pump will be removed. Or if the pump fails to work they will have the pump removed. For some patients the pump will be implanted but a problem is found that requires a second operation to fix. The costs of removing the pump or having a second operation to correct a problem are reported in Table 11.12.

Table 11.12 Cost of removing the pump due to major infection (2010/11 prices)

		Cost	Inpatient stay	reference
Pump removal	**Cost of having pump implanted less the cost of the pump**	£13,895 - £9,706 = £4,449	5 days	Cost of implant procedure taken from Sampson 2002. Cost of pump and catheters taken from the East Midlands Specialised Commissioning Group - Commissioning Policy for Intrathecal Baclofen. 25/09/2009 and uplifted to 2010/11 costs
Catheter revision or other correction	**2nd operation required to fix a problem with the pump**	£4,163	1.5 days	Reference cost for catheter 18 years or under NHS reference costs 2010/11

Outcomes

No studies were identified that demonstrated the predictive value of the ITB test. Patients only had a pump implanted if the test was positive. After discussion with the GDG it appears that clinicians are able to predict which patients will benefit from ITB treatment from their clinical characteristics. The test is used to demonstrate the effectiveness of ITB to the patient and help decide treatment goals.

The baseline analysis assumes no improvement in quality of life for children and young people who have the pump implanted and this is the same effect as standard therapy, a conservative assumption to reflect that little good quality comparative evidence is available. It is assumed that staying on standard therapy resulted in no quality of life improvements, but also no deterioration.

The analysis was also run using the long-term quality of life effects from Sampson 2002 (Table 11.7).

Synthesis of costs and outcomes

The cost of care for a population of 100 children and young people was calculated for each arm. Table 11.13 reports the number of specific events (test results, adverse events) throughout the clinical pathway and the total cost for children who were tested prior to planned treatment. Table 11.14 shows the same data for children who were not tested prior to treatment and were identified as suitable to have an ITB pump based on clinical judgement alone.

Table 11.13 Population numbers, mean and total cost of intrathecal baclofen treatment with testing (N=100) (figures are rounded from the model)

	Number
Patients having a test	100
Major infection due to test	1
Minor infection due to test	1
Patients with positive test result	94
Patients with negative test result	6
Patients who stay on standard therapy	9
Patients who have pump implanted after positive test result	91
Patients who have an infection during surgery	5
Patients who have second surgery to fix a problem with the pump	3

Patients who have pump removed	6
Patients with pump at 5 year follow-up	84
Total cost of care of children and young people tested before pump implanted	£2,142,330
Cost per patient	£21,423

Table 11.14 Population numbers, mean and total cost of intrathecal baclofen treatment without testing (N=100) (figures are rounded from the model)

	Number
Patients who have pump removed	15
Infection from surgery	6
Number of participants who have further surgery to fix a problem with the pump	3
Number of participants with pump at 5 year follow-up	85
Total cost of care of children and young people not tested before pump implanted	**£2,137,040**
Cost per patient	**£21,370**

Table 11.15 Population numbers, mean and total cost of standard treatment (N=100) (figures are rounded from the model)

	Number	**Cost per patient**	**Total cost**
Total cost of care of children and young people remaining on standard treatment	100	£97	£9,686

In an economic evaluation a new treatment is always compared with another treatment, or standard care. We are interested in the additional benefit of the new treatment above standard treatment and whether this incremental benefit is worth the additional cost. Using the baseline assumption of no improvement in health related quality of life with CITB therapy, standard therapy should be chosen because implanting the pump incurs costs with no improvement in health. However, if the analysis is run using the quality of life outcomes from Sampson 2002 then using the ITB pump is cost effective compared to standard therapy in wheelchair users with moderate spasm-related pain (Table 11.17). The analysis suggests that implanting the pump without testing is less costly and more effective than testing first using these inputs, but the differences in the overall costs and benefits is small (£21,423 versus £21,370 per person, and 1.70 versus 1.71 QALYs over 5 years).

Table 11.16 Quality of life improvement scores for category 3 (wheelchair users with moderate spasm-related pain) from Sampson 2002 used in sensitivity analysis

Treatment arm	**Estimated mean quality of life improvement per year**	**Total quality of life improvement over 5 years per person** **Discounted at 3.5%**
Standard treatment	0	0
Intrathecal baclofen pump with no test	0.43	2.01
Intrathecal baclofen pump with testing	0.43	2.01

Table 11.17 Sensitivity analysis - Incremental cost effectiveness results using quality of life outcomes from Sampson 2002 category 3 (wheelchair users with moderate spasm-related pain; benefits discounted by 3.5%)

Treatment arm	Effects	Incremental effects	Costs	Incremental costs	Incremental cost effectiveness ratio
Standard treatment	0		£9,686		
Intrathecal baclofen pump with no test	171.1	171.1	£2,137,040	£2,127,353	**£12,431**
Intrathecal baclofen pump with testing	169.7	-1.4	£2,142,330	£5,290	dominated

The incremental cost effectiveness results for all three categories of patients taken from Sampson 2002 are as follows:

- category 1, £19,798 bedbound patients experiencing severe spasm-related pain
- category 2, £10,691 bedbound patients who were not in pain
- category 3, £12,431 wheelchair users with moderate spasm-related pain.

Table 11.18 Sensitivity analysis - Incremental cost effectiveness results using quality of life outcomes from Sampson 2002 category 3 (benefits discounted by 1.5%)

Treatment arm	Effects	Incremental effects	Costs	Incremental costs	Incremental cost effectiveness ratio
Standard treatment	0		£9,686		
Intrathecal baclofen pump with no test	177.6	177.6	£2,137,040	£2,127,353	**£11,967**
Intrathecal baclofen pump with testing	176.2	-1.5	£2,142,330	£5,290	dominated

Discussion

There is considerable uncertainty in this model given the limited clinical evidence available to show the effectiveness of the pump. Only one RCT was identified with a very small study population of children and young people, but it was not a long-term study. Therefore the baseline assumption for this model was that the ITB pump would have no effect on quality of life and therefore could not be cost effective. This was tested in a sensitivity analysis using estimated quality of life scores from Sampson 2002. Using these quality of life scores the ITB pump may be a cost effective treatment compared to standard treatment. The EQ-5D scores from Sampson 2002 were estimated by the authors, and included adults and children with different causes of spasticity and so these scores may not be representative of the improvement in children and young people who have spasticity as a result of a non-progressive brain disorder.

Given the lack of evidence for improvement in quality of life the model was used to calculate what level of effectiveness would be needed for the pump to be found cost effective at the NICE threshold of £20,000 per QALY. If the ITB pump improves quality of life by more than 0.26 each year for the 5 year lifetime of the pump, then implanting a pump would be cost effective by the NICE threshold. The effectiveness of testing is also uncertain. If there are no adverse events related to testing then the QALYs gained are equal for both the group having testing and the group not having testing. But there is still an additional cost related to testing patients, £1,837 per patient. Testing may avoid pumps being removed due to lack of effect, as patients who will not have a beneficial effect may be identified at the test stage. Although in this analysis, the costs of testing outweighed the cost of additional surgeries required to remove the pump. There would be a quality of life decrement if the pump is removed but it would be short-term. The GDG believes that testing is a valuable part of the treatment, as in some cases reducing spasticity can have a negative effect and then the pump would not be appropriate. Also the test would allow children and young people and their parents or carers to understand the effects of ITB and so make informed treatment choices and feel confident in giving consent.

The main costs are related to implanting the pump. Sensitivity analysis could be performed varying the costs included in the model. Given that standard therapy is so much cheaper than continuous ITB, the other costs included in the model, for example treating infections, are minor compared to the overall cost of testing and implanting the ITB pump. The costs used in this model were uplifted from 1999 costs and these may not be representative of the true current costs. A document for the East Midlands Specialised Commissioning Group on the Commissioning Policy for Intrathecal Baclofen for paediatrics, showed the costs of implanting an ITB pump for one year using 2009 costs. (http://www.emscg.nhs.uk/Library/P008V2EMSCGPolicyforIntrathecalBaclofen.pdf (accessed 12 October 2010); see Table 11.19).

Table 11.19 Cost of intrathecal baclofen pump for year for paediatrics (uplifted to 2010/11 prices) (East Midlands Specialised Commissioning Group)

Element of procedure	Cost
Test dose	**£1,077**
Implant procedure	£ 926
Device and catheters	£ 9,706
Refills (4 per year)	£3,698
Total	**£15,407**

The costs from Sampson 2002 were more detailed and so used in the model. Using the East Midlands costs, the overall cost with the test and including a 5 year follow up was £28,213. This is higher than the costs used in the model, but when tested in the model these higher costs did not change the direction of the results.

Conclusion

ITB is much more expensive than standard treatment and its clinical value is uncertain. This analysis illustrates the trade-off between the benefits of treatment, the risks, and the costs. This is based on very limited, low quality data which suggests that the efficacy, and the risks and adverse events associated with this treatment are not well known. A more detailed evaluation of the costs, benefits, and risks of ITB require more long-term data, especially as this analysis suggests that ITB may be beneficial and cost effective in some groups of children but not all children.

11.6 Orthopaedic surgery

Health economic question

What is the cost effectiveness of orthopaedic surgery in preventing or treating musculoskeletal deformity compared to no surgery in children with spasticity caused by a non-progressive brain disorder?

Literature review

No published health economic evaluations were identified in the literature search conducted for this review question.

Further analysis

Introduction

Given the lack of clinical evidence for the outcomes considered important for this question it was not possible to develop an economic evaluation. The guideline covers children with considerable variation in impairment from those with spasticity in a single muscle to children with severe spasticity affecting all limbs and appropriate surgical management procedures will vary between patients. Like the other interventions for spasticity considered for economic evaluation, the goals of therapy will be individualised to the child within the family and will change in different contexts. The outcomes of importance will therefore vary depending on the specific goal. As with physical therapy and orthoses, it was not possible to undertake an evaluation that would provide meaningful results in which the GDG would have confidence.

Methods

A cost analysis was requested by the GDG and is presented here. NHS reference costs from 2010-11 were found for various types of surgery. The cost of surgery varies depending on the limb, whether it is minor or major surgery, and there is a 60% uplift to tariffs for children when surgery is performed in a specialist children's hospital.

Resource use and costs

Reference costs (for 2010-11) were found for hip, knee, foot, hand, shoulder and upper arm, elbow and lower arm procedures. They were classed as non-trauma, categories one and two. The reference costs were grouped by procedure and whether it was minor, intermediate or major surgery. Within these groups a weighted average cost was calculated from all procedures for categories one and two, with or without complications. Costs ranged from £1,855 (minor hand procedures) to £6,241 (major hip procedures). With the children's tariff uplift these become £2,969 to £9,986. The average length of stay ranged from 1 day for hand procedures, to 15 days for major hip procedures. Scoliosis or surgery for other spinal deformities cost on average £1,797 (£2,874 with uplift) and required on average 3 days in hospital.

These costs are for a finished consultant episode and so do not include rehabilitation physical therapy in the community after surgery.

Conclusion

Long-term outcomes are needed in order to develop a useful economic evaluation to assess surgery compared to no surgery. The question on timing of surgery and the need for monitoring would benefit from an economic evaluation. The increased costs of routinely monitoring children can be compared to the potential improvements in the effectiveness of surgery and reduction in need for further interventions. Further research would be useful in this area.

11.7 Selective dorsal rhizotomy

Health economic question

What is the cost effectiveness of SDR in children and young people with spasticity caused by a non-progressive brain disorder?

Literature review

No published health economic analyses were identified for this question. The NICE IPAC, which developed 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE IPG 373), had access to an unpublished dissertation presenting a pilot economic analysis of SDR in the UK (Edwards 2010). It was developed to determine whether a full-scale economic analysis of SDR was needed and whether SDR should continue to be offered in the UK. The analysis was based on a group of patients treated at the Robert Jones and Agnes Hunt Orthopaedic and District Hospital NHS Trust who had undergone SDR and had been regular patients from 5 years old to post-adolescence and comprehensive hospital records were available. The costs and outcomes for this group were retrospectively analysed.

The comparison group was four patients with spastic diplegia who had not been selected for SDR for minimal clinical reasons. It was expected that these patients would have followed a very similar pattern of musculoskeletal development and impairment to the SDR group had they not undergone SDR.

The small numbers of patients included in the analysis makes the results of the economic evaluation uncertain, as was explained in the discussion of the dissertation. The literature review for this clinical question was limited. The only statistically significant benefit reported was a reduction in tone in lower extremity joints. As no good quality long term data was available it is not possible to say from the evidence whether the initial reduction in tone reported would lead to long term, clinically significant benefits.

Further analysis

Introduction

It was not possible to develop a cost effectiveness analysis as it is necessary to have final outcomes and the GDG were unable to extrapolate the reduction in tone to a potential long term clinically significant improvement in function.

Methods

Evidence from an unpublished study would not normally be included in a NICE clinical guideline. However, the study provided useful estimates of the resource use and costs which the GDG were able to include in their considerations of SDR. The cost analysis developed for the dissertation (Edwards 2010) was very detailed and gives a thorough understanding of the costs involved in SDR, the number of consultations needed and begins to look at the potential impact on need for further surgery. The costs are reproduced in this section. In order to understand how SDR fits into the NHS this cost data needs to be reviewed alongside good quality comparative long-term effectiveness data with a large enough population to capture the risks as well as the benefits.

Resource use and costs

A report for the Australian Medical Services Advisory Committee outlined the requirements for a centre to offer SDR. An experienced multidisciplinary team is necessary and a key aspect of the service is patient selection and monitoring. The surgery is performed by a paediatric neurosurgeon supported by specialists in paediatric anaesthesia, paediatric perioperative pain management, paediatric rehabilitation and intra-operative spinal monitoring. Post-operative care involves input from specialists in neurosurgery, paediatric rehabilitation, orthotics, orthopaedic surgery, physiotherapy, occupational therapy, nursing psychology and social work. The report stated that the procedure is not technically difficult and staff can be trained quickly (Medical Services Advisory Committee 2006).

A cost analysis was conducted for each patient in the Edwards 2010 study. A data collection sheet was used to record all contacts with the hospital or one of its outreach services in schools and clinics in other Trusts. Contact episodes were separately identified as outpatient appointments, multidisciplinary team sessions, gait assessments, orthotics supplies, hospital admissions, surgical or other in-patient interventions, and admissions for physiotherapy top-up.

They use a bottom-up approach where resource use for nine patients receiving SDR was recorded and then costs applied, rather than taking tariffs or reference costs for episodes (Tables 11.20-11.23).

Table 11.20 Unit costs for treatment (source: Edwards 2010)

Initial clinical screening and pre-operative assessment	Cost
Initial outpatient appointment	£94
Gait assessment	£1,245
X-ray (spine and hips)	£25
Magnetic resonance imaging of brain and spinal cord	£2,467
Paediatric consultant review of imaging (15 minutes)	£21

Pre-operative assessment clinic	
Pre-op clinic attendance	£94
Dietitian (30 minutes)	£13
Psychologist (1 hour)	£57
Orthotist (1 hour)	£30

Table 11.21 Resource use and unit costs for SDR procedure (source: Edwards 2010)

SDR procedure and recovery	Cost
Theatre time	£3,600
Theatre – two surgeons for 4 hours	£634
Special tooling – gold anspach drill	£130
Intra-operative spinal monitoring	
Spinal monitoring	£2,680
Bioengineering support (4 hours)	£54
Recovery	
Recovery – paediatric nurses (2) (mean 1 hour in recovery)	£40

Table 11.22 Resource use and unit costs for rehabilitation on ward after SDR (source: Edwards 2010)

Rehabilitation on Ward (7 weeks)	Cost
Consultant ward round (20 minutes per visit)	£148
Ward costs	£8,459
Dietician (30 minutes)	£13
Psychologist (30 minutes)	£28
Physiotherapy – group session	£277
Physiotherapy – individual session	£2,217
Hydrotherapy	£623
Orthotics – contracture correction devices (CCDs) supplied to 15% of children	£201
Orthotist to fit and supply CCDs (1.5 hours)	£45
Therapeutic electrical stimulation	£160

Table 11.23 Total costs for SDR assessment, procedure and follow-up (source: Edwards 2010)

Total Costs of SDR	Cost
Net total	**£21,135**
Overheads	£4,227
Grand Total	**£25,362**

The study did not include the cost of additional follow-up clinic visits since all patients are followed up routinely post-surgery. The costs of ankle foot orthosis and footwear whilst on the ward were not included because a high proportion of children with spastic diplegia routinely wear ankle foot orthoses. The neurophysiological spinal monitoring equipment was treated as a sunk cost as it is used for other spinal surgery and so was not included in the costing.

The mean cost of care for the SDR patients (from age 5 years to end of adolescent growth (16 years girls, 18 years boys)) was £67,478 (median £71,404, range £47,511 to £86,880). In the non-SDR group the mean cost of care was £63,542 (median £56,890, range £44,842 to £95,570).

The study reported all the patient contacts for each group including musculoskeletal surgery and inpatient days including top-up physiotherapy admission. They found the number of outpatient visits showed no significant variation between groups group (32.9 outpatient visits for SDR group compared to 30.3 for non-SDR group). Non-SDR patients underwent an average of 3 periods of surgery in total and SDR an average of 1.9 (this includes the SDR surgery and periods of surgery after SDR), although the SDR patients spent longer in hospital (83 days compared to 57.5 in the non-SDR group). However, these are small patient numbers.

Conclusion

The cost data presented in the dissertation was thorough and provides useful information. Again these are small patient numbers and so it would not be productive to compare the groups. There is considerable uncertainty surrounding the effectiveness of SDR. In order to provide a useful analysis for decision making we would need to understand the long-term benefits and risks of treatment compared to the next best alternative. A “what-if” analysis working backwards from the NICE threshold for cost-effectiveness to determine what level of effectiveness would be needed for SDR to be considered was suggested. The GDG had limited clinical experience with patients who had had SDR and did not feel able to estimate the potential efficacy of SDR in the long-term compared to physiotherapy or orthopaedic surgery given the published evidence available. A ‘what-if’ analysis relies on clinical justification of the efficacy estimates to be useful for decision making and the GDG did not feel they would be able to support any guesses they would make with confidence.

11.8 Overall conclusions

Given the lack of published evidence, further comparative research is necessary to capture benefits of interventions for spasticity in children and young people. These outcomes need to be expressed in terms of function, pain, adverse events and quality of life ideally using the EuroQol Group’s EQ-5D instrument (a child friendly version is available) or the Health Utilities Index (which was developed for children). Although other goals are important, NICE considers evidence of cost effectiveness of interventions across all health states in a population in terms of QALYs. Without evidence of cost effectiveness expressed in terms of QALYs, it is not possible to determine whether interventions designed to benefit children and young people with spasticity represent a good use of resources when compared with other competing calls on those same resources in the NHS.

Long-term data on outcomes are needed for the ITB pump, orthopaedic surgery and SDR because these are invasive and expensive treatments with risks associated. Also the studies should be designed to allow subgroup analysis by severity of spasticity in terms of the GMFCS, and also limb involvement (hemiplegia, diplegia, and quadriplegia). Studies should be designed to allow data on resource use to be collected to allow cost analysis. Cost effectiveness analysis comparing treatments for each subgroup will provide better information for decision making.

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13 Abbreviations and glossary

13.1 Abbreviations

AFO	ankle-foot orthosis
AHA	Assisting Hand Assessment (reported in some research studies as Assisted Hand Assessment)
ANCOVA	analysis of covariance
ANOVA	analysis of variance
AROM	active range of movement (reported in some research studies as active range of motion)
BADS	Barry-Albright Dystonia Scale
BFMS	Burke-Fahn-Marsden Scale
BNFc	British National Formulary for Children
BoNT	botulinum toxin
BoNT-A	botulinum toxin type A
BoNT-B	botulinum toxin type B
CHQ	Child Health Questionnaire
CHQ-PF50	Child Health Questionnaire – Parent Form 50
CI	confidence interval
CIMT	constraint-induced movement therapy
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CITB	continuous pump-administered intrathecal baclofen
COPM	Canadian Occupational Performance Measure
COPM-P	Canadian Occupational Performance Measure – Performance
COPM-S	Canadian Occupational Performance Measure – Satisfaction
CSF	cerebrospinal fluid
GABA	gamma-aminobutyric acid
GAS	goal attainment scaling (reported in some research studies as goal assessment scaling or scale)
GAS T-score	goal attainment scaling T-score (reported in some research studies as goal assessment scaling or scale T-score)
GDG	guideline development group
GGI	Gillette Gait Index
GMFCS	Gross Motor Functional Classification System

GMFM	Gross Motor Function Measure
GMFM-66	Gross Motor Function Measure 66-item score
GMFM-88	Gross Motor Function Measure 88-item score
GMFM-A	Gross Motor Function Measure – Dimension A (lying and rolling)
GMFM-B	Gross Motor Function Measure – Dimension B (sitting)
GMFM-C	Gross Motor Function Measure – Dimension C (crawling and kneeling)
GMFM-D	Gross Motor Function Measure – Dimension D (standing)
GMFM-E	Gross Motor Function Measure – Dimension E (walking, running and jumping)
GMPM	Gross Motor Performance Measure
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRAFO	ground reaction force ankle-foot orthosis
HAFO	hinged ankle-foot orthosis
HTA	Health Technology Assessment
ICD-10	International Classification of Diseases
ICER	incremental cost effectiveness ratio
ICF Framework	International Classification of Functioning, Disability and Health
IPAC	Interventional Procedures Advisory Committee
IPG	interventional procedure guidance
ITB	intrathecal baclofen
MAS	Modified Ashworth Scale
MACS	Manual Ability Classification System
MAUULF	Melbourne Assessment of Unilateral Upper Limb Function
MD	mean difference
MTS	Modified Tardieu Scale
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NDT	neurodevelopmental treatment
NHS	National Health Service
NHS EED	NHS Economic Evaluation Database
NICE	National Institute for Health and Clinical Excellence
NS	not (statistically) significant
OR	odds ratio
OTHP	occupational therapy home programme
PEDI	Pediatric evaluation of disability inventory
PedsQL	Pediatric quality of life inventory
PLSAFO	posterior leaf spring ankle-foot orthosis
PODCI	Pediatric Outcomes Data Collection Instrument
PROM	passive range of movement (reported in some research studies as passive range of motion)

PSSRU	Personal Social Services Research Unit
QALY	quality adjusted life year
QUEST	Quality of Upper Extremity Skills Test
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomised controlled trial
RR	relative risk
SAFO	solid ankle-foot orthosis (sometimes referred to as a rigid ankle-foot orthosis)
SCPE	Surveillance of Cerebral Palsy in Europe
SD	standard deviation
SDR	selective dorsal rhizotomy
SE	standard error
SEMLS	single-event multilevel surgery
SIGN	Scottish Intercollegiate Guidelines Network
SMO	supramalleolar orthosis
SPC	summary of product characteristics
TLSO	thoracic-lumbar-sacral orthosis
UK	United Kingdom
UMNL	upper motor neurone lesion
USA	United States of America
VAS	Visual Analogue Scale
WHO	World Health Organization
WMD	weighted mean difference

13.2 Glossary

Abnormal torsion	Abnormal twisting of a bone resulting from abnormal muscle tone
Acetylcholine	A chemical produced by the nervous system to send messages from one nerve to another or from nerve to muscle. One of the neurotransmitters
Acquired brain injury	A brain injury that occurs after the neonatal period (more than 28 days after birth)
Active range of movement	The range through which a child or young person can move a specific joint themself
Ankle dorsiflexion	Movement of the foot at the ankle joint in an upward direction
Ankle plantarflexion	Movement of the foot at the ankle joint in a downward direction
Anti-muscarinic	A drug that inhibits the action of acetylcholine at muscarinic receptors
Ataxia	A disorder of control of movement that impairs balance. It may involve the trunk (truncal ataxia) or the limbs. In some children and young people it may result from sensory deficits
Athetosis	A disorder characterised by slow, sinuous or writhing movement. Athetosis and chorea (see below) are often seen together and it can be difficult to distinguish one from the other

Bilateral cerebral palsy	Cerebral palsy affecting both sides of the body
Bilateral spasticity	Spasticity affecting both sides of the body
Bimanual therapy	An approach to physical therapy in which the child or young person has unrestrained use of both arms (see constraint-induced movement therapy)
Bony deformity	Distortion, irregularity or deviation of bones, often resulting from abnormal muscle tone
Botulinum toxin type A treatment	A neurotoxin produced by the bacterium *Clostridium botulinum* that blocks neurotransmitter release at peripheral cholinergic nerve terminals. Injection into a muscle reduces spasticity. Type A is one of seven serologically distinct toxin types. Botulinum toxin type A is manufactured by laboratory fermentation of *C botulinum* cultures which are reconstituted with saline before intramuscular injection
Cerebral palsy	A group of permanent disorders of the development of movement and posture that limit activity and are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems
Cholinergic	Relating to nerve cells where acetylcholine is a neurotransmitter
Chorea	A disorder characterised by involuntary, purposeless and irregular movement affecting proximal or distal joints. Chorea and athetosis (see above) are often seen together and it can be difficult to distinguish one from the other
Constraint-induced movement therapy	An approach to physical therapy in which an unaffected arm is temporarily restrained to encourage use of the other arm
Continuous pump-administered intrathecal baclofen treatment	Direct administration of baclofen into the fluid-filled space around the spinal cord (the intrathecal space) using a catheter and infusion pump. The pump is implanted in the abdominal cavity and allows a continual controlled delivery of baclofen adjusted according to need
Contracture	Shortening of muscle tendons, ligaments and soft tissues resulting in a limitation of joint movement. Usually, muscle shortening is the primary abnormality, but prolonged immobility or scarring may also contribute
Diplegia	A type of cerebral palsy in which the lower limbs are affected, and the upper limbs may be less severely affected or unaffected
Distal joint	A joint situated away from the centre of the body or the point of attachment
Dynamic orthosis	A non-rigid orthosis designed to allow some movement. A dynamic thumb abduction splint may be used where there is a 'thumb in palm' deformity
Dyskinesia	A term used to include movement disorders such as athetosis, chorea, dystonia and tics
Dystonia	Involuntary, sustained, or intermittent muscle contractions that cause twitching and repetitive movements, abnormal postures or both. It can be precipitated by attempts to move, change in position, and by emotion (such as excitement or anxiety)
Equinus deformity	Abnormal ankle plantarflexion (see above). This can, for example, result in the child or young person walking on tiptoe
Fine motor function	The ability to use small muscle groups, often in co-ordination with the eyes, to perform precision activities such as writing or fastening buttons
Focal dystonia	Dystonia involving a specific muscle or group of muscles

Focal spasticity	Spasticity involving a specific muscle or group of muscles
Function	The ability to perform normal activities or actions. Such function may be impaired by spasticity and associated motor disorders and by the complications of spasticity
Gait analysis	A detailed approach to analysing the component phases of walking using instrumentation or video analysis in addition to clinical observation. This is undertaken to evaluate a child or young person's ability and style of walking and to plan or assess treatment
Gait assessment	Assessment of walking based on clinical observation with or without formal gait analysis. This is undertaken to evaluate an child or young person's ability and style of walking and to plan or assess treatment
Gross motor function	The ability to use large muscle groups to perform body movements such as sitting, standing, walking and running
Gross Motor Function Classification System	A five-level classification system that describes the gross motor function of a person with cerebral palsy on the basis of their self-initiated movement with particular emphasis on their sitting, walking, and wheeled mobility: level I, walks without restrictions; level II, walks without assistive devices; level III, walks with assistive devices; level IV, has limited self-mobility; level V, has severely limited self-mobility even with assistive devices
Hemiplegia	Weakness or paralysis of an arm and leg on one side of the body
Hip abduction	Lateral movement of the lower limb at the hip joint away from the central line of the body
Hip displacement	Hip migration (see below) of greater than 30%
Hip migration	Movement of the top of the thigh bone that connects with the pelvis (the femoral head) from its normal position in the socket joint of the hip (the acetabulum). This movement is often measured by reporting the degree of displacement seen on X-ray (known as the hip migration percentage)
Hypertonia	Abnormally increased resistance to externally imposed movement about a joint. Hypertonia includes spasticity, dystonia, and rigidity
International Classification of Functioning, Disability and Health	The World Health Organization's classification (often referred to as the ICF framework) that expresses how a person with a health condition functions in their daily life (rather than focusing on a disease process). The framework takes account of interactions between a person's state of health, their environment, and personal factors through domains termed 'body function and structure' and 'activity and participation'
Intrathecal baclofen testing	Direct injection of baclofen into the fluid-filled space around the spinal cord (the intrathecal space) using a lumbar puncture needle or a temporary spinal catheter in order to assess the likely response to continuous pump-administered baclofen treatment
Kyphosis	Abnormal curvature of the spine when viewed from the side of the body that results in a hunched or slouching position
Lower limb	The region of the body that extends from the pelvic girdle, and includes the buttock, hip, thigh, knee, shin, calf, ankle and foot. Anatomically, the term leg includes that part of the lower limb below the knee
Low-load active stretching	Stretching of a muscle by contracting an opposing muscle, for example, the child or young person may pull their foot upwards (dorsiflexion) by contracting the muscles at the front of the leg thereby stretching the calf muscles
Low-load passive stretching	Stretching of a muscle by application of an external force, for example, a physiotherapist may move or position the child or young person's limb to

	achieve this
Monoplegia	Weakness or paralysis of a single limb
Motor disorder	An umbrella term used to describe disorders primarily affecting movement
Motor function	The ability to produce voluntary movement through the interaction of the central nervous system (brain and spinal cord), peripheral nervous system (nerves) and the muscles
Muscle-strengthening therapy	Any physiotherapy programme used to improve muscle strength
Muscle tone	The normal state of continuous passive partial contraction in a resting muscle. Muscle tone is important in maintaining posture. Increased muscle tone (hypertonia) is associated with an abnormal resistance to passive stretch, while reduced muscle tone (hypotonia) is associated with floppiness of the limbs or trunk and poor posture
Musculoskeletal anatomy	The bones, joints and skeletal muscles and their associated nerves
Musculoskeletal complication of spasticity	A complication of spasticity affecting the musculoskeletal system
Network of care	Linked groups of healthcare professionals and organisations working in an agreed and co-ordinated manner to deliver a clinical service. A network is not constrained by existing professional, organisational or institutional boundaries
Network team	A multidisciplinary group of healthcare and other professionals working in a network of care to deliver a clinical service
Neurology	The medical specialty concerned with the anatomy, function and disorders of nerves and the nervous system
Neurosurgery	Surgery on any part of the nervous system
Non-progressive brain disorder	A condition caused by an injury to or abnormal development of the brain or its function that is not neurodegenerative
Occupational therapy	A professional discipline that promotes health and wellbeing through engagement in meaningful and useful activities based on an analysis of physical, environmental and other factors to identify barriers to function and participation
Optimisation of function	To enhance the performance of an activity or action as much as is possible
Optimisation of movement	To enhance the performance of body movement as much as is possible
Orthopaedic surgery	Surgery aimed at preventing or improving conditions involving the musculoskeletal system
Orthosis (plural, orthoses)	An artificial device or appliance used to support, align, prevent, or correct deformities or to improve musculoskeletal function
Orthotics	The medical specialty concerned with the provision and use of orthoses
Passive range of movement	The degree of motion through which a joint can be moved by an outside force without active participation by the child or young person themself (for example, movement by another person)
Postural management	A planned programme of activities or interventions aimed at improving or supporting a child or young person's posture
Postural management equipment	Apparatus used to maintain or improve a child or young person's posture and function, for example, special seating, night-time support, standing supports or orthoses
Proximal joint	A joint situated near to the centre of the body or the point of attachment of a

	limb to the trunk
Physical therapy	Physiotherapy and/or occupational therapy
Physiotherapy	A professional discipline that aims to improve health, wellbeing and quality of life by facilitating movement, function and participation
Pyramidal	Relating to the pyramidal tract of the central nervous system that is involved in the control of voluntary movement. It originates in the sensorimotor areas of the cerebral cortex and descends through the brain stem to the spinal cord
Quadriplegia	Paralysis or weakness affecting the both the arms and legs
Range of movement	The range of motion, usually measured in degrees, through which a joint can move
Rigid orthosis	An inflexible artificial device or appliance used to support, align, prevent, or correct deformities or to improve musculoskeletal function
Sarcoplasmic reticulum	A network of smooth-surfaced tubules surrounding each myofibril within smooth and striated muscle tissue which stores calcium and releases it on electrical stimulation
Scoliosis	An abnormal lateral curvature of the spine viewed from in front of or behind the child or young person
Secondary complication of spasticity	An adverse effect on musculoskeletal structure that occurs as a result of spasticity (for example, a contracture or abnormal torsion)
Secondary consequence of spasticity	Any effect experienced by a child or young person as a result of spasticity. This may be symptomatic (for example, pain or difficulty walking) or a complication affecting the structure of the musculoskeletal system (see secondary complication of spasticity)
Selective dorsal rhizotomy	A neurosurgical procedure in which some of the sensory nerves that contribute to spasticity in the lower limb are cut at the point where they enter the spinal cord
Serial casting	The successive use of casts with the aim of progressively lengthening muscles and other non-bony tissues such as ligaments and tendons thereby reducing the effect of contractures by passive stretching to gradually improve the range of movement
Single-event multilevel orthopaedic surgery	Musculoskeletal surgery where a number of procedures are performed at one time
Spasticity	A specific form of hypertonia in which one or both of the following are present: • the resistance to externally imposed movement increases with increasing speed of stretch and varies with the direction of joint movement • the resistance to externally imposed movement increases rapidly beyond a threshold speed or joint angle.
Spinal fusion	A surgical procedure where two or more vertebrae are joined to prevent movement between them
Skeletal muscle	Striated muscle that is connected at either or both ends of a bone, that usually crosses a joint, and that forms part of the mechanical system to move parts of the skeleton
Task-focused active-use therapy	A physiotherapy technique where a specific goal is identified and the child or young person carries out exercises or activities using the affected limb or limbs to improve their performance
Trunk	The torso or body excluding the head and limbs

Unilateral cerebral palsy	Cerebral palsy affecting one side of the body
Unilateral spasticity	Spasticity affecting one side of the body
Upper limb	The arm, including from the shoulder, axilla, upper arm, elbow, forearm, wrist and hand

Appendices A to L are in a separate file