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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Appendices A–M are in a separate file.

1 Guideline summary

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

GDG members

Paul Eunson (Chair)	Consultant Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh
Gordon Allan	General Practitioner, Methil, Fife
Liz Barnes	Parent and carer member, Freelance Writer, Trustee of Hemihelp, London
Lucinda Carr	Consultant Paediatric Neurologist, Great Ormond Street Hospital for Children
Stephenie Cawker	Clinical Specialist Physiotherapist, Neurodisabilities, Great Ormond Street Hospital for Children
Elspeth Dixon	Parent and carer member, Senior Specialist Learning Disability Physiotherapist, Adult Learning Disability Team, Herefordshire
Christina Gericke	Specialist Paediatric Occupational Therapist (retired May 2011), Royal Hampshire Country Hospital, Winchester
Alec Musson	Superintendant Physiotherapist, Paediatric Physiotherapy Team, Leeds Teaching Hospitals NHS Trust
James Robb	Consultant Orthopaedic Surgeon, Royal Hospital for Sick Children, Edinburgh
Trudy Ward	Interim Head of Community Children's Nursing, (formerly Specialist Clinical Lead Nurse, Childhood Neuro-disability), Sussex Community NHS Trust.
Jane Williams	Consultant Community Paediatrician, Nottingham University Hospitals NHS Trust

National Collaborating Centre for Women's and Children's Health (NCC-WCH)

Lauren Bardisa-Ezcurra	Research fellow (until April 2011)
Zosia Beckles	Information scientist
Shona Burman-Roy	Senior research fellow
Katherine Cullen	Health economist
Juliet Kenny	Project manager
Moira Mugglestone	Director of guideline development (from June 2011)
Stephen Murphy	Clinical co-director (children's health)

External advisers

Christopher Morris	Senior Research Fellow in Child Health, Peninsula Medical School, University of Exeter and Honorary Principal Orthotist, Nuffield Orthopaedic Centre, Oxford
Andrew Roberts	Consultant Orthopaedic Surgeon, The Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry

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Julie Hodge Allen, Khalid Ashfaq, Wahab Bello, Hannah Rose Douglas, Rupert Franklin, Rosalind Lai, Emma Newbatt, Edmund Peston, Wendy Riches and Roz Ullman at the NCC-WCH

1.2 Foreword (or executive summary)

The final published guideline will include a foreward or executive summary

1.3 Care pathway

The care pathways are presented in separate files for the stakeholder consultation

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.

1.4 Key priorities for implementation

Number	Recommendation	See section
	Principles of care	**4**
1	Offer immediate referral to a local multidisciplinary child development team that can be accessed when needed and is linked to regional specialist centres.	4
4	Offer a management programme that is: • individualised • goal focused • developed and implemented in partnership with the child or young person and their family or carers.	4
5	Local multidisciplinary child development teams and regional specialist centres should enable children and young people (and when appropriate their parents or carers) to be partners in the development and implementation of management programmes by offering: • relevant information and educational materials • regular opportunities for discussion and • advice on the child or young person's developmental potential and how different treatment options may affect this potential.	4
9	Monitor the child or young person for: • progression of spasticity • development of secondary consequences of spasticity • response to treatments • the need for changes to individualised goals and • the need for timely referral to regional specialist centres.	4
11	Offer adjunctive physical therapy following treatments involving botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy to ensure effectiveness of these treatments.	4

Number	Recommendation	See section
13	Before starting treatment, regional specialist centres should ensure that local multidisciplinary child development teams have allocated resources for locally provided post-treatment services.	4
	Physical therapy (physiotherapy and occupational therapy	**4**
14	Offer to refer children and young people to a physiotherapist who is a member of the local multidisciplinary child development team.	4
	Intrathecal baclofen	**8**
79	Consider treatment with continuous pump-administered intrathecal baclofen if, despite the use of non-invasive treatments, spasticity, with or without dystonia, is causing difficulties with any of the following: • pain or muscle spasms • posture or function • self-care (or ease of care in the case of parents or carers).[i]	8
	Orthopaedic surgery	**9**
103	Offer children and young people referral to an orthopaedic surgeon if there is clinical or radiological evidence of hip displacement or spinal deformity.	9
106	Monitor children and young people to identify displacement of the hip and spinal deformity.	9

1.5 Recommendations

Number	Recommendation	See section
	Principles of care	**4**
1 (KPI)	Offer immediate referral to a local multidisciplinary child development team that can be accessed when needed and is linked to regional specialist centres.	4
2	The local multidisciplinary child development team should be experienced in the management of spasticity in children and young people and include a paediatrician, a paediatric physiotherapist and have access to a paediatric occupational therapist.	4
3	Access to a paediatric occupational therapist is needed for children and young people with spasticity that affects the upper limb.	4
4 (KPI)	Offer a management programme that is: • individualised	4

[i] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

Number	Recommendation	See section
	• goal focused • developed and implemented in partnership with the child or young person and their family or carers.	
5 (KPI)	Local multidisciplinary child development teams and regional specialist centres should enable children and young people (and when appropriate their parents or carers) to be partners in the development and implementation of management programmes by offering: • relevant information and educational materials • regular opportunities for discussion and • advice on the child or young person's developmental potential and how different treatment options may affect this potential.	4
6	When formulating a management programme take into account the impact of treatment schedules on family circumstances.	4
7	Identify and agree with children and young people (and where appropriate their parents or carers) goals and assessments that: • are appropriate for their age and development • will aim to improve their body function and structure and activity and participation in line with the domains of the World Health Organization's International Classification of Functioning, Disability and Health.[ii]	4
8	Record and communicate the child or young person's individualised goals within the local multidisciplinary child development team and with all healthcare professionals who care for them in different settings.	4
9 (KPI)	Monitor the child or young person for: • progression of spasticity • development of secondary consequences of spasticity • response to treatments • the need for changes to individualised goals and • the need for timely referral to regional specialist centres.	4
10	Do not offer botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy to children and young people unless they are participating actively in a programme of care and physical therapy.	4
11 (KPI)	Offer adjunctive physical therapy following treatments involving botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy to ensure effectiveness of these treatments.	4
12	Healthcare professionals in regional specialist centres who assess children and young people's suitability for oral drugs, botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy should communicate with the child or young person's local multidisciplinary child development team to ensure compatibility and continuity of local	4

[ii] World Health Organization International Classification of Functioning, Disability and Health (ICF), available from www.who.int/classifications/icf/en/

Number	Recommendation	See section
	and specialist services.	
13 (KPI)	Before starting treatment, regional specialist centres should ensure that local multidisciplinary child development teams have allocated resources for locally provided post-treatment services.	4
	Physical therapy (physiotherapy and occupational therapy)	**4**
14 (KPI)	Offer to refer children and young people to a physiotherapist who is a member of the local multidisciplinary child development team.	4
15	Offer children and young people a physical therapy programme tailored to their individual needs and aimed at specific goals, such as: • enhancing skill development and improving function • enhancing the ability to participate in everyday activities • preventing or delaying the onset of complications such as contractures.	4
16	When formulating physical therapy programmes for children and young people take account of: • the views of the child or young person and their parents or carers • the likelihood of achieving the intended goals of treatment • the implications for the child or young person and their family in implementing the plan, including the time and effort involved and potential barriers (for example, barriers associated with particular cultural practices).	4
17	Consider task-focused active-use therapies such as constraint-induced movement therapy followed by bimanual therapy to enhance manual skills.	4
18	Consider structuring task-focused active-use therapy as an intensive programme over a short time period (for example, 4–8 weeks).	4
19	Consider muscle-strengthening therapy where assessment suggests that muscle weakness is contributing to loss of function or joint deformity.	4
20	Direct muscle-strengthening therapies towards specific goals and incorporate progressive repetitive exercises performed against resistance.	4
21	Consider postural management strategies to: • prevent or slow the development of contractures in children and young people at risk of developing these • enable the child or young person to take part in activities appropriate to the child or young person's stage of development.	4
22	As part of postural management consider an individualised physical therapy programme that includes: • resting positions and • low-load active or passive stretching over 24 hours.	4
23	Offer training to parents and carers involved in delivering postural	4

Number	Recommendation	See section
	management programmes.	
24	Assess whether any equipment or techniques used in the physical therapy plan is safe and appropriate, for example in children or young people with any of the following: • poorly controlled co-existing epilepsy • respiratory compromise • risk of aspiration • risk of bone fracture due to osteoporosis (for example, children and young people who are non-ambulatory, malnourished or taking anticonvulsant therapy).	4
25	For children and young people who are at risk of bone fractures due to osteoporosis (for example, children and young people who are non-ambulatory, malnourished or taking anticonvulsant therapy), consider sustained low-load stretching to prevent or limit contractures and joint deformity. Depending on the individual child or young person's circumstances (for example recent history of fractures, bone pain, broken skin), consider low-load stretching and weight bearing including use of orthoses or serial casting.	4
26	Monitor children and young people at risk of developing functional difficulties related to their condition. Consider a programme of daily maintenance activities for children and young people with or at risk of developing functional difficulties.	4
27	Consider the use of serial casting after botulinum toxin type A treatment to improve passive range of movement if muscle tightness is identified alongside dynamic spasticity. To improve the cast's tolerability and allow better stretch of muscle, do not apply serial casts for 2-4 weeks after botulinum toxin type A treatment.	4
28	Offer children and young people and their parents or carers verbal and written information about physical therapy interventions needed to achieve intended goals. This information should emphasise possible advantages as well as difficulties and possible adverse effects (for example time commitment and discomfort) to enable them to participate in choosing a suitable physical therapy programme.	4
29	Reassess at regular intervals all children and young people receiving a programme of physical therapy to ensure that: • the intended goals are being achieved • the therapy programme remains appropriate to the child or young person's individual needs.	4
30	When considering 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
31	Physical therapists should have a central role in preparing young people (and their parents or carers) for transition and transfer to adult	4

Number	Recommendation	See section
	physical therapy services (for example, helping them to take responsibility for their own physical therapy).	
	Orthoses	**5**
	General principles	5
32	Consider orthoses for children and young people with spasticity to: • improve posture • facilitate upper limb function • improve walking efficiency • prevent or slow development of contractures • prevent or slow hip migration.	5
33	Determine realistic goals for treatment with orthoses based on a careful individual assessment, and discuss the options, risks and benefits of wearing them with children and young people and their parents or carers.	5
34	Ensure that orthoses have been designed, sized and fitted correctly.	5
35	Inform children and young people with orthoses and their parents and carers: • how to apply them • when to wear them and for how long • when and where to seek further advice.	5
36	Ensure that an orthotist is involved when a custom-made orthosis is being used.	5
37	Minimise delays in the supply of orthoses after measurement and in the repair of orthoses.	5
38	Review orthotic use at every contact with the local multidisciplinary child development team to ensure that orthoses: • are still acceptable to the child or young person and their parents or carers • remain in good repair • remain appropriate to intended treatment goals • remain well fitting • are being used as advised • are not causing discomfort or pain • are not causing injury • are not causing sleep disturbance.	5
	Cautions in the use of orthoses	5
39	Assess whether orthoses 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 their appearance.	5
40	Advise about the risk of pressure sores with orthoses.	5
41	Inform children and young people and their parents or carers to remove orthoses that are causing pain that cannot be relieved immediately through repositioning of the limb in the orthosis or	5

Number	Recommendation	See section
	adjustment of the strapping.	
42	When deciding whether to offer an orthosis, balance the benefits against the risks and potential consequences of muscle wasting through lack of muscle use. Discuss these with the child or young person and their parents or carers.	5
43	Be cautious in offering rigid orthoses to children and young people with severe spasticity or dyskinesis because rigid orthoses are often poorly tolerated in this group.	5
	Botulinum toxin type A injection and orthoses	5
44	Consider an orthosis after treatment with botulinum toxin type A.	5
45	Consider treatment with botulinum toxin type A if this is likely to improve the tolerability of an orthosis.[iii]	5
	Overnight use of orthoses	5
46	Consider overnight use of orthoses. If an orthosis is used overnight: • check that overnight use does not disturb sleep • use night resting splints for muscles that control two joints (for example, the ankle and knee, in the case of the gastrocnemius muscle).	5
	Lower limb orthoses	5
47	When deciding whether to offer an ankle–foot orthosis, balance the benefits against the risk of worsened gait in children and young people with: • hip or knee contractures • femoral or tibial anteversion. Discuss these with the child or young person and their parents and carers.	5
48	Consider ground reaction 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
49	For children and young people with equinus deformities that impair their gait consider: • a solid ankle–foot orthosis if they have good control of knee or hip extension • a hinged ankle–foot orthosis if they have poor control of knee or hip extension.	5
50	In children whose motor development is between 8 months and 2 years consider offering supramalleolar orthoses or supportive orthotic footwear instead of ankle–foot orthoses.	5
51	Consider ankle–foot orthoses for children and young people with serious functional limitations (GMFCS levels 4 and 5) to improve foot	5

[iii] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

Number	Recommendation	See section
	position for sitting, transfers between sitting and standing, and assisted standing.	
52	Inform children and young people and their parents and carers that ankle–foot orthoses intended to stretch muscles (for example, rigid, hinged or ground-reaction force ankle–foot orthoses) should usually be worn for at least 6 hours each day.	5
53	Consider knee gaiters for children and young people with knee flexion deformities.	5
54	Consider hip orthoses: • to improve function if scissoring is causing difficulties with sitting, standing or walking • to limit hip adduction and reduce the risk of hip migration.	5
	Upper limb and trunk orthoses	5
55	Consider the following 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 thumb abduction splint if the child or young person has a 'thumb in palm' deformity).	5
56	Consider offering body trunk orthoses to children and young people for the management of spasticity with co-existing scoliosis or kyphosis if this will help with sitting.	5
	Oral drugs	**6**
57	Consider oral diazepam if spasticity is contributing to: • discomfort or pain • muscle spasms (for example night-time muscle spasms) • functional disability and • a rapid effect is desirable (for example, in pain crisis).	6
58	Consider oral baclofen if spasticity is contributing to: • discomfort or pain • muscle spasms • functional disability and • a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).	6
59	Start oral diazepam treatment with a single dose at bedtime. If the clinical response is unsatisfactory consider: • increasing the dose or • adding a daytime dose.	6
60	Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect.	6
61	If oral diazepam is used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.	6

Number	Recommendation	See section
62	Continue using oral diazepam or oral baclofen if they have a clinical benefit and are well tolerated, but consider whether to stop treatment every time the child or young person's management programme is reviewed and at least every 6 months.	6
63	If adverse effects (such as drowsiness) occur with oral diazepam or oral baclofen consider reducing the dose or stopping treatment.	6
64	If the clinical response to oral diazepam or oral baclofen used alone is unsatisfactory within 4–6 weeks, stop using the drug or consider a trial of combination treatment with both oral diazepam and oral baclofen.	6
	Botulinum toxin type A	**7**
	When to use botulinum toxin type A	7
65	Consider botulinum toxin type A where 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 concerns about appearance to the child or young person.[iv]	7
66	Consider botulinum toxin type A where focal spasticity of the lower limb is: • impeding gross motor function • compromising care and hygiene • causing pain • disturbing sleeping patterns • impeding tolerance of other treatments, such as orthoses and use of equipment to support posture • causing cosmetic concerns to the child or young person.[v]	7
67	Do not offer botulinum toxin type A in children and young people: • with severe muscle weakness • with a previous adverse reaction or allergy • who are currently taking aminoglycosides.	7

68	Consider botulinum toxin type A with caution if:
	• the child or young person has any of the following
	  ○ a bleeding disorder or is receiving anti-coagulation therapy
	  ○ generalised spasticity
	  ○ fixed muscle contractures
		7

[iv] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

[v] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

Number	Recommendation	See section
	○ marked bony deformity **or** • where there are concerns about the child or young person engaging with post-treatment adjunctive therapy.[vi]	
69	Consider using botulinum toxin type A to treat rapid-onset spasticity causing abnormal postures and soft-tissue shortening after acquired brain injury.[vii]	7
	Assessment	7
70	Local multidisciplinary child development teams and regional specialist centres involved in the assessment and administration of botulinum toxin type A should have expertise in child neurology, child development and musculoskeletal assessment in order to decide on: • the need for botulinum toxin type A • administration of botulinum toxin type A • offering repeat injections.	7
71	Include movement and motor function in assessments for treatment with botulinum toxin type A and involve a paediatric physiotherapist or paediatric occupational therapist.	7
72	Ensure that children and young people who receive treatment with botulinum toxin type A are offered timely access to orthotic services (see recommendation 44).	7
	Treatment	7
73	Consider using ultrasound-guided injection or electrical muscular stimulation when injecting botulinum toxin type A into muscles.[viii]	7
74	Minimise distress to the child or young person undergoing treatment with botulinum toxin type A by considering the need for the: • topical or systemic analgesia or anaesthesia • sedation.	7
75	Local multidisciplinary child development teams and regional specialist centres involved in the assessment and administration of botulinum toxin type A should: • monitor effectiveness of the first botulinum toxin type A injection by repeating pre-injection assessment 6-12 weeks after the injection (both assessments should preferably be performed by the same healthcare professionals) • monitor effectiveness of subsequent botulinum toxin type A	7

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Number	Recommendation	See section
	injections and the need for further injections at 3–6 months.	
76	If the clinical response to treatment is satisfactory review the child or young person's goals and consider repeat injections if: • the problem that prompted initial treatment returns after treatment wears off • new goals are identified.[ix]	7
77	Inform children and young people and their parents and carers: • how to recognise serious but rare complications associated with botulinum toxin type A (swallowing difficulties and breathing difficulties) • that these complications may arise during the first week after botulinum toxin type A treatment, and • that the child or young person should return to hospital immediately if they occur.	7
78	Consider injecting botulinum toxin type A into more than one muscle, but ensure that: • maximum doses are not exceeded • a clear functional goal is identified • the child or young person and their parents or carers understand the possible side effects.[x]	7
	Intrathecal baclofen	**8**
	When to consider intrathecal baclofen	8
79 (KPI)	Consider treatment with continuous pump-administered intrathecal baclofen if, despite the use of non-invasive treatments, spasticity, with or without dystonia, is causing difficulties with any of the following: • pain or muscle spasms • posture or function • self-care (or ease of care in the case of parents or carers).[xi]	8
80	Be aware that children and young people who benefit from continuous pump-administered intrathecal baclofen typically have: • moderate to severe motor function problems (GMFCS level 3-5) • bilateral spasticity affecting upper and lower limbs.[xii]	8
81	When considering continuous pump-administered intrathecal	8

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[x] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.
[xi] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.
[xii] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.

Number	Recommendation	See section
	baclofen, balance the benefits against the risk of reducing spasticity if that spasticity supports function (for example, by compensating for muscle weakness) which may have adverse consequences. Discuss this with the child or young person and their parents and carers.[xiii]	
	Intrathecal baclofen testing	8
82	In children and young people being considered for treatment with continuous pump-administered intrathecal baclofen perform intrathecal baclofen testing to assess therapeutic effect and to check for adverse effects.[xiv]	8
83	Before starting intrathecal baclofen testing inform children and young people and their parents or carers verbally and in writing about: • what the test will entail • how the test might predict successful treatment with continuous pump-administered intrathecal baclofen and achievement of individualised goals • adverse effects of continuous pump-administered intrathecal baclofen that might be predicted by testing • adverse effects that might be associated with intrathecal baclofen testing.[xv]	8
84	Inform children and young people and their parents or carers verbally and in writing about continuous pump-administered intrathecal baclofen. The information should include all of the following: • the surgical procedure used for implantation of the infusion pump • the need for regular hospital follow-up visits • requirements for pump maintenance • risks associated with implantation of the pump, pump-related complications, and adverse effects that might be associated with continuous pump-administered intrathecal baclofen infusion.	8
85	Intrathecal baclofen testing should be: • performed by a regional specialist centre that is able to carry out the necessary assessments • undertaken in an inpatient setting to ensure safety and to allow a thorough assessment of outcomes.[xvi]	8
86	Before intrathecal baclofen testing, a pre-test assessment should be performed, including where necessary, an assessment of joint range of movement while the child or young person is under general anaesthesia.	8
87	The test dose or doses of intrathecal baclofen should be administered using a catheter inserted under general anaesthesia.[xvii]	8

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Number	Recommendation	See section
88	Assess the response to intrathecal baclofen testing using standardised outcome measures within 3-5 hours of administration or later if the effects of the general anaesthetic have not worn off.	8
89	Take account of individualised goals and the following criteria for a satisfactory response to intrathecal baclofen: • reduction in spasticity or dystonia • reduction in pain or muscle spasms • improved posture and function, including head control • improved self-care (or ease of care in the case of parents or carers).	8
90	Discuss with the child or young person and their parents or carers their subjective assessments of the response to intrathecal baclofen testing. Subjective assessments should include reports on self-care (or ease of care in the case of parents or carers). Consider using a standardised questionnaire to document their assessments.	8
91	Pre- and post-test assessments should be performed by the same healthcare professionals in the regional specialist centre.	8
	Continuous pump-administered intrathecal baclofen	8
92	Perform implantation of 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 89).[xviii]	8
93	Be aware of the following potential contraindications to treatment with continuous pump-administered intrathecal baclofen: • the child or young person is too small to accommodate an infusion pump • co-existing medical conditions (for example, uncontrolled epilepsy and coagulation disorders) • intercurrent infections (systemic or around operative sites) which can increase the risks associated with continuous pump-administered intrathecal baclofen temporarily • spinal fusion • malnutrition which increases the risk of post-surgical complications (including infection and delayed healing) • some respiratory conditions.	8
94	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 regional specialist centre.	8
95	Monitor the response to continuous pump-administered intrathecal baclofen. Take account of individualised goals and the criteria for a satisfactory response to intrathecal baclofen (see recommendation 89).	8
96	Inform children and young people and their parents or carers verbally	8

[xvii] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.
[xviii] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.

Number	Recommendation	See section
	and in writing: • about safe and effective management of continuous pump-administered intrathecal baclofen • about the effects of intrathecal baclofen, possible adverse effects, and symptoms and signs suggesting the dose is too low or too high • about safe and effective management of the infusion pump, including correct pump settings and the potential for pump-related complications • that it is dangerous to stop the continuous pump-administered intrathecal baclofen infusion suddenly • that the child or young person will need to attend hospital for follow-up appointments, for example to refill and reprogram the infusion pump • that continuous pump-administered intrathecal baclofen should not be stopped before seeking advice from a healthcare professional.	
97	If the response to continuous pump-administered intrathecal baclofen is unsatisfactory (see recommendation 89) offer continued support from the local multidisciplinary care team and consider referral for specialist support.	8
98	In children and young people with spasticity and co-existing scoliosis exercise caution and if the child or young person: • has not yet undergone spinal fusion, implant the infusion pump before performing spinal fusion • has undergone spinal fusion be aware that the operative procedure for implanting the pump will be more difficult technically and may not be possible.[xix]	8
99	Titrate the dose of intrathecal baclofen after continuous pump-administered intrathecal baclofen pump implantation to optimise effectiveness and reassess the child or young person's achievement of their individualised goals.[xx]	8
100	Repeat assessments after titration to determine the response to the new dose. The post-titration assessment should be performed by the same healthcare professionals in the regional specialist centre that performed the pre- and post-implantation assessments.	8
101	If treatment with continuous pump-administered intrathecal baclofen is judged to be unsatisfactory (see recommendation 89) and the infusion pump system has been confirmed to be working, consider reducing the dose gradually to determine whether spasticity and associated symptoms increase.	8
102	When the infusion pump is coming to the end of its lifespan, consider reducing the dose gradually to enable the child or young person to decide whether or not to have a new pump.[xxi]	8

[xix] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.
[xx] At the time of publication (October 2011), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years. Informed consent should be obtained and documented.
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Number	Recommendation	See section
	Orthopaedic surgery	**9**
	Referral	9
103 (KPI)	Offer children and young people referral to an orthopaedic surgeon if there is clinical or radiological evidence of hip displacement or spinal deformity.	9
104	Consider referring a child or young person for an orthopaedic opinion if any of the following indications is present: • the posture of an upper limb is causing difficulties with putting on or taking off clothing • hand or upper limb function is limited by functionally short muscles (where spasticity prevents muscles stretching to their full length during functional tasks), pain or an unfavourable limb posture • a contracture of the shoulder, elbow, wrist or hand causes difficulty with skin crease hygiene • lower limb function is limited by functionally short muscles or an unfavourable limb posture • walking is limited by functionally short lower limb muscles, joint contracture, abnormal torsion of the femur or tibia, foot deformity, or lower limb pain • the cosmetic appearance of the upper limb causes significant concern for the child or young person.	9
105	Consider orthopaedic surgery as an adjunct to other interventions because timely surgery can prevent deterioration and ameliorate function.	9
	Monitoring	9
106 (KPI)	Monitor children and young people to identify displacement of the hip and spinal deformity.	9
107	Clinically monitor all children and young people for signs of hip migration and recognise the following as evidence of hip displacement: • abnormal hip migration percentage (more than 30%) • increasing hip migration percentage • deterioration in hip abduction • pain arising from the hip • reduced range of hip movement • increased hip muscle tone • decreased ability or tolerance for sitting or standing because of worsening hip joint contracture or bony deformity • clinically important leg length difference • increasing difficulty of perineal care or hygiene.	9
108	Perform a hip X-ray to monitor hip migration: • by the age of 18 months in children with bilateral cerebral palsy • in children with poor prognosis for walking (total body involved), delayed walking or who are using an external support for spastic diplegia • in children or young people with signs of hip displacement	9

Number	Recommendation	See section
	(see recommendation 107).	
109	Repeat the hip X-ray every 6 months in children and young people with hip migration percentage greater than 15% or in whom hip migration percentage is increasing by more than 10% per year.	9
	Before undertaking orthopaedic surgery	9
110	Before undertaking orthopaedic surgery discuss and agree with the child or young person and their parents or carers a rehabilitation programme and how and where it will be delivered. The programme may include: • inpatient care and subsequent follow-up • physical therapy • orthoses • other adjunctive treatments, such as oral drugs and botulinum toxin type A.	9
	Performing orthopaedic surgery	9
111	Orthopaedic surgery should: • be undertaken by surgeons experienced in the concepts and techniques of performing such surgery in this group of patients and • take place in a paediatric setting.	9
112	Aim to perform single-event multilevel orthopaedic surgery to improve gait (rather than as staged surgical episodes) informed by a thorough preoperative functional assessment, preferably including a pre-operative gait analysis and interpretation of the results by a surgical team with experience in such analyses.	99
	Assessment	9
113	Assess outcomes of gait-improvement orthopaedic surgery 1–2 years after performing the surgery. Use the same criteria for pre- and post-operative assessments.	9
	Selective dorsal rhizotomy	**10**
114	Offer selective dorsal rhizotomy to improve walking ability only in the context of clinical research.	10

1.6 Key research recommendations

Number	Research recommendation	See section
	Selective dorsal rhizotomy	**10**
23	Does selective dorsal rhizotomy followed by intensive rehabilitation performed between the ages of 3 and 9 years in children who are in GMFCS level 2 or 3 result in good community mobility as a young adult?	10

Number	Research recommendation	See section

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 in GMFCS level 2 or 3 (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; 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 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

Number	Research recommendation	See section
	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).	
	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 which factor is the greatest inhibitor of functional ability. The studies should incorporate classification of functional ability based on validated scales, such as the gross motor functional classification system (GMFCS).	4
	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 in GMFCS level 4 or 5 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 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, they	4

Number	Research recommendation	See section
	do not have severe contractures and they are usually easily occupied).	
	Botulinum toxin	**7**
14	What is the effectiveness of botulinum toxin type A when used routinely or according to clinical need in children and young people who are in GMFCS levels 1 to 3? 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 functional 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 improving 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 in GMFCS levels 1 to 3. Further research is needed to evaluate the effectiveness of botulinum toxin type A, 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.	7
	Intrathecal baclofen	**8**
19	What is the effectiveness of continuous pump-administered intrathecal baclofen compared with usual care in children and young people who are in GMFCS level 4 or 5? 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 spasticity (specifically pain or muscle spasms, posture or function, or ease of care). Such children and young people will typically be in GMFCS level 4 or 5. 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	8

Number	Research recommendation	See section
	factors.	

1.7 Research recommendations

Number	Research recommendation	See section
	Physical therapy (physiotherapy and occupational therapy)	**4**
1 (KRR)	What are the greatest inhibitors of functional ability in children and young people with upper motor neuron lesions?	4
2 (KRR)	What is the optimal postural management programme using a standing frame in children aged 1–3 years?	4
3	What is the effectiveness of 24-hour postural management programmes in non-ambulatory children and young people with spastic quadriplegia?	4
4	What is the optimal duration for the passive stretch component of physical therapy?	4
5	What is the effectiveness of activity-based context-focused physical therapy compared with child-focused physical therapy in children and young people who are in GMFCS levels 1 to 3?	4
6	What is the effectiveness and optimal age for modified constraint-induced movement therapy (CIMT)?	4
	Orthoses	**5**
7	What is the effectiveness of a prolonged stretch of the calf muscles with a HAFO compared to an AFO worn for a shorter time in children and young people with spastic hemiplegia?	5
8	What of the effectiveness of wearing a HAFO to prevent an equinus foot posture compared to an AFO or SAFO?	5
9	What is the effectiveness of wearing an AFO after surgery compared to not wearing an AFO in children and young people with lower limb spasticity?	5
10	What is the effectiveness of dynamic thermoplastic orthoses compared to static orthoses in children and young people with spastic hemiplegia who have abnormal posturing?	5
11	What is the 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 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 in GMFCS levels 1 to 5?	6
13	What is the effectiveness of night-time oral baclofen or oral diazepam combined with physical therapy and a night-time postural control	6

Number	Research recommendation	See section
	system compared to physical therapy and a night-time postural control system only in children and young people who are in GMFCS levels 1 to 5?	
	Botulinum toxin	**7**
14 (KRR)	What is the effectiveness of BoNT A when used routinely or according to clinical need in children and young people who are in GMFCS levels 1 to 3?	7
15	What is the 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 in GMFCS levels 1 to 3?	7
16	What is the effectiveness of BonT A for reducing muscle pain?	7
17	What is the effectiveness of BoNT A compared to BoNT B for reducing spasticity while minimising side effects?	7
	Intrathecal baclofen	**8**
18	What is the effectiveness of ITB testing in terms of improving functional outcomes in children and young people who are in GMFCS level 2?	8
19 (KRR)	What is the effectiveness of CITB compared to usual care in children and young people who are in GMFCS level 4 or 5?	8
20	What is the effectiveness of gait analysis as an assessment tool in studies to evaluate interventions such as CITB?	8
	Orthopaedic surgery	**9**
21	What is the effectiveness of soft tissue surgery in terms of preventing hip dislocation?	9
22	What is the effectiveness of SEMLS in terms of producing benefits that continue after skeletal maturity has been achieved?	9
	Selective dorsal rhizotomy	**10**
23 (KRR)	Does selective dorsal rhizotomy followed by intensive rehabilitation performed between the ages of 3 and 9 years in children who are in GMFCS level 2 or 3 result in good community mobility as a young adult?	10
24	What is the effectiveness of SDR compared to CITB in children and young people who are in GMFCS level 4 or 5?	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 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, co-existing motor disorders and their early musculoskeletal complications in children and young people from birth up to 19 years who have non-progressive brain disorders.

What are spasticity and co-existing motor disorders?

Muscle spasticity is defined as an increase in resistance to muscle stretch proportional to the velocity at which the muscle is stretched. 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 single lesions 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, we 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 (CP) is the most common condition responsible for an UMNL in children and young people. The incidence of CP is not known, but its prevalence is 186 per 100,000 population, such that a total of 110,000 people are affected in the United Kingdom (UK; Department of Health 2005).

In the definition of CP, 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 CP.

Prematurity is a strong risk factor for development of an UMNL and CP (Surman 2009). Forty percent of antenatal or perinatal acquired CP occurs in children who are born prematurely and who may have additional non-neurological complications of prematurity (for example, chronic gastrointestinal disorders). Such disorders may worsen spasticity and dystonia (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 CP. The common pathology in prematurity-related CP 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 CP. 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 CP 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 CP may not be given a definite diagnosis until they are aged 2 years.

Between 10% and 20% of children with cerebral palsy have a postnatal acquired brain injury (ABI) as the cause of their CP (ref needed).

What is acquired brain injury?

ABI, which refers to brain injury that occurs after the neonatal period, 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 CP may have a pure dystonic syndrome, but the majority of children and young people with a pure dystonia have a genetic syndrome of 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 CP. There is no strong reason for not using the same system in children and young people who have a motor impairment following ABI. The traditional system used the terms monoplegia, diplegia, hemiplegia, and quadriplegia. Recently CP 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 (ref needed – SCPE).

Motor impairment can also be described in terms of the severity of functional motor impairment, which can be graded with the Gross Motor Functional Classification System (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 an 88-item measure of skills in rolling, sitting, crawling, standing, walking and running. 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 (levels 1 to 5).

In clinical practice, a simple grading system of community mobility, household mobility and wheel chair user may be used because this does not require an understanding of the GMFCS.

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 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 functions and structures' and 'activities and participations' 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 the problem areas.

Variability in condition in terms of the child or young person

The child or young person with a non-progressive brain disorder 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. Therapy should be tailored to meet the problems faced by the individual child or young person, 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 occupational therapy) is considered to be the mainstay of treatment for children and young people with motor disorders. Many techniques and 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 these drugs. Newer drugs, licensed for use in adults, are used off-licence in children and young people in many areas.

Botulinum toxin 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 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 (ITB), 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 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, which has been the subject of a NICE Interventional Procedure Guidance ('Selective dorsal rhizotomy for spasticity in cerebral palsy', NICE Interventional procedure guidance 373), is currently available in only one centre in England and Wales. The procedure requires prolonged post-operative rehabilitation, and there are concerns about 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 CP. The role of surgery has changed, however. Soft-tissue surgery is performed less frequently in the 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 postoperative 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 has to be added to the cost of equipment, house adaptations, and loss of parental earnings to present 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 therapy. Monitoring the effect of an intervention over the course of several years is not easy, and for some of these approaches there is a limited theoretical framework. It may be difficult, therefore, to plan a programme of therapy for the 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 nonprogressive 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 therapy will be.

Planning therapy 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 therapy (for example, pain from muscle spasticity can be treated with oral drugs, BoNT-A, ITB, or postural programmes). There is more to life than therapy, 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 therapies for individual children or young people. Parents and carers also need guidance on choosing the most appropriate therapy, and to ensure that the time, effort and their own 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 with spasticity, co-existing motor disorders and their early musculoskeletal complications caused by non-progressive brain disorders

- 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 with spasticity, co-existing motor disorders and their early musculoskeletal complications caused by non-progressive brain disorders and their families and other carers who are involved in making decisions about the most appropriate management choices.

2.3 Related NICE guidance

- 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE Interventional procedure guidance 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 Interventional procedure guidance 373) were used for the SDR review. The search for the physiotherapy review was limited by date (the search was limited to articles published after 1970), and the remaining searches were not limited by date. 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 the GRADE 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 (high, moderate, low, or very low) 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 studie, 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 only included on their advice (see Appendix E).

The type of review question determines the highest level of evidence that may be sought. For issues of therapy or 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 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. For dichotomous outcomes, where a 95% confidence interval for a RR or 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 95% confidence interval was entirely below 0.75 or entirely above 1.25 or entirely between 0.75 to 1.25, the outcome was not downgraded for imprecision and the result could be interpreted as being clinically significant. 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.

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 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 relative risks (RRs) or odds ratios (ORs) with 95% CIs, and continuous outcomes were presented as mean differences 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 risk ratios (RRs), pooled odds ratios (ORs), or weighted mean differences (WMDs). Forest plots for all meta-analyses conducted for the guideline are presented in Appendix J. 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. [These details will apply to the final published guideline; for the stakeholder consultation GRADE findings are presented in full 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 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 occupational therapy)
- orthoses
- botulinum toxin (BoNT) injections
- continuous (pump-administered) intrathecal baclofen (CITB)
- orthopaedic surgery
- selective dorsal rhizotomy (SDR).

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

The GDG considered using the EQ-5D, but had reservations about its application in children and young people. No studies were found that used 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 research 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 ten 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]

4 Physical therapy (physiotherapy and occupational therapy)

Introduction

Children with developmental and physical problems due to upper motor neurone (UMN) damage usually receive physiotherapy or occupational therapy. These two categories of physical therapy are referred to collectively as therapy in this guideline, and physiotherapists and occupational therapists are referred to collectively as therapists.

Therapy usually starts when developmental concerns first arise, or at the time of injury, and it continues throughout throughout childhood and through to adult life. Therapists use a proactive and preventative approach centred on understanding the causes of current functional problems and how hese impact upon the child or young person's ability to develop and maintain skills and participate in home and school-life, and in the wider community. As well as managing functional problems, therapists have a large educational and advisory role helping children and young people, and their families, understand their conditions and prognoses.

Spasticity is usually one physical feature of a more complex movement disorder caused as a result of UMN damage. Advances in 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 WHO's ICF domains (ref needed). The link between these domains is not clearly defined but it is recognised that negative and compensatory phenomena resulting from UMN damage (such as 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 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 therapy goals and interventions. Therapists recognise that a child's cognitive ability, personality, health and fitness, family situation, comorbidities, environment and social context have a significant impact on activity and participation. Many 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.

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, increased family stress, emotional difficulties and additional care needs. Therapists are vital in recognising and managing these limitations, referring on to colleagues for advice and further management where necessary. Therapy is used in conjunction with other interventions such as oral drugs, orthopaedic surgery and SDR to improve effectiveness and aid rehabilitation.

Therapists have a wide range of skills and treatment options, and while there are similarities between approaches, clinical practice varies depending on a therapist's individual knowledge and skills, the model of service delivery favoured, and the needs assessment. The amount and type of therapy received can vary widely. The evidence for the effects of therapy interventions and benefits for

treating movement problems is considered in this chapter. The review conducted for the guideline focused specifically on the following therapy interventions:

- 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 (FSP), seating solutions including moulded seats, knee blocks, sleep systems, and standing frames)
- task- focused active use therapy (active use therapy or constraint-induced movement therapy (CIMT), and bimanual training).

No related NICE guidance was identified for this review question.

Review question

What is the effectiveness of physical therapy (physiotherapy and 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

In total there were 10 studies in 12 publications addressing four comparisons as follows:

- active use versus no active use (three RCTs reported in four publications; Aarts 2010; Aarts 2011; Katz-Leurer 2009; Novak 2009)
- strengthening vesus usual care not including strengthening (five RCTs reported in six publications)
- serial casting versus usual care not including serial casting (one RCT)
- early casting after BoNT versus delayed casting after BoNT (one RCT).

Evidence profiles

Active use versus no active use

The three parallel RCTs reported in four publications were identified for inclusion compared active use therapy versus no active use therapy (Aarts 2010; Aarts 2011; Katz-Leurer 2009; Novak 2009). Two trials (Katz-Leurer 2009; Novak 2009) were conducted in populations of children who had unilateral and bilateral spasticity and therapy was based on repitition of exercises to facilitate performance of goals or daily activities. The Aarts trial (Aarts 2010; Aarts 2011) was conducted in population of children with unilateral spasticity only. In this trial the intervention was described as constraint induced movement therapy ie that children were encouraged to actively use their affected arm during treatment and use of their unaffected arm was limited, in this occastion, by using a sling. The GDG considered CIMT to be a form of active use therapy

None of the studies reported reduction of spasticity.

One study (Aarts 2011) reported range of movement in the upper limb.

Number of studies	Number of patients		Effect		Quality
	Active use therapy	No active use therapy	Relative (95% CI)	Absolute (95% CI)	

Active range of motion 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
Active range of motion 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
Passive range of motion 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
Passive range of motion 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
Active range of motion 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
Active range of motion 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
Passive range of motion 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
Passive range of motion 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 higher)	HIGH

* Calculated by the NCC-WCH

Three RCTs reported outcomes relevant to optimisation of function and movement (Aarts 2010; Katz-Leurer 2009; Novak 2009).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Active use therapy	**No active use therapy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Assisting hand assessment at week 9 (range 0 to 100, change from baseline) (Better indicated by higher values)					
1 study (Aarts 2010)	28	22	-	MD 4.3 higher (0.28 to 8.32 higher)	MODERATE
Assisting hand assessment at week 17 (range 0 to 100, change from baseline) (Better indicated by					

higher values)					
1 study (Aarts 2010)	28	22	-	MD 4.70 higher (1.58 to 7.82 higher)	MODERATE
Goal assessment scale at week 9 (% children who showed an increase of 2 point 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
Goal assessment scale at week 17 (% children who showed an increase of 2 point 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
Goal assessment T-score at week 8 - 4wk Occupational therapy home programme (OTHP) group (Better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-	HIGH
Goal assessment T-score at week 8 - 8wk OTHP group (Better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-	HIGH
Goal assessment T-score at week 8 – 4wk vs. 8wk OTHP group (Better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-	MODERATE
Canadian Occupational Performance Measure - Performance at week 8 - 4wk OTHP group (Better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-	HIGH
Canadian Occupational Performance Measure - Performance at week 8 - 8wk OTHP group (Better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-	HIGH
Canadian Occupational Performance Measure - Performance at week 8 - 4wk vs. 8wk OTHP (Better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-	MODERATE
Canadian Occupational Performance Measure - Performance at week 9 (range 0 to 10) (Better indicated by higher values)					
1 study (Aarts 2010)	28	22	-	-	HIGH
Canadian Occupational Performance Measure - Performance at week 17 (range 0 to 10, change from baseline) (Better indicated by higher values)					
1 study (Aarts 2010)	28	22	-	MD 2.00 higher (1.20 to 2.80 higher)*	HIGH

Walking speed at 6 weeks (change from baseline, m/s) (10m walk test) (Better indicated by higher values)					
1 study (Katz-Leurer 2009)	10	10	-	MD 0.03 higher (0.06 lower to 0.12 higher)	LOW

* Calculated by the NCC-WCH

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

Number of studies	Number of patients		Effect		Quality
	Active use therapy	No active use therapy	Relative (95% CI)	Absolute (95% CI)	
Canadian Occupational Performance Measure – Satisfaction (COPM-S) at week 8 - 4wk Occupational therapy home programme (OTHP) group (range 0 to 10, change from baseline) (Better indicated by higher values)					
1 study (Novak 2009)	11	12	-	-	HIGH
(COPM-S) at week 8 - 8wk OTHP group (range 0 to 10, change from baseline) (Better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-	HIGH
(COPM-S) at week 8 - 4wk OTHP vs. 8 wk OTHP (Better indicated by higher values)					
1 study (Novak 2009)	12	12	-	-	MODERATE
(COPM-S) at week 9 (range 0 to 10, change from baseline) (Better indicated by higher values)					
1 study (Aarts 2010)	28	22	-	-	HIGH
(COPM-S) at week 17 (range 0 to 10, change from baseline) (Better indicated by higher values)					
1 study (Aarts 2010)	28	22	-	MD 2.00 higher (1.20 to 2.80 higher)*	HIGH

* Calculated by the NCC-WCH

No 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 therapist by telephone or in an interview if encountered. No adverse events were reported.

Number of studies	Number of patients		Effect		Quality
	4 or 8 wks Occupational therapy (OT) home programme	No OT home programme	Relative (95% CI)	Absolute (95% CI)	
Adverse events					
1 study (Novak 2009)	0/24 (0%)	0/12 (0%)	-	-	LOW

Strengthening versus usual care not including strengthening

The five parallel RCTs identified for inclusion compared strengthening programmes (progressive resistive exercises) versus usual care (Dodd 2003; Dodd 2004; Fowler 2010; Lee 2008; Liao 2007; Unger 2006). The five trials were reported in six publications because Dodd 2004 was a follow-up study after Dodd 2003. No evidence was found for other strengthening interventions, such as treadmill training and rebound therapy.

None of the studies reported reduction of spasticity.

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

Number of studies	Number of patients		Effect		Quality
	Strengthening	Usual care	Relative (95% CI)	Absolute (95% CI)	
Gross motor function measure (GMFM) 88-goal dimension score at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Liao 2007)	103	104	-	MD 8.6 higher*	LOW
GMFM D-standing at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Lee 2008)	9	8	-	MD 0.6 lower*	MODERATE
1 study (Dodd 2003)	11	10	-	MD 1 lower*	MODERATE
GMFM D-standing at 18 weeks (change from baseline) (Better indicated by higher values)					
1 study (Dodd 2003)	11	9	-	MD 0.9 lower*	MODERATE
GMFM E-walking, running and jumping at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Lee 2008)	9	8	-	MD 1 higher*	MODERATE
1 study (Dodd 2003)	11	10	-	MD 3.2 higher*	MODERATE
GMFM E-walking, running and jumping at 18 weeks (change from baseline) (Better indicated by higher values)					
1 study (Dodd 2003)	11	9	-	MD 5.9 higher*	MODERATE
GMFM-66 total (change from baseline at 12 weeks) (Better indicated by higher values)					
1 study (Fowler 2010)	29	29	-	MD 0.7 higher*	MODERATE
GMFM total at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Lee 2008)	9	8	-	MD 0 higher*	MODERATE
1 study (Dodd 2003)	11	10	-	MD 1.2 higher*	MODERATE
GMFM total at 18 weeks (change from baseline) (Better indicated by higher values)					
1 study (Dodd	11	9	-	MD 2 higher*	MODERATE

2003)					
Walking speed (m/min) at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Liao 2007)	10	10	-	MD 9.2 higher*	LOW
Walking speed (cm/sec) at 6 weeks (change from baseline) (Better indicated by higher values)					
1 study (Lee 2008)	9	8	-	MD 25.5 higher	MODERATE
Walking speed (m/min) at 6 weeks (10m walk test) (change from baseline) (Better indicated by higher values)					
1 study (Dodd 2003)	11	10	-	MD 0.4 lower*	MODERATE
Walking speed (mm/s) at 8 weeks (change from baseline) (Better indicated by higher values)					
1 study (Unger 2006)	24	13	-	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	28	-	MD 2.2 higher*	MODERATE
Walking speed (m/min) at 18 weeks (10m walk test) (change from baseline) (Better indicated by higher values)					
1 study (Dodd 2003)	11	9	-	MD 0.7 lower*	MODERATE
Timed stair (s) at 6 weeks (change from baseline) (Better indicated by lower values)					
1 study (Dodd 2003)	11	9	-	MD 5.6 lower*	MODERATE
Timed stair (s) at 18 weeks (change from baseline) (Better indicated by lower values)					
1 study (Dodd 2003)	11	9	-	MD 0.4 lower*	MODERATE

* Calculated by the NCC-WCH

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

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

Number of studies	**Number of patients**		**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	13	-	MD 0.1 lower*	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	13	-	MD 2.9 higher*	LOW
Self-perception (Global self-worth) at 18 weeks (score 0 to 4) (Better indicated by lower values)					
1 study (Dodd 2004)	10	6	-	MD 0.02 higher*	LOW

* Calculated by the NCC-WCH

Two RCTs investigated adverse effects (Dodd 2003; Fowler 2010).

Number of studies	Number of patients		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 3/11 3/11 (27.3%)	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%)4	0/29 (0%)	-	-	LOW

* Calculated by the NCC-WCH

None of the studies reported acceptability and tolerability.

Serial casting versus usual care not including serial casting

The cross-over RCT identified for inclusion compared serial casting versus usual care (McNee 2007).

The study did not report reduction of spasticity, but did report optimisation of movement at the ankle joint (PROM).

Optimisation of movement:

Number of studies	Number of patients		Effect		Quality
	Serial casting	Usual care	Relative (95% CI)	Absolute (95% CI)	
Walking speed (m/s, tridimensional gait analysis) (Change from baseline at 12 weeks) (Better indicated by higher values)					
1 study (McNee 2007)	9	9	-	MD 0.030 lower (0.18 lower to 0.13 higher)	LOW
Passive range of motion-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
Passive range of motion-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

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

Number of studies	Number of patients		Effect		Quality
	Serial casting	Usual care	Relative (95% CI)	Absolute (95% CI)	
Walking speed (m/s, tridimensional gait analysis) (Change from baseline at 12 weeks) (Better indicated by higher values)					
1 study (McNee 2007)	9	9	-	MD 0.03 lower (0.18 lower to 0.13 higher)	LOW

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 study reported outcomes relevant to reduction of spasticity and optimisation of movement of the joint (PROM).

Number of studies	Number of patients		Effect		Quality
	Early casting post botulinum neurotoxin (BoNT)	Delayed casting post BoNT	Relative (95% CI)	Absolute (95% CI)	
Gastrosoleus spasticity (Modified Tardieu) (degrees) 3 months after casting (Better indicated by lower values)					
1 study (Newman 2007)	6	6	-	MD 9.20 higher (1.37 to 17.03 higher)	LOW
Passive range of motion 3 months after casting (Better indicated by higher values)					
1 study (Newman 2007)	6	6	-	MD 2.00 higher (6.76 lower to 10.76 higher)	LOW
Gastrosoleus spasticity (Modified Tardieu) (degrees) 6 months after casting (Better indicated by higher values)					
1 study (Newman 2007)	6	6	-	MD 15.00 higher (4.42 to 25.58 higher)	LOW
Passive range of motion 6 months after casting (Better indicated by higher values)					

1 study (Newman 2007)	6	6	-	MD 0.40 lower (10.39 lower to 9.59 higher)	LOW

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

The study reported adverse effects.

Number of studies	Number of patients		Effect		Quality
	Early casting post botulinum neurotoxin (BoNT)	Delayed casting post BoNT	Relative (95% CI)	Absolute (95% CI)	
Adverse effects: Pain					
1 study (Newman 2007)	3/6 (50%)	0/6 (0%)	-	-	LOW

The study did not report acceptability and tolerability.

Evidence statement

Active use versus no active use

No evidence was identified in relation to reduction of spasticity.

With regard to optimisation of range of movement, one RCT provided evidence that there were no statistically significant differences in active or passive ROM wrist extension at 9 or 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 (MODERATE). The same study reported that there were no statistically significant differences in active ROM elbow extension at 9 or 17 weeks, or in passive ROM elbow extension at 9 weeks (MODERATE), although a statistically significant improvement was found in passive ROM elbow extension at 17 weeks. (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 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 provided evidence of a statistically significant improvement in goal attainment (GAS 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) A further RCT provided evidence of a statistically significant improvement in goal attainment (GAS T scores) and performance (COPM-P scores) at 8 weeks in children who received a 4-week occupational therapy (OT) home programme and children who received the same programme for 8 weeks as compared to children who did not receive the programme. (HIGH) However, there were no statistically significant differences in goal attainment (GAS T scores) or performance (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 a statistically significant improvements in performance (COPM-P 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) One RCT reported no statistically significant difference in walking speed (10-minute walk test) 6 weeks after children received a 6-week home-based task-oriented exercise programme (including sit to stand and step up exercises) as compared to children who did not receive the programme. (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 occupational therapy home programme and those who received the same programme for 8 weeks as compared to children who did not receive the programme. (HIGH) However there were no statistically significant differences between the children who received the 4-week programme and those who received the 8-week programme. (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 occupational therapy home programme or in children who did not receive the programme. (LOW)

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, one RCT reported no statistically significant difference in function (GMFM 88-goal dimension) at 6 weeks in children who received a strengthening programme for 6 weeks as compared to children who received their regular therapy instead of the programme. (LOW) A further RCT reported no statistically significant difference in function (GMFM D-standing) at 6 weeks in children who received a strengthening programme for 5 weeks as compared to children who received conventional therapy for 5 weeks. (LOW) One RCT reported no statistically significant difference in function (GMFM D-standing) at 18 weeks after children received a 6-week strengthening programme as compared to children who received usual care instead of the programme. (LOW) A further RCT reported no statistically significant difference in function (GMFM E-walking, running and jumping) at 6 weeks in children who received a strengthening programme for 5 weeks as compared to children who received conventional therapy for 5 weeks. (LOW) Another RCT reported no statistically significant difference in function (GMFM E-walking, running and jumping) at 18 weeks after children received a 6-week strengthening programme as compared to children who received usual care instead of the programme. (LOW) A further RCT reported no statistically significant difference in function (GMFM-66 total) at 12 weeks after children received a 12-week strengthening programme as compared to children who did not receive the programme. (LOW) Another RCT reported no statistically significant difference in function (GMFM total) at 6 weeks in children who received a strengthening programme for 5 weeks as compared to children who received conventional therapy for 5 weeks. (LOW) One RCT reported no statistically significant difference in function (GMFM total) at 18 weeks after children received a 6-week strengthening programme as compared to children who received usual care instead of the programme. (LOW) One RCT reported no statistically significant difference in the walking speed (10-minute walk test) at 6 weeks in children who received a strengthening programme for 6 weeks as compared to children who received their usual therapy only. (LOW) Another RCT provided evidence of a statistically significant improvement in walking speed at 6 weeks (computerised gait analysis) in children who received a strengthening programme for 5 weeks as compared to children who received conventional therapy for 5 weeks. (MODERATE) A further RCT reported no statistically significant difference in walking speed (10-minute walk test) at 6 weeks after children received a 6-week strengthening programme as compared to children who received usual care instead of the programme. (MODERATE) Another RCT reported no statistically significant difference in walking speed (three-dimensional gait analysis) at 8 weeks in children who received a strengthening programme for 8 weeks as compared to children who did not receive the programme.(LOW) Another RCT reported no statistically significant difference in walking speed (30-second walk test) at 12 weeks after children received a 12-week strengthening programme as compared to children who did not receive the programme.(MODERATE) One RCT reported no statistically significant difference in walking speed (10-minute walk test) at 18 weeks after children received a 6-week strengthening programme as compared to children who received usual care instead of the programme. (MODERATE) The same RCT found no statistically significant difference in the timed stair test at 6 or 18 weeks after children started a 6-week strengthening programme as compared to children who received usual care instead of the programme. (MODERATE)

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

With regard to quality of life, one RCT reported no statistically significant difference in self-perception of functional competence at 8 weeks in children who received a strengthening programme for 8 weeks as compared to children who did not receive the programme. (MODERATE) However, the same RCT reported a statistically significant improvement in self-perception of body image at 8 weeks in children who received the strengthening programme for 8 weeks as compared to children who did not receive the programme. (MODERATE) One RCT reported no statistically significant difference in self-perception-Global Self Worth at 18 weeks after children received a 6-week strengthening programme as compared to children 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 complained of pressure on the shoulder, mild-foot discomfort or mild ankle discomfort. No episodes of these adverse events were reported in the control group who did not receive the intervention. (MODERATE) A further RCT reported that 58.6% of children who received a 12-week strengthening programme complained of mild pain, soreness, or muscle cramping and 3.4% of children in the strengthening programme experienced a skin rash related to the equipment used. No episodes of these adverse events were reported in the control group who did not receive the intervention. (MODERATE)

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 passive range of motion-ankle dorsiflexion (knee flexed) at 12 weeks after children received serial casting as compared to when the same children did not receive casting (MODERATE). The RCT also reported no statistically significant difference in passive range of motion-ankle dorsiflexion (knee extended) at 12 weeks after children received serial casting as compared to when the same children did not receive casting. (LOW)

With regard to optimisation of function, one RCT reported no statistically significant difference in walking speed (tridimensional gait analysis) at 12 weeks after children received serial casting as compared to when the same children did not receive casting. (LOW) No evidence was identified in relation to pain (reduction of pain), quality of life, adverse effects, or acceptability and tolerability.

No evidence was identified in relation to optimisation of function, 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 (modified Tardieu) at 3 and 6 months in children who received casting immediately after botulinum toxin injection as compared to those children who received casting 4 weeks after botulinum toxin injection for the treatment of spastic equines. (LOW) The same RCT reported no statistically significant difference after 3 months or 6 months in passive range of movement at the ankle between children who received casting immediately after botulinum toxin injection and those who received casting 4 weeks after botulinum toxin injection for the treatment of spastic equinus. (LOW)

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

With regard to adverse effects, one RCT provided evidence that 50% of children who received casting immediately after botulinum toxin injection complained of pain whereas none of the children who received casting 4 weeks after botulinum toxin injection for the treatment of spastic equinus complained of pain. (LOW) the same RCT reported evidence that 50% of children who received casting immediately after botulinum toxin injection required a change of cast within 48 hours of having their first cast applied because of pain.

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 botulinum toxin versus botulinum toxin only
- postural management versus usual care not including postural management
- passive stretching versus usual care not including passive stretching.

Health economics

There is very limited good quality evidence of effectiveness for therapy and those studies that were identified showed equivocal results in the short term. A simple cost analysis showed 1 hour per week of therapy would cost approximately £2,000 a 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 available currently.

Evidence to recommendations

Important research outcomes in therapy

Although therapy might not alter spasticity the GDG considered that this should be assessed and that Ashworth, modified Ashworth, and Tardieu scales were appropriate measures as they are widely used in research. Optimisation of movement was prioritised as it this is a prime aim in therapy. Active range of movement was considered a useful indicator of selective muscle control and hence a potentially important outcome. Passive range of movement was also considered important because muscle tightness may be improved by therapy. Walking speed and distance (endurance) were also considered to be clinically important measures because improvement would increase the ability to participate in activities and join in with peers. Optimisation of function is often the cornerstone of therapy programmes and was, therefore, considered to be an important outcome. The GDG prioritised the assisted hand assessment (AHA), the SHUE, goal attainment scaling (GAS), the PEDI and the GMFM (66- or 88-item versions) as commonly employed measures of function. 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 (QoL) were also considered important as outcomes of therapy, and the GDG chose the COPM satisfaction and performance scales (both subjective scales), the child health questionnaire, PedsQL and CP Quad as useful measures. Pain was regarded as an important outcome, in that the GDG consensus was that therapy might have a role in the management of painful muscle spasms and chronic pain more generally, and the GDG agreed that outcomes reported based on objective pain scales should be included. Certain adverse effects might be anticipated with therapy, including pain and discomfort. Injury might also be important, and such effects were included as important outcomes. Finally, acceptability and tolerability of therapy interventions was considered by the GDG to be a key outcome.

The evidence

The available evidence related to four key areas of 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. Therapy typically consists of functional activities carried out with instruction and demonstration followed by feedback. Repetition and practice are considered to be critically important. Functional activities include dialy maintainence activities such as standing to do something and brushing one's teeth.

Moderate- to high-quality evidence from RCTs supported the effectiveness of active use therapy consisting of constraint-induced movement therapy (CIMT) followed by bimanual training in improving upper limb function. There was evidence suggesting improved hand function and goal attainment 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. Before 8 years of age, children with spasticity are still developing their mobility and their hand-skill strategies. The GDG considered that active-use therapy provided in the context of the child's normal activities, for instance at the nursery or at home, was more likely to prove effective than those developed in a more abstract setting.

One RCT provided moderate- to high-quality evidence for significant improvements in goal attainment using individualised home occupational therapy delivered over 4 or 8 weeks. The programme interventions varied greatly depending on individual goals, and they included specific goal-directed training, parent education, handwriting task training, recreation and sports therapy, play therapy and CIMT. In addition to these active-use interventions, other therapy strategies employed included positive behaviour support, the use of adaptive equipment, strength training and orthotics. Using these diverse interventions there were improvements for both the 4- and 8-week groups in relation to goal attainment (GAS), participation (COPM-P) and reported satisfaction (COPM-S). There was no significant difference between the groups. 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 GDG considered that this study highlighted the importance of individualised therapy and this was reflected in the recommendations.

Regarding active-use therapy, the GDG believed that it would be important to determine the optimal duration and frequency of therapy needed to acquire and maintain skills. One 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. This did not provide evidence that this approach achieved the outcome of improved walking speed.

Muscle strengthening

The studies of 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 programme was 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 therapy, was that muscle strengthening could be a useful goal in appropriately selected individuals. In children and young people 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 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 individuals. This might be especially true for those who otherwise have a limited opportunity to participate in exercise programmes.

The GDG therefore recommended that consideration should 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 joint deformity. The GDG recommended that strengthening therapies should 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. For example, 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 orthotic device).

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 GDG consensus was that any effect derived from this approach might be expected to be short-lived, and so they did not recommend it.

One study reported that serial casting improved passive range of movement (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 serial casting or orthoses was more likely to be effective in maintaining soft tissue length and preventing or limiting deformity.

Although there is a lack of comparative studies on serial casting is employed following botulinum toxin injection treatment with and without subsequent serial casting, it is common practice to employ serial casting in this setting with the aim of enhance 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 botulinum toxin 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 botulinum toxin treatment did not alter the therapeutic effect, but 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 musculo-skeletal deformity. Despite this, the GDG noted that no studies were identified that examined the effectiveness of postural management. 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 plan, 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 considered that training and support of family members or carers was key to successful postural management. It was also essential that the 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. It was important when assessing individual and family needs to consider the acceptability of the therapy programme to the child or young person and their family or carers. Only through regular reassessment is it possible to determine whether a management programme is achieving its intended goals. Over time, as the child grows and develops, the postural management plan is likely to need to be modified. The GDG made recommendations with regard to these aspects of postural management.

Considerations regarding risk and benefit

The GDG considered that benefits derived from physical therapy would obviously need to be balanced against any significant disadvantage. Adverse events associated with physical therapy were likely to be relatively uncommon and often minor or manageable by modification of the physical therapy programme (for example, minor injury, discomfort or pain). Intensive therapy could be associated with significant disruption to the lives of children and young people and to their parents or

carers, and careful account needed to be taken of this. In this context the GDG made 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.

Considerations regarding resource implications

Provision of therapy throughout childhood has significant resource implications. The GDG recognised that based on the published literature the evidence of effectiveness for various commonly employed physical therapy interventions, including regimens aimed at muscle strengthening, stretching and postural management, was limited. Nevertheless, they 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 suitable selected individuals they were an essential component of management. The strongest evidence related to the use of task-focused active-use therapy. In particular, there was some evidence that this approach could improve function and quality of life. Although long-term benefit needed to be examined, the available evidence suggested that intensive goal-directed active-use therapy showed functional improvement at least in the short term. Even in those with an existing fixed deformity, 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 therapy suggested long-term benefits are to be obtained,

The GDG also recognised that the remit of the physical therapist goes well beyond that of directly providing the physical interventions of therapy. The therapist also has a key role in undertaking a specialist assessment of the needs of the individual child, and in recommending and arranging provision of specialist equipment intended to optimise function and to prevent slow progression of deformity and disability. Such equipment may also have an important role in facilitating supportive care for the child or young person. The GDG recognised that the cost of such equipment may be substantial, especially in those with more severe motor dysfunction (for example, GMFCS levels 4 and 5).

The physical therapist is also involved in providing support, education and training for children and young people and their families and carers. This is an essential component of the service currently provided. There is little research evidence available on the impact that such measures have had on improving the ability of children and young people and their families and carers to cope, or on quality of life or their ability to participate in physical therapy regimens. 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, botulinum toxin injection treatment, intrathecal baclofen or orthopaedic surgery may be necessary to improve function and prevent or ameliorate disability and deformity. However, in children and youg 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 offered only in a research context), post-operative rehabilitation with appropriate therapy considered to be essential.

Other considerations

The GDG recognised the importance of co-morbidities when considering an appropriate programme of physical therapy. Potentially important examples were the use of postural equipment in those with poorly controlled epilepsy or respiratory compromise, the use of techniques such as passive stretching in those likely to have osteoporosis, and the use of certain types of postural therapy in those at risk of aspiration.

The GDG also emphasised in their 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 possible. 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 plans for physical therapy healthcare professionals should, therefore, consider potential barriers to implementation and seek ways of overcoming such barriers to provide physical therapy plans that are acceptable to the individual child or young person in their family and cultural circumstances.

The GDG believes that appropriate information sharing and the use of written educational materials may facilitate physical therapy. In particular, when children and young people and their families have a proper understanding of the condition and its management, and of realistic goals of physical therapy and are partners in the agreed programme of 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.

The GDG considered that supporting therapy might be particularly difficulty during times of change, in particular when individuals are moving to a new supporting service or a new environment. Transition and transfer to adult services was recognised as a particular challenge. Therapists could have an important role in facilitating such processes, in preparing the way for such changes and, where appropriate, in helping individuals to participate more in the management of their own conditions.

As stated in the introduction to this chapter the GDG have considered physical therapy to mean either physiotherapy or occupational therapy and as such ‘physical therapy’ has been used throughout the recommendations to incorporate both. The GDG did acknowledge though that the first therapy professional children and young people are referred to in clinical practice is a physiotherapist, rather than an occupations therapist, and this is reflected in their recommendation to offer a referral to a physiotherapist in the first instance. All children and young people should also have access to an occupational therapist through the local multidisciplinary child development team (see section below on principles of care for more details).

In formulating their recommendations the GDG considered that the word ‘participation’ that is used in the ICF was synonymous with taking part in daily activities and both phrases are used in the recommendations interchangeably.

Principles of care

The GDG’s considerations in relation to the evidence identified for this review question and others identified some common themes, and the GDG concluded that these were best addressed through the development of recommendations defining overarching principles of care.

Patient-important outcomes were key 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 to promote independence and quality of life through to adult life. The management of spasticity, co-existing motor disorders and their secondary complications involves a long-term commitment for the child or young person and their family. The success of the clinical aspects of management should be viewed in the framework of the the World Health Organization’s (WHO’s) International Classification of Functioning, Disability and Health (ICF; http://www.who.int/classifications/icf/en/). Thus, 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 need 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 orthotic device, enabling a child to keep up with peers and participate more fully in life, whereas for another child, 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, and to construct an individualised care plan to suit individual needs when considered in a holistic view.

The specific issues and associated actions that the GDG identified as important principles of care for children and young people with nonprogressive motor disorders were as follows.

- All children and young people with spasticity, co-existing disorders and early muscular-skeletal complications caused by nonprogressive motor disorders should be referred to a local multidisciplinary child development team without delay. The multidisciplinary team should be linked to a regional specialist centre because of the potential need for expertise and treatments available only through such centres.
- Although the GDG did not identify evidence regarding the specific composition of local multidisciplinary child development teams to ensure effectiveness, they recognised that a range of treatment options used alone, in combination, or sequentially should be offered and that this requires access to various types of healthcare professional, including physiotherapists, occupational therapists, paediatricians, and orthopaedic surgeons. The GDG considered that local multidisciplinary child development teams should be able to provide access to physical therapy, orthoses and oral drugs as a minimum and potentially treatment botulinum toxin type A. Regional specialist centres may provide access to the other interventions including: botulinum toxin type A, CITB, orthopaedic surgery. The GDG's view was that all healthcare professionals involved in care should have expertise specific to the management of spasticity, co-existing disorders and early muscular-skeletal complications in children and young people. The GDG's recommendation mirrors guidance contained in 'Selective dorsal rhizotomy for spasticity in cerebral palsy' (NICE interventional procedure guidance 373), which highlights 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. The SDR team would normally include a physiotherapist, a paediatrician and surgeons, all with specific training and expertise (see Chapter 10).
- The GDG 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. Such programmes should take a holistic view of the child or young person, be supported by opportunities for children and young people and their parents and carers to access information and education about treatments. Discussion of developmental potential, and how this might be influenced by different treatments, was also highlighted as an important element of care.
- The GDG recognised the importance of communication between healthcare professionals of different types and those in different settings, again reflecting the importance of the range of treatment options available and how they may be used in combination or sequentially.
- Monitoring for progression of spasticity, development of its secondary consequences, response to treatment, changes to goals and, where appropriate, timely referral to specialist centres, were also identified as important elements of care.
- Based on the guideline reviews for the effectiveness of botulinum toxin and orthopaedic surgery, the GDG concluded that active participation in a programme of care and therapy was an essential prerequisite of such treatments The GDG also highlighted the need for adjunctive therapy to be arranged before starting such treatments.

1 Recommendations

Number	Recommendation
	Principles of care
1 (KPI)	Offer immediate referral to a local multidisciplinary child development team that can be accessed when needed and is linked to regional specialist centres.
2	The local multidisciplinary child development team should be experienced in the management of spasticity in children and young people and include a paediatrician, a paediatric physiotherapist and have access to a paediatric occupational therapist.
3	Access to a paediatric occupational therapist is needed for children and young people with spasticity that affects the upper limb.
4 (KPI)	Offer a management programme that is: • individualised • goal focused • developed and implemented in partnership with the child or young person and their family or carers.
5 (KPI)	Local multidisciplinary child development teams and regional specialist centres should enable children and young people (and when appropriate their parents or carers) to be partners in the development and implementation of management programmes by offering: • relevant information and educational materials • regular opportunities for discussion and • advice on the child or young person's developmental potential and how different treatment options may affect this potential.
6	When formulating a management programme take into account the impact of treatment schedules on family circumstances.
7	Identify and agree with children and young people (and where appropriate their parents or carers) goals and assessments that: • are appropriate for their age and development • will aim to improve their body function and structure and activity and participation in line with the domains of the World Health Organization's International Classification of Functioning, Disability and Health.[22]
8	Record and communicate the child or young person's individualised goals within the local multidisciplinary child development team and with all healthcare professionals who care for them in different settings.
9 (KPI)	Monitor the child or young person for: • progression of spasticity • development of secondary consequences of spasticity • response to treatments • the need for changes to individualised goals and • the need for timely referral to regional specialist centres.
10	Do not offer botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy to children and young people unless they are participating actively in a programme of care and physical

[22] World Health Organization International Classification of Functioning, Disability and Health (ICF), available from www.who.int/classifications/icf/en/

Number	Recommendation
	therapy.
11 (KPI)	Offer adjunctive physical therapy following treatments involving botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy to ensure effectiveness of these treatments.
12	Healthcare professionals in regional specialist centres who assess children and young people's suitability for oral drugs, botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy should communicate with the child or young person's local multidisciplinary child development team to ensure compatibility and continuity of local and specialist services.
13 (KPI)	Before starting treatment, regional specialist centres should ensure that local multidisciplinary child development teams have allocated resources for locally provided post-treatment services.
	Physical therapy (physiotherapy and occupational therapy)
14 (KPI)	Offer to refer children and young people to a physiotherapist who is a member of the local multidisciplinary child development team.
15	Offer children and young people a physical therapy programme tailored to their individual needs and aimed at specific goals, such as: • enhancing skill development and improving function • enhancing the ability to participate in everyday activities • preventing or delaying the onset of complications such as contractures.
16	When formulating physical therapy programmes for children and young people take account of: • the views of the child or young person and their parents or carers • the likelihood of achieving the intended goals of treatment • the implications for the child or young person and their family in implementing the plan, including the time and effort involved and potential barriers (for example, barriers associated with particular cultural practices).
17	Consider task-focused active-use therapies such as constraint-induced movement therapy followed by bimanual therapy to enhance manual skills.
18	Consider structuring task-focused active-use therapy as an intensive programme over a short time period (for example, 4–8 weeks).
19	Consider muscle-strengthening therapy where assessment suggests that muscle weakness is contributing to loss of function or joint deformity.
20	Direct muscle-strengthening therapies towards specific goals and incorporate progressive repetitive exercises performed against resistance.
21	Consider postural management strategies to: • prevent or slow the development of contractures in children and young people at risk of developing these • enable the child or young person to take part in activities appropriate to the child or young person's stage of development.
22	As part of postural management consider an individualised physical therapy programme that includes: • resting positions and • low-load active or passive stretching over 24 hours.

Number	Recommendation
23	Offer training to parents and carers involved in delivering postural management programmes.
24	Assess whether any equipment or techniques used in the physical therapy plan is safe and appropriate, for example in children or young people with any of the following: • poorly controlled co-existing epilepsy • respiratory compromise • risk of aspiration • risk of bone fracture due to osteoporosis (for example, children and young people who are non-ambulatory, malnourished or taking anticonvulsant therapy).
25	For children and young people who are at risk of bone fractures due to osteoporosis (for example, children and young people who are non-ambulatory, malnourished or taking anticonvulsant therapy), consider sustained low-load stretching to prevent or limit contractures and joint deformity. Depending on the individual child or young person's circumstances (for example recent history of fractures, bone pain, broken skin), consider low-load stretching and weight bearing including use of orthoses or serial casting.
26	Monitor children and young people at risk of developing functional difficulties related to their condition. Consider a programme of daily maintenance activities for children and young people with or at risk of developing functional difficulties.
27	Consider the use of serial casting after botulinum toxin type A treatment to improve passive range of movement if muscle tightness is identified alongside dynamic spasticity. To improve the cast's tolerability and allow better stretch of muscle, do not apply serial casts for 2-4 weeks after botulinum toxin type A treatment.
28	Offer children and young people and their parents or carers verbal and written information about physical therapy interventions needed to achieve intended goals. This information should emphasise possible advantages as well as difficulties and possible adverse effects (for example time commitment and discomfort) to enable them to participate in choosing a suitable physical therapy programme.
29	Reassess at regular intervals all children and young people receiving a programme of physical therapy to ensure that: • the intended goals are being achieved • the therapy programme remains appropriate to the child or young person's individual needs.
30	When considering 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.
31	Physical therapists should have a central role in preparing young people (and their parents or carers) for transition and transfer to adult physical therapy services (for example, helping them to take responsibility for their own physical therapy).

1

Number	Research recommendation
1 (KRR)	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 gross motor functional classification system (GMFCS).
2 (KRR)	What is the optimal postural management programme using a standing frame in children aged 1–3 years?
3	What is the effectiveness of 24-hour postural management programmes in non-ambulatory children and young people with spastic quadriplegia? **Why this is important** Children who are in GMFCS level 4 or 5 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 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, they do not have severe contractures and they are usually easily occupied).
4	What is the optimal duration for the passive stretch component of physical therapy?
5	What is the effectiveness of activity-based context-focused physical therapy compared with child-focused physical therapy in children and young people who are in GMFCS levels 1 to 3?
6	What is the effectiveness and optimal age for modified constraint-induced movement therapy (CIMT)?

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 physiotherapy, occupational therapy or botulinum toxin therapy. They may also be used following surgery. They may be used to facilitate function (for example, improving hand use) or they may be used 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 assisting enhanced 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 individual'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, 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 were considered.

- Solid ankle-foot othosis (SAFO): the 'solid' or 'rigid' AFO prevents dorsiflexion and plantar flexion. It is used to prevent excessive plantar flexion or knee hyperextension during walking or standing. Knee hyperextension is a common problem, and tends to induce foot plantar flexion automatically.
- Posterior leaf spring AFO (PLSAFO): this supports the foot and ankle, preventing excessive plantar flexion and knee extension. 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 AFO (HAFO): this has a 'block' incorporated that can prevent dorsiflexion or plantar flexion depending on individual need. For most children and young people the aim is prevention of plantar flexion, but those prone to a 'crouch' gait may benefit from control of dorsiflexion.
- Ground reaction AFO (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 some ankle movement in the sagittal plane and has the potential to control foot inversion and eversion.

- Prescribed footwear: the review question also considers the use of footwear that is 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 functional orthoses that are intended to hold the hip in a neutral position throughout the gait cycle or when standing or sitting.
- Upper limb orthoses: these include prefabricated, neoprene and thermoplastic upper limb orthoses. They can be static orthoses designed to prevent abnormal postures or functional (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 thoracolumbosacral 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, ankle-foot orthoses, knee splints, and upper limb orthoses) as compared to no orthoses to optimise movement and function, to prevent or treat contractures in children with spasticity and with or without other motor disorders caused by a non-progressive brain disorder?

Description of included studies

In total six studies were included in this review and they addressed four comparisons as follows.

- SAFOs versus no treatment in children and young people with diplegia and hemiplegia (five randomised comparative studies; Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005)
- HAFOs with plantarflexion stop versus SAFOs in children and young people with diplegia and hemiplegia (the same five randomised comparative studies; Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005)
- PLSOs versus SAFOs in children and young people with diplegia and hemiplegia (three randomised comparative studies; Buckon 2001; Buckon 2004a; Sienko-Thomas 2002)
- SMOs versus SAFOs in children and young people with diplegia (one study; Carlson 1997).

Evidence profiles

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

Five randomised comparative studies were identified for inclusion and these compared SAFOs to no treatment (Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005). The data for this comparison were not presented adequately enough for extraction from a further study (Carlson 1997).

The five randomised comparative studies examined outcomes assessing optimisation of movement (Buckon 2001; Buckon 2004a; Rethlefsen 1999; Sienko-Thomas 2002; Radtka 2005)

1 Diplegia

Number of studies	Number of patients		Effect		Quality
	Solid ankle-foot orthosis (SAFO) Mean	No SAFO Mean	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion Initial contact (diplegia) (Better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs	-	MD = 3.6 higher (1.42 higher to 5.78 higher)*	LOW
Ankle dorsiflexion Initial contact (diplegia) (Better indicated by higher values)					
1 study (Buckon 2004a)	16	16	-	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	12	-	MD = 15.23 higher (11.02 higher to 19.44)*	LOW
Ankle dorsiflexion, terminal stance (diplegia) (Better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs	-	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	12	-	MD = 12.80 higher (8.35 higher to 17.25 higher)*	LOW
Peak dorsiflexion stance (diplegia) (Better indicated by higher values)					
1 study (Buckon 2004a)	16	16	-	MD = 6.80 higher (0.03 lower to 13.63 higher)*	LOW
Peak dorsiflexion time, % (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 9.00 higher (0.36 lower to 18.36 higher)*	LOW
Peak dorsiflexion swing (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 10.80 higher (3.46 higher to 18.14 higher)*	MODERATE
Range (Better indicated by higher values) (diplegia)					
1 study (Buckon	16	16	-	MD = 19.10 lower (26.59	MODERATE

2004a)				lower to 11.61 lower)*	
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.00 higher (3.46 lower to 3.46 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 2.00 higher (7.30 lower to 3.30 higher)*	LOW
Knee, initial contact (degrees) (Better indicated by higher values) (diplegia)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs	-	MD = 1.00 lower (6.15 lower to 4.15 higher)*	LOW
Knee, terminal stance (degrees) (Better indicated by higher values) (diplegia)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs		MD = 1.00 lower (5.28 lower to 3.28 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.04 lower (0.18 lower to 0.10 higher)*	LOW
Velocity (cm/sec) (Better indicated by higher values)					
1 study (Radtka 2005)	40 limbs	40 limbs		MD = 0.40 higher (-4.03 lower to 4.83 higher)*	LOW

1 * Calculated by the NCC-WCH

2 Hemiplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Solid ankle-foot orthosis (SAFO) Mean	**No SAFO Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ankle dorsiflexion Initial contact (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29		MD = 13.00 higher (10.42 higher to 15.58 higher)*	MODERATE
Peak dorsiflexion stance (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29		MD = 5.00 higher (2.47 higher to 7.53 higher)*	MODERATE

Ankle dorsiflexion Dynamic Range (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		MD = 15.00 lower (17.73 lower to 12.27 lower)*	MODERATE
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		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	19		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	19		MD = 0.04 higher (0.02 lower to 0.09 higher)*	LOW

* Calculated by the NCC-WCH

Two randomised comparative studies examined outcomes assessing optimisation of function (Buckon 2004a and Rethlefsen 1999)

Diplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Solid ankle-foot orthosis (SAFO) Mean	**No SAFO Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.40 higher (1.51 lower to 2.31 higher)*	LOW
GMFM Walking/Running/Jumping (Better indicated by higher values) (diplegia)					
1 study (Buckon	16	16	-	MD = 3.50 higher (4.31	LOW

2004a)				lower to 11.31 higher)*	
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 1.40 higher (0.65 lower to 3.45 higher)*	LOW
PEDI Mobility Caregiver assistance (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.30 higher (0.64 lower to 1.24 higher)*	LOW

1 * Calculated by the NCC-WCH

2 Hemiplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Solid ankle-foot orthosis (SAFO) Mean	**No SAFO Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.40 higher (0.40 lower to 1.20 higher)*	LOW
GMFM Walking/Running/Jumping (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.50 higher (1.79 lower to 2.79 higher)*	LOW
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.40 higher (0.39 higher to 2.41 higher)*	LOW
Ascent PEDI Item 54 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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
Descent PEDI Item 59 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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

3 * Calculated by the NCC-WCH

No 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

Five studies examined the comparison of HAFO versus SAFO (Radtka 2005; Buckon 2001; Buckon 2004a; Sienko-Thomas 2002; Rethlefsen 1999).

Four randomised comparative studies assessed optimisation of movement (Buckon 2004a; Radtka 2005; Sienko-Thomas 2002; Rethlefsen 1999).

Diplegia

Number of studies	Number of patients		Effect		Quality
	Hinged ankle-foot orthosis (HAFO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion Initial contact (diplegia) (Better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs	-	MD = 1.00 higher (0.94 lower to 2.94 higher)*	LOW
1 study (Buckon 2004a)	16	16	-	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	12	-	MD = 1.72 lower (6.61 lower to 3.17 higher)*	LOW
Ankle dorsiflexion, terminal stance (diplegia) (Better indicated by higher values)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs	-	MD = 5.00 higher (2.82 higher to 7.18 higher)*	LOW
1 study (Radtka 2002)	12	12	-	MD = 4.63 higher (0.38 higher to 8.88 higher)*	LOW
Peak dorsiflexion stance(diplegia) (Better indicated by higher values)					
1 study (Buckon 2004a)	16	16	-	MD = 6.10 higher (1.27 higher to 10.93 higher)*	MODERATE
Peak dorsiflexion time, % (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 10.00 higher (3.18 higher to 16.82 higher)*	MODERATE
Peak dorsiflexion swing (Better indicated by higher values) (diplegia)					

1 study (Buckon 2004a)	16	16	-	MD = 1.10 higher (2.75 lower to 4.95 higher)*	LOW
Range (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 5.90 higher (2.54 higher to 9.26 higher)*	MODERATE
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 2.00 higher (2.22 lower to 6.22 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 4.00 higher (0.90 lower to 8.90 higher)*	LOW
Knee, initial contact (degrees) (Better indicated by higher values) (diplegia)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs		MD = 2.00 higher (2.92 lower to 6.92 higher)*	LOW
Knee, terminal stance (degrees) (Better indicated by higher values) (diplegia)					
1 study (Rethlefsen 1999)	42 limbs	42 limbs		MD = 2.00 higher (2.28 lower to 6.28 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.06 lower (0.20 lower to 0.08 higher)*	LOW
Velocity (cm/sec) (Better indicated by higher values)					
1 study (Radtka 2002)	12	12		MD = 4.93 higher (12.12 lower to 21.98 higher)*	LOW
Velocity, m/minute (Better indicated by higher values) (diplegia)					
1 study (Rethlefsen 1999)	40 limbs	40 limbs		MD = 0.90 higher (3.75 lower to 5.55 higher)*	LOW

1 * Calculated by the NCC-WCH

2 Hemiplegia

Number of	Number of patients	Effect	Quality

studies	Hinged ankle-foot orthosis (HAFO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion Initial contact (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (1.02 lower to 3.02 higher)*	LOW
Peak dorsiflexion stance (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29	-	MD = 5.00 higher (2.21 higher to 7.79 higher)*	MODERATE
Ankle dorsiflexion Dynamic Range (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29[7]	29[8]	-	MD = 5.00 higher (3.21 higher to 6.79 higher)*	MODERATE
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (1.29 lower to 3.29 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	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	19	-	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	19	P = No significant difference (reported)	MD = 0.02 lower (0.07 lower to 0.04 higher)*	LOW

* Calculated by the NCC-WCH

Three studies examined optimisation of function (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002).

1 Diplegia

Number of studies	Number of patients		Effect		Quality
	Hinged ankle-foot orthosis (HAFO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.30 lower (2.31 lower to 1.71 higher)*	LOW
GMFM Walking/Running/Jumping (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.40 higher (7.02 lower to 7.82 higher)*	LOW
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.70 lower (2.78 lower to 1.38 higher)*	LOW
PEDI Mobility Caregiver assistance (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16[9]	16[10]	-	MD = 0.10 higher (0.73 lower to 0.93 higher)*	LOW
Ascent PEDI Item 54 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
1 study (Sienko-Thomas 2002)	12/19	9/19	1.33 (0.74 to 2.39)	RD = 0.16 higher (0.15 fewer to 0.47 higher)*	LOW
Descent PEDI Item 59 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
1 study (Sienko-Thomas 2002)	10/19	7/19	1.43 (0.69 to 2.96)	RD = 0.16 higher (0.15 fewer to 0.47 higher)*	LOW

2 * Calculated by the NCC-WCH

3 Hemiplegia

Number of studies	Number of patients		Effect		Quality
	Hinged ankle-foot orthosis (HAFO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.10 lower (0.61 lower to 0.41 higher)*	LOW

GMFM Walking/Running/Jumping (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (0.79 lower to 2.79 higher)*	LOW
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.10 lower (1.11 lower to 0.91 higher)*	LOW
Ascent PEDI Item 54 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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
Descent PEDI Item 59 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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

* Calculated by the NCC-WCH

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

Posterior leaf spring ankle foot orthosis versus solid ankle foot orthosis

Three studies examined the comparison of posterior leaf spring AFO versus SAFO (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002).

All three studies examined outcomes for optimisation of movement (Buckon 2001; Buckon 2004a; Sienko-Thomas 2002).

Diplegia

Number of studies	Number of patients		Effect		Quality
	Posterior leaf spring ankle-foot orthosis (PLSAFO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Ankle dorsiflexion Initial contact (diplegia) (Better indicated by higher values)					
1 study (Buckon 2004a)	16	16	-	MD = 0.20 lower (3.35 lower to 2.95 higher)*	LOW
Peak dorsiflexion stance(diplegia) (Better indicated by higher values)					
1 study (Buckon 2004a)	16	16	-	MD = 2.30 higher (2.12 lower to 6.72 higher)*	LOW

Peak dorsiflexion time, % (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 2.00 higher (7.01 lower to 11.01 higher)*	LOW
Peak dorsiflexion swing (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.30 lower (3.85 lower to 3.25 higher)*	LOW
Range (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 4.00 higher (1.11 higher to 6.89 higher)*	MODERATE
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.00 higher (3.83 lower to 3.83 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 3.00 higher (2.30 lower to 8.30 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.07 higher (0.06 lower to 0.20 higher)*	LOW

* Calculated by the NCC-WCH

Hemiplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Posterior leaf spring ankle-foot orthosis (PLSAFO) Mean	**Solid ankle-foot orthosis (SAFO) Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ankle dorsiflexion Initial contact (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29		MD = 2.20 lower (4.49 lower to 0.09 higher)*	LOW
Peak dorsiflexion stance (hemiplegia) (Better indicated by higher values)					
1 study (Buckon 2001)	29	29		MD = 5.00 higher (2.21 higher to 7.79 higher)*	MODERATE

Ankle dorsiflexion Dynamic Range (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		MD = 4.00 higher (2.21 higher to 5.79 higher)*	MODERATE
Ankle range Dorsiflexion knee extension, degree (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 1.00 higher (1.02 lower to 3.02 higher)*	LOW
Dorsiflexion knee flexion, degrees (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		MD = 1.00 higher (1.58 lower to 3.58 higher)*	LOW
Velocity, m/s (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29		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	19		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	19		MD = 0.03 higher (0.04 lower to 0.09 higher)*	LOW

* Calculated by the NCC-WCH

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

Diplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Posterior leaf spring ankle-foot orthosis (PLSAFO) Mean	**Solid ankle-foot orthosis (SAFO) Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.20 lower (2.25 lower to 1.85 higher)*	LOW
GMFM Walking/Running/Jumping (Better indicated by higher values) (diplegia)					

1 study (Buckon 2004a)	16	16	-	MD = 0.20 higher (7.01 lower to 7.41 higher)*	LOW
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.30 higher (1.72 lower to 2.32 higher)*	LOW
PEDI Mobility Caregiver assistance (Better indicated by higher values) (diplegia)					
1 study (Buckon 2004a)	16	16	-	MD = 0.10 lower (1.19 lower to 0.99 higher)*	LOW

1 * Calculated by the NCC-WCH

2 Hemiplegia

Number of studies	**Number of patients**		**Effect**		**Quality**
	Posterior leaf spring ankle-foot orthosis (PLSAFO) Mean	**Solid ankle-foot orthosis (SAFO) Mean**	**Relative (95% CI)**	**Absolute (95% CI)**	
Gross motor function measure (GMFM) Standing (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.20 lower (0.71 lower to 0.31 higher)*	LOW
GMFM Walking/Running/Jumping (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.50 higher (1.29 lower to 2.29 higher)*	LOW
Pediatric evaluation of disability inventory (PEDI) Mobility Functional skills (Better indicated by higher values) (hemiplegia)					
1 study (Buckon 2001)	29	29	-	MD = 0.20 lower (1.21 lower to 0.81 higher)*	LOW
Ascent PEDI Item 54 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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
Descent PEDI Item 59 (proportion of children who keep up with peers) (Better indicated by higher values) (hemiplegia)					
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

* Calculated by the NCC-WCH

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

Comparisons to no treatment or no orthosis

Supramalleolar foot orthosis versus solid ankle foot orthosis

One study was identified for inclusion and this compared SMO with (Carlson 1997). The study examined outcomes assessing optimisation of movement.

Diplegia

Number of studies	Number of patients		Effect		Quality
	Supramalleolar orthosis (SMO) Mean	Solid ankle-foot orthosis (SAFO) Mean	Relative (95% CI)	Absolute (95% CI)	
Velocity (m/s) - group mean (Better indicated by higher values)					
1 study (Carlson 1997)	11	11	-	MD = 0.00 (0.16 lower to 0.16 higher)*	LOW
Ankle dorsiflexion angle at foot strike (degrees) - group mean (Better indicated by higher values)					
1 study (Carlson 1997)	11	11	-	MD = 6.70 lower (12.15 lower to 1.25 lower)*	MODERATE

* Calculated by the NCC-WCH

No studies reported optimisation of function, 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 randomised comparative studies examined outcomes assessing optimisation of movement.

Three randomised studies of children and young people with diplegia reported significantly greater mean ankle dorsiflexion at initial contact with a SAFO compared to no SAFO (LOW to MODERATE). The mean differences ranged from 3.6 to 15.23 degrees higher. However, one study analysed results by limb, and another reported a post hoc analysis of data.

Two randomised studies of children with diplegia compared the effects of a SAFO and no SAFO on mean ankle dorsiflexion at terminal stance. Whilst one study found no statistically significant differences in results (study analysed results by limb) (LOW), the other study found a mean increase in ankle dorsiflexion at terminal stance of 12.8 degrees favouring wearing a SAFO compared to no SAFO (post hoc analysis of data). (LOW)

One randomised study of children with diplegia found that although the percentage peak dorsiflexion time and peak dorsiflexion in stance was improved when a SAFO was worn compared to no SAFO, these differences were not statistically significant (LOW). The same study reported that use of a SAFO peak dorsiflexion swing was significantly higher compared to no SAFO (MODERATE), but that range of movement was significantly greater when no SAFO was worn compared to when one was not worn. (MODERATE)

No significant differences were reported in degrees of ankle dorsiflexion range with knee extended or flexed in one randomised study of children with diplegia. (LOW)

One study of children and young people with diplegia reported no significant differences between SAFO and no SAFO assessments of degrees for knee position at initial contact or at terminal stance. (LOW)

No statistically significant differences were reported in walking velocity achieved when wearing a SAFO compared to no SAFO in three randomised studies involving children and young people with diplegia. (LOW)

One randomised study of children and young people with hemiplegia reported that use of a SAFO statistically significantly improved ankle dorsiflexion at initial contact and peak dorsiflexion in stance compared to no SAFO. (MODERATE) However, the same study found that ankle dorsiflexion dynamic range was significantly greater when no SAFO was worn compared to when a SAFO was worn. (MODERATE)

One randomised study of children and young people with hemiplegia found no significant differences in degrees of dynamic range of ankle dorsiflexion with knee extended or flexed in children with hemiplegia. (LOW)

One randomised study of children and young people with hemiplegia found no significant differences in walking velocity when SAFO use was compared to no SAFO use. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in speed of going up and down stairs when wearing a SAFO as compared to no SAFO. (LOW)

Two randomised comparative studies assessed optimisation of function. No significant differences were identified in gross motor function measure (GMFM) standing scores or walking, running and jumping scores when SAFO use was compared to no SAFO in one study of children and young people with diplegia. (LOW)

One randomised study of children and young with diplegia found no significant differences in pediatric evaluation of disability inventory (PEDI) mobility functional skills or PEDI mobility caregiver assistance scores when SAFO use was compared to no SAFO use. (LOW)

No significant differences were identified in GMFM standing scores or walking, running and jumping scores when SAFO use was compared to no SAFO use in one study of children and young people with hemiplegia. (LOW)

One randomised study of children and young people with hemiplegia reported a significant improvement in PEDI mobility functional skills scores when wearing SAFOs compared to not wearing SAFOs. (MODERATE) A subgroup analysis of 19 of the participants reported no significant differences in the proportion of children and young people able to keep up with their peers in going up and down stairs when wearing a SAFO compared to no SAFO. (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

Five randomised comparative studies assessed optimisation of movement.

Three randomised studies in children and young people with diplegia reported no significant differences in ankle dorsiflexion at initial contact when HAFO use was compared to SAFO use. (LOW)

Two randomised studies in children and young people with diplegia found significant increases in ankle dorsiflexion at terminal stance when a HAFO was compared to a SAFO (one was a post hoc analysis and in the other ‘number of limbs’ was the unit of analysis). (LOW)

One randomised study in children and young people with diplegia found that peak dorsiflexion at stance and peak dorsiflexion time percentage and peak dorsiflexion range were all significantly improved, (MODERATE) when a HAFO was worn compared to a SAFO, but that there were no

significant differences between the groups for peak dorsiflexion swing. (LOW) The term 'peak dorsiflexion time percentage' was not defined in the article. No significant differences were reported in degrees of ankle dorsiflexion range with knee extended or flexed in children and young people wearing a HAFO or a SAFO. (LOW)

One study of children and young people with diplegia reported no significant differences between HAFO and SAFO assessments of degrees for knee position at initial contact or at terminal stance. (LOW)

No significant differences were reported in velocity achieved when wearing a HAFO compared to a SAFO in three randomised studies in children and young people with diplegia. (LOW)

No significant differences were reported in ankle dorsiflexion at initial contact when HAFO use was compared to SAFO use in one study of children and young people with hemiplegia. (LOW)

One study of children and young people with hemiplegia reported significantly improved peak dorsiflexion at stance and active range of ankle dorsiflexion when a HAFO was worn compared to when a SAFO was used. (MODERATE)

No significant differences in degrees of ankle dorsiflexion dynamic range were found with knee extended or flexed when wearing a HAFO or SAFO in one study involving children and young people with hemiplegia. (LOW)

No significant differences were reported in velocity achieved when wearing a HAFO compared to a SAFO in one study involving children and young people with hemiplegia. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in velocity ascent or descent achieved when wearing a HAFO compared to a SAFO. (LOW)

Three studies examined optimisation of function. No significant differences were identified in GMFM standing scores or walking, running and jumping scores when HAFO use was compared to SAFO use in one randomised study of children and young people with diplegia. (LOW)

One randomised study of children and young people with diplegia found no significant differences in PEDI mobility functional skills or PEDI mobility caregiver assistance scores when HAFO use was compared to SAFO use. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in the proportion of children and young people able to keep up with their peers in ascent or descent of stairs when wearing a HAFO compared to a SAFO. (LOW)

No significant differences were identified in GMFM standing scores or walking, running and jumping scores when HAFO use was compared to SAFO use in one study of children and young people with hemiplegia. (LOW)

One randomised study of children and young people with hemiplegia found no significant differences in PEDI mobility functional skills scores when HAFO use was compared to SAFO use. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in the proportion of children and young people able to keep up with their peers in ascent or descent of stairs when wearing a HAFO compared to a SAFO. (LOW)

Posterior leaf spring ankle foot orthosis versus solid ankle foot orthosis

Three studies examined outcomes for optimisation of movement. No significant differences were identified in ankle dorsiflexion at initial contact, peak dorsiflexion, percentage peak dorsiflexion time or peak dorsiflexion swing at stance when PLS AFO use was compared to SAFO use in children and young people with diplegia. (LOW)

Range of ankle dorsiflexion was significantly improved when PLS AFO was used compared to SAFO use in one study of children and young people with diplegia. (LOW)

No significant differences were identified in degrees of ankle dorsiflexion range with knee extended or flexed in children and young people with diplegia wearing a PLS AFO or a SAFO. (LOW)

No significant differences were identified in velocity achieved when wearing a PLS AFO compared to a SAFO in one study of children and young people with diplegia. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in velocity ascent or descent achieved when wearing a PLS AFO compared to a SAFO. (LOW)

No significant differences were identified in ankle dorsiflexion at initial contact when PLS AFO use was compared to SAFO use in one study of children and young people with hemiplegia. (LOW)

Use of a PLS AFO significantly improved peak dorsiflexion at stance and ankle dorsiflexion dynamic range compared to when a SAFO was worn. (MODERATE)

No significant differences were reported in degrees of ankle dorsiflexion range with knee extended or flexed in children and young people with hemiplegia wearing a PLS AFO or a SAFO. (LOW)

No significant differences were identified in velocity achieved when wearing a PLS AFO compared to a SAFO in one study of children and young people with hemiplegia (LOW). A subgroup analysis based on 19 of the participants reported no significant differences in velocity ascent or descent achieved when wearing a HAFO compared to a SAFO. (LOW)

Three studies examined outcomes for optimisation of function. No significant differences were identified in GMFM standing scores or walking, running and jumping scores when PLS AFO use was compared to SAFO use in children and young people with diplegia. (LOW)

One randomised study of children and young people with diplegia found no significant differences in PEDI mobility functional skills or PEDI mobility caregiver assistance scores when PLS AFO use was compared to SAFO use. (LOW)

No significant differences were identified in GMFM standing scores or walking, running and jumping scores when PLS AFO use was compared to SAFO use in one study of children and young people with hemiplegia. (LOW)

One randomised study of children and young people with hemiplegia found no significant differences in PEDI mobility functional skills scores when PLS AFO use was compared to SAFO use. (LOW) A subgroup analysis based on 19 of the participants reported no significant differences in the proportion of children and young people able to keep up with their peers in ascent or descent of stairs when wearing a PLS AFO compared to a SAFO. (LOW)

Comparisons to no treatment or no orthosis

Supramalleolar foot orthosis versus solid ankle foot orthosis

One randomised study examined outcomes assessing optimisation of movement. No significant differences in velocity were reported when use of a SMO was compared to a SAFO. (LOW) In the same study, ankle dorsiflexion angle at foot strike was significantly higher with SAFO use compared to SMO use. (MODERATE)

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.

Health economics

The clinical evidence for this question was limited and the evidence that was identified was of low quality. A simple cost analysis was conducted to understand the costs associated with having an orthosis fitted.

The analysis assumed that a child or young person would be offered the following appointments:

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

Orthotists start at band 5 and can work up to band 7 as a senior orthotist. Only one-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[23] (band 5 median) to represent the cost of an orthotist the appointments would cost about £27 (for 40 minutes) to £62 (for 1.5 hours) to supply and fit an orthosis if the orthotist were employed by the NHS. Private companies may provide the orthotist's time as a loss leader and in this case there would be no cost associated with appointments.

The cost of a single AFO is about £120 to £300. Lower limb orthoses are usually custom made, whereas upper limb orthoses can be products supplied from stock.

The orthosis needs 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.

The minimum age at which a child can be fitted for an orthosis is 17-18 months and orthoses can be worn throughout the growing period.

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 will 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 have commented on the need to monitor patients to assess goals and also record tolerability and side effects. This information may be useful to assess the cost-effectiveness of orthoses when the guideline is updated.

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 and to prevent contractures and deformity. The outcomes of importance will vary depending on the specific goal. The GDG agreed the following outcomes to be important: measures of optimisation of function, including gross motor function measure (GMFM), paediatric evaluation of disability inventory (PEDI) and goal attainment scaling (GAS); improving or maintaining range of movement, for example in the use of night-time resting splints to improve posture and prevent deformity; active and passive range of movement, quality of life, as measured by the child health questionnaire (CHQ). Based on their clinical experience, the GDG included muscle spasticity 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.

[23] £42 per hour of client contact with a community physiotherapist, £40 with a hospital physiotherapist – the mean was used. Unit costs of health and social care 2010, PSSRU.

Studies have used foot and knee position as indicators of efficacy 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 gross motor function classification system (GMFCS) levels 1 to 3. 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 postures during walking, 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 those at GMFCS level 4 or 5 or MACS levels 4 or 5 there is a greater risk of deformity. Here, the passive range of movement (ROM) 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 provided some evidence supporting a beneficial effect with the various forms of AFO (SAFO, HAFO, PLSAFO) in relation to ankle dorsiflexion during the gait cycle in children with diplegia or hemiplegia, but the findings were often inconsistent across studies. No improvement in walking speed was identified. No improvement in function as measured by gross motor function measure (GMFM) or PEDI was shown. 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 and important role in the management of spasticity in children and young people. The GDG considered that orthoses can have an important role in improving posture, facilitating upper limb function, improving walking efficiency, and preventing or slowing the development of contractures and hip migration. The GDG recommended that these objectives be considered in relation to the individual child or young person, through a careful assessment of the goals that may be realistic for that individual.

No adverse effects were identified in the evidence and there was no evidence regarding acceptability and tolerance of orthoses. Side effects may have a major impact on the child or young person's ability and willingness to accept or tolerate an orthosis. In the GDG's experience, discomfort, skin injury, sleep disturbance, etc. are more likely to occur if orthoses are badly designed, ill-fitting or worn. When custom-made orthoses are used the GDG recommended that an orthotist should be involved. Adverse effects should mainly be preventable with careful design and fitting of the devices.

Trade-off between net health benefits and resource use

Orthoses can be expensive. 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 therapist in assessment, supply, fitting, and regular reviews. However, if an orthosis meets the intended outcomes, is acceptable to the child or young person, and causes no harm then it can be considered to be cost effective. Although the evidence did not identify 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 also have resource implications.

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. A total of six prospective comparative studies were included in the guideline review. These studies examined the efficacy of various ankle foot orthoses in children with diplegia or hemiplegia. The children had randomised allocation of treatment sequences to allow comparison. For all of the outcomes studied the quality of the evidence was rated as low. The GDG considered that the findings from the studies should be treated with some caution.

There was no evidence suitable for inclusion in relation to the use of wrist or hand orthoses, thumb abduction orthoses, elbow orthoses, knee orthoses, spinal (thoracic lumbar sacral) orthoses, hip abduction orthoses, or prescribed footwear.

Other considerations

Based on their expertise and experience, and taking account of the available evidence, the GDG made recommendations for the use of orthoses in the following specific circumstances.

Lower limb orthoses

The GDG recommended that for children and young people in GMFCS 4 or 5 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 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 efficacy 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 individual had good control of knee and hip extension then a SAFO should be considered, but if not then a HAFO might be preferred as this would be less likely to cause over-extension. The GDG also agreed that AFOs can worsen gait in those with fixed lower limb deformities, such as hip or knee contractures and femoral or tibial anteversion.

The GDG also considered that children and young people with serious functional limitations (GMFCS levels 4 and 5) should be offered AFOs to improve foot position for sitting, transfers and assisted standing.

Any child fitted for an AFO should be advised that it should be worn for at least 6 hours a day to maximise effectiveness.

Given their effect in restricting ankle movement, AFOs can potentially make it more difficult for an individual to stand up, and the GDG therefore advised that in young children who are in the process of learning to stand up consideration be given to the use of SMOs or supportive orthotic footwear.

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

Although there was no supportive evidence, the GDG believed that knee gaiters should be considered for those with knee flexion deformity because the support these provided would improve posture and function and might assist in preventing the development of fixed contractures.

Again, although clinical trial evidence was lacking, the GDG believed that hip orthoses were helpful in some individuals. They recommended their use be considered in those with lower limb scissoring if this was causing functional difficulty in relation to sitting, standing or walking. They also recommended considering their use to limit hip adduction in order to reduce the risk of hip migration.

Upper limb orthoses

There was no published evidence on which to base recommendations on the use of orthoses 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 those 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, an individual 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 contracture. However, a dynamic orthosis should be considered to help with hand function. For example, a thumb abduction splint for those with a 'thumb in palm' deformity may be helpful. Dynamic thermoplastic orthoses that allow limited flexion and extension at the wrist may facilitate better function than a rigid wrist hand orthosis.

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 on the optimal duration they believed this to be a reasonable recommendation.

Body trunk orthoses

There was an absence of evidence regarding the use of body trunk orthoses. The GDG considered that while thoracolumbosacral orthoses (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.

Orthoses in association with other treatment options

There was no evidence comparing the use of orthoses with other treatments. The GDG noted that orthoses are usually used together with other interventions, such as physiotherapy or botulinum toxin injection. The GDG recommended that consideration be given to the use of an orthosis after botulinum toxin therapy because this might well increase the effectiveness of that treatment by optimising joint position when spasticity is reduced.

Monitoring and assessment of orthoses

The GDG has made recommendations on the need for regular monitoring and on giving advice to the child or young person and their parents or carers regarding the correct use of the device, and when and how to seek advice if concerns arise. Recommendations were made in this regard to reduce the risk and optimise efficacy and acceptability and tolerability.

The GDG view was that an orthotist should be involved when using a custom-made orthosis to ensure that it is designed, sized and fitted properly and its comfort and use monitored. Specialist orthotists can discuss with parents and carers how to apply orthoses, when to wear them and for how long, and when and from whom to seek further advice. This should include advice about the use of orthotics overnight. Parents and carers need to ensure that an orthotic is not disturbing the child's or young person's sleep, as well as the circumstances where resting splints should be used, for example for muscles controlling two joints.

The orthotist should minimise delays as this can be associated with reduced effectiveness and this may result in complications. Once fitted, there should be regular reviews of the othosis to ensure maximum efficiency in achieving individualised goals. The reviews need to cover all aspects of orthotics use, including acceptability and appropriateness to the child or young person, checks of the condition, fit and correct use of the othosis, 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 othosis to that individual. The health care professional undertaking the review should also look for signs of muscle wastage or reduced sensation. They should also be aware that rigid orthoses for children may not be well tolerated in children and young people with severe spasticity.

The GDG recommended that if an orthosis causes pain for which there is no immediate remedy it should be removed without delay. 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. Most such difficulties are rapidly relieved by modifying, changing or removing the orthosis. The GDG were aware, based on their experience, that children and young people with severe spasticity or dyskinesis may tolerate solid orthoses poorly, and recommended that caution be exercised in such cases. The GDG recommended that consideration be given to whether the use of botulinum toxin injection therapy might in some cases improve tolerance of orthoses. Reduction in spasticity would be expected to facilitate patient comfort and optimal joint positioning with orthoses. A longer-term risk was that of muscle wasting and weakness resulting from immobilisation. 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. 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.

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 their level of comfort. Such orthoses are being used increasingly with children and young people with spasticity, despite mixed evidence regarding their effectiveness. Further evaluation is needed as to their effectiveness and for which children and young people.

Recommendations

Number	Recommendation
	Orthoses
	General principles
32	Consider orthoses for children and young people with spasticity to: • improve posture • facilitate upper limb function • improve walking efficiency • prevent or slow development of contractures • prevent or slow hip migration.
33	Determine realistic goals for treatment with orthoses based on a careful individual assessment, and discuss the options, risks and benefits of wearing them with children and young people and their parents or carers.
34	Ensure that orthoses have been designed, sized and fitted correctly.
35	Inform children and young people with orthoses and their parents and carers: • how to apply them • when to wear them and for how long • when and where to seek further advice.
36	Ensure that an orthotist is involved when a custom-made orthosis is being used.
37	Minimise delays in the supply of orthoses after measurement and in the repair of orthoses.
38	Review orthotic use at every contact with the local multidisciplinary child development team to ensure that orthoses: • are still acceptable to the child or young person and their parents or carers • remain in good repair • remain appropriate to intended treatment goals • remain well fitting • are being used as advised • are not causing discomfort or pain • are not causing injury • are not causing sleep disturbance.
	Cautions in the use of orthoses
39	Assess whether orthoses 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 their appearance.
40	Advise about the risk of pressure sores with orthoses.

Number	Recommendation
41	Inform children and young people and their parents or carers to remove orthoses that are causing pain that cannot be relieved immediately through repositioning of the limb in the orthosis or adjustment of the strapping.
42	When deciding whether to offer an orthosis, balance the benefits against the risks and potential consequences of muscle wasting through lack of muscle use. Discuss these with the child or young person and their parents or carers.
43	Be cautious in offering rigid orthoses to children and young people with severe spasticity or dyskinesis because rigid orthoses are often poorly tolerated in this group.
	Botulinum toxin type A injection and orthoses
44	Consider an orthosis after treatment with botulinum toxin type A.
45	Consider treatment with botulinum toxin type A if this is likely to improve the tolerability of an orthosis.[24]
	Overnight use of orthoses
46	Consider overnight use of orthoses. If an orthosis is used overnight: • check that overnight use does not disturb sleep • use night resting splints for muscles that control two joints (for example, the ankle and knee, in the case of the gastrocnemius muscle).
	Lower limb orthoses
47	When deciding whether to offer an ankle–foot orthosis, balance the benefits against the risk of worsened gait in children and young people with: • hip or knee contractures • femoral or tibial anteversion. Discuss these with the child or young person and their parents and carers.
48	Consider ground reaction 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.
49	For children and young people with equinus deformities that impair their gait consider: • a solid ankle–foot orthosis if they have good control of knee or hip extension • a hinged ankle–foot orthosis if they have poor control of knee or hip extension.
50	In children whose motor development is between 8 months and 2 years consider offering supramalleolar orthoses or supportive orthotic footwear instead of ankle–foot orthoses.
51	Consider ankle–foot orthoses for children and young people with serious functional limitations (GMFCS levels 4 and 5) to improve foot position for sitting, transfers between sitting and standing, and assisted standing.
52	Inform children and young people and their parents and carers that ankle–foot orthoses intended to stretch muscles (for example, rigid, hinged or ground-reaction

[24] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

Number	Recommendation
	force ankle–foot orthoses) should usually be worn for at least 6 hours each day.
53	Consider knee gaiters for children and young people with knee flexion deformities.
54	Consider hip orthoses: • to improve function if scissoring is causing difficulties with sitting, standing or walking • to limit hip adduction and reduce the risk of hip migration.
	Upper limb and trunk orthoses
55	Consider the following 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 thumb abduction splint if the child or young person has a 'thumb in palm' deformity).
56	Consider offering body trunk orthoses to children and young people for the management of spasticity with co-existing scoliosis or kyphosis if this will help with sitting.

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Number	Research recommendation
7	What is the effectiveness of a prolonged stretch of the calf muscles with a HAFO compared to an AFO worn for a shorter time in children and young people with spastic hemiplegia?
8	What of the effectiveness of wearing a HAFO to prevent an equinus foot posture compared to an AFO or SAFO?
9	What is the effectiveness of wearing an AFO after surgery compared to not wearing an AFO in children and young people with lower limb spasticity?
10	What is the effectiveness of dynamic thermoplastic orthoses compared to static orthoses in children and young people with spastic hemiplegia who have abnormal posturing?
11	What is the 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?

3

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. It was, therefore, important to examine the evidence regarding the effectiveness and safety of these therapies.

Diazepam is thought to directly augment 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 and therefore diminishing the force of the muscles contractions, but it is not selective on the muscles it acts upon. It is metabolised in 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 when 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 the cholinergic interneurons. Treatment with trihexyphenidyl is thought to reduce cholinergic transmission and redress the balance leading to a decrease in dystonia.

Other 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

In total there were eight studies in nine publications addressing four comparisons as follows:

- diazepam versus placebo or no treatment (one RCT; Mathew 2005a; Mathew 2005b)
- baclofen versus placebo or no treatment (three RCTs; McKinlay 1980; Milla 1977; Scheinberg 2006)
- dantrolene versus placebo or no treatment (three RCTs; Denhoff 1975; Haslam 1974; Joynt 1980)
- trihexyphenidyl versus placebo or no treatment (one RCT; Rice 2008).

Evidence profiles

Oral diazepam versus placebo or no treatment

Two reports of a parallel RCT conducted in India (Mathew 2005a; Mathew 2005b) compared the effects of a single bedtime dose of diazepam to placebo in children with spasticity of varying severities. Children who were in distress due to painful spasms were excluded from the study.

One report (Mathew 2005b) provided evidence on reduction of spasticity.

Number of studies	Number of patients		Effect		Quality
	Diazepam	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean reduction of muscle tone score (modified Ashworth scale) at 15 -20 days; bedtime half dose diazepam 0.5mg if <8.5kg, 1mg if >8.5kg bodyweight vs. placebo: (Better indicated by higher values)					
1 study (Mathew 2005b)	59	55	-	MD = 8.00	MODERATE
Mean reduction of muscle tone score (modified Ashworth scale) at 15 - 20 days : bedtime full dose diazepam 1mg if <8.5kg, 2mg >8.5kg bodyweight vs. placebo: (Better indicated by higher values)					
1 study (Mathew 2005b)	59	55	-	MD = 12.79	MODERATE

Neither report provided outcomes relevant to optimisation of movement or function, pain (reduction of pain), or quality of life.

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

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

One report (Mathew 2005a) provided evidence on outcomes relevance to acceptability and tolerability.

Number of studies	Number of patients		Effect		Quality
	Diazepam	Placebo	Relative (95% CI)	Absolute (95% CI)	
Child's disposition during activities of daily living at 15 - 20 days: bedtime dose diazepam (Better indicated by higher values)					
1 study (Mathew 2005a)	59	55	-	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 diazepam (Better indicated by higher values)					
1 study (Mathew 2005a)	59	55	-	MD 7.31 higher (6.78 to 7.84 higher)	MODERATE
Child's behavioural profile at 15 - 20 days: bedtime dose diazepam (Better indicated by higher values)					
1 study (Mathew 2005a)	59	55	-	MD 7.35 higher (6.74 to 7.96 higher)	MODERATE

* Calculated by the NCC-WCH

Oral baclofen versus placebo or no treatment

Three cross-over RCTs compared the effects of oral baclofen and placebo (McKinlay 1980; Milla 1977; Scheinberg 2006).

All three RCTs reported reduction of spasticity.

Number of studies	Number of patients		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	2/20	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	0/20	RR 11 (0.65 to 186.62)*	-	LOW
Reduced muscle tone (Ashworth scale) reported by investigators					
1 study (McKinlay 1980)	-	-	-	-	LOW
Reduced muscle tone or better movement reported by physiotherapist					
1 study (McKinlay 1980)	14/209	5/20	RR 2.8 (1.26 to 6.22)*	45 more per 100 (from 6 more to 130 more)*	MODERATE
Mean Tardieu score at wk12 of treatment (Better indicated by lower values)					
1 study (Scheinberg 2006)	15	15	-	4.4 lower	MODERATE

* Calculated by the NCC-WCH

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

Number of studies	Number of patients		Effect		Quality
	Baclofen	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Pediatric evaluation of disability inventory (PEDI) self care score at wk12 of treatment: (Better					

indicated by higher values)					
1 study (Scheinberg 2006)	15	15	-	1.5 lower	MODERATE
Mean PEDI mobility at wk12 of treatment: (Better indicated by higher values)					
1 study (Scheinberg 2006)	15	15	-	1.5 lower	MODERATE
Mean PEDI social function at wk12 of treatment: (Better indicated by higher values)					
1 study (Scheinberg 2006)	15	15	-	0.2 lower	MODERATE
Mean Goal assessment T score (GAS T) at wk12 of treatment: (Better indicated by higher values)					
1 study (Scheinberg 2006)	15	15	-	6.6 higher	MODERATE
Gait assessment performance improved (interstep distance and angle of the foot to the direction of walking)					
1 study (McKinlay 1980)	8/20	4/20	RR = 2.00 (0.72 to 5.59)*	20 more per 100 (from 6 fewer to 92 more)*	LOW

1 * Calculated by the NCC-WCH

2 No studies reported outcomes relevant to pain.

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

Number of studies	**Number of patients**		**Effect**		**Quality**
	Baclofen	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Adverse effects					
1 study (Milla 1977)	5/20	0/20	RR = 11 (0.65 to 186.62)*	-	LOW
Adverse effects (parental reports)					
1 study (McKinlay 1980)	8/20	1/20	RR = 8 (1.1 to 58.19)*	35 more per 100 (from 1 more to 100 more)*	LOW
Drowsiness (therapist and teacher reports)					
1 study (McKinlay 1980)	6/15	4/15	RR = 1.5 (0.53 to 4.26)*	13 more per 100 (from 13 fewer to 87 more)*	MODERATE

4 * Calculated by the NCC-WCH

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

Number of studies	**Number of patients**		**Effect**		**Quality**
	Baclofen	**Placebo**	**Relative**	**Absolute**	

			(95% CI)	(95% CI)	
Wish to continue child's treatment (parental report)					
1 study (McKinlay 1980)	-	-	-	-	LOW
Willingness to continue with the medication their child was on (parental report)					
1 study (Sheinberg 2006)	6/155	4/156	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)	6/157	7/158	RR = 0.86 (0.38 to 1.95)*	7 fewer per 100 (from 28 fewer to 44 more)*	MODERATE

* Calculated by the NCC-WCH

No studies reported outcomes relevant to quality of life.

Oral dantrolene versus placebo

Three RCTs compared the effects of oral dantrolene and placebo (Denhoff 1975; Haslam 1974; Joynt 1980). Two were cross-over RCTs (Denhoff 1975; Haslam 1974), and one was a parallel RCT (Joynt 1980).

Two RCTs reported outcomes relevant to reduction of spasticity.

Number of studies	Number of patients		Effect		Quality
	Dantrolene	Placebo	Relative (95% CI)	Absolute (95% CI)	
Motor tone assessment					
1 study (Haslam 1974)	59	55	-	0.609 higher	LOW
Scissoring					
1 study (Haslam 1974)	59	55	-	0.381 higher	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)	-	MODERATE
Passive range of motion (PROM)					
1 study (Haslam 1974)	59	55	-	0.565 higher	LOW
Spontaneous range of motion (ROM)					
1 study (Haslam 1974)	59	55	-	0.522 higher	LOW

* Calculated by the NCC-WCH

Two RCTs reported outcomes relevant to optimisation of function.

Number of	Number of patients	Effect	Quality

studies	Dantrolene	Placebo	Relative (95% CI)	Absolute (95% CI)	
Improvement in motor functioning					
1 study (Denhoff 1975)	10/26	8/26	-	-	LOW
Improvement in activities of daily living and behaviour – staff assessment					
1 study (Denhoff 1975)	11/20	2/20	-	-	VERY LOW
Improvement in activities of daily living and behaviour – parent's assessment					
1 study (Denhoff 1975)	12/28	2/28	-	-	LOW
Overall assessments (neurological, orthopaedic, motor, activities of daily living and behaviour)					
1 study (Denhoff 1975)	28	28	-	-	LOW
Activities of daily living using multiple performance tests at 9 weeks (e.g. as time taken to screw and unscrew two halves of barrels of three sizes and time taken to button and unbutton buttons of three different sizes)					
1 study (Joynt 1980)	11	9	-	-	LOW

* Calculated by the NCC-WCH

No studies reported outcomes relevant to pain (reduction in pain) or to quality of life.

One RCT reported outcomes relevant to adverse effects.

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

No studies reported outcomes relevant to acceptability and tolerability.

Oral trihexyphenidyl versus placebo

One cross-over RCT compared the effects of high-dose trihexyphenidyl and placebo. (Rice 2008)

One RCT reported outcomes relevant to reduction of dystonia.

Number of studies	Number of patients		Effect		Quality
	Trihexyphenidyl (THP)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Barry-Albright Dystonia Scale (BAD) score: (Better indicated by lower values)					
1 study (Rice 2008)	16	16	-	-	LOW

One RCT reported outcomes relevant to optimisation of function.

Number of studies	Number of patients		Effect		Quality
	Trihexyphenidyl (THP)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Quality of upper extremity skills test (QUEST) score (Better indicated by higher values)					
1 study (Rice 2008)	16	16	-	-	LOW
Mean Goal assessment scale (GAS) score (Better indicated by higher values)					
1 study (Rice 2008)	16	16	-	-	VERY LOW
Mean Canadian occupational performance measure (COPM) score (performance) (Better indicated by higher values)					
1 study (Rice 2008)	16	16	-	-	VERY LOW

No studies reported outcomes relevant to pain (reduction in pain) or to quality of life.

One RCT reported outcomes relevant to adverse effects.

Number of studies	Number of patients		Effect		Quality
	Trihexyphenidyl (THP)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Adverse effects					
1 study (Rice 2008)	16/163	6/164	-	-	LOW

One RCT reported outcomes relevant to acceptability and tolerability

Number of studies	Number of patients		Effect		Quality
	Trihexyphenidyl (THP)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Canadian occupational performance measure (COPM) score (satisfaction) (Better indicated by higher values)					
1 study (Rice 2008)	16	16	-	-	LOW

Evidence statement

Oral diazepam versus placebo or no treatment

With regard to reduction of spasticity, one parallel RCT found that muscle tone (modified Ashworth score) was statistically significantly reduced in children with spasticity of varying severities who were given a single bedtime half or full dose of diazepam compared with placebo. (MODERATE)

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

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

With regard to acceptability and tolerability, one parallel RCT found that the child's disposition during activities of daily living, the burden of caring for the child on the family and the child's behavioural profile were statistically significantly improved in children with spasticity of varying severities who were given a single bedtime half or full dose of diazepam compared with children who received placebo. (MODERATE)

Oral baclofen versus placebo or no treatment

With regard to reduction of spasticity, one cross-over RCT reported a statistically significant improvement in spasticity of one level on the Ashworth scale when children with diplegia, hemiplegia and quadriplegia were given baclofen compared with placebo. (LOW) However there was no statistically significant difference in improvement in spasticity of two or more levels on the Ashworth scale between treatment periods. (LOW) One cross-over RCT reported that there was no statistically significant difference in muscle tone observed by the study investigators when children with spasticity were given baclofen compared with placebo. (LOW) One cross-over RCT found that statistically significantly more children with spasticity had a reduction in muscle tone or better movement (assessed by therapists) when they were given baclofen compared with placebo. (MODERATE) One cross-over RCT found no statistically significant differences in mean Tardieu scores when children with spastic or spastic dystonic quadriplegia were given baclofen compared with placebo. (MODERATE)

With regard to optimisation of function, one cross-over RCT found that there were no statistically significant differences in mean change scores in PEDI self care, mobility or social function assessments when children with spastic or spastic dystonic quadriplegia were given baclofen compared to placebo. (All MODERATE) One cross-over RCT provided evidence that mean GAS T scores were statistically significantly improved when children with spastic or spastic dystonic quadriplegia were given baclofen compared to placebo. (MODERATE). One cross-over RCT found that there was no statistically significant difference in the number of children with spasticity achieving improved gait performance when given baclofen compared to placebo. (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 found that 25% of children experienced side effects related to baclofen's therapeutic effect (4 sedation, 1 hypotonia) during treatment. There were no side effects reported when placebo was given. (LOW) One cross-over RCT found that 89% of parent-reported side effects were seen in children receiving baclofen and in half of these cases reduction of dose of baclofen relieved side effects. (LOW). One cross-over RCT reported that therapists and teachers reported that daytime drowsiness occurred statistically significantly more frequently when children were taking baclofen compared to placebo. (LOW) One cross-over RCT, which titrated the baclofen dose more slowly than the other two included RCTs, found that 40% of parents reported adverse effects during the baclofen treatment period compared to 27% of parents during the placebo period. (MODERATE)

With regard to acceptability and tolerability, one cross-over RCT found that one parent (5%) would have continued with active treatment (should their guess about the active treatment period be correct). (LOW) One cross-over RCT found that 40% of parents would have continued with baclofen compared to 27% who would have continued with placebo. (MODERATE) and that positive findings were reported by 40% of parents during the baclofen treatment period compared with 47% of parents during the placebo period. (MODERATE)

Oral dantrolene versus placebo

With regard to reduction of spasticity, one cross-over RCT found no statistically significant differences in muscle tone when children with spasticity and learning disabilities were given dantrolene compared with placebo. (LOW) However, scissoring was statistically significantly improved when dantrolene was given compared with placebo. (LOW) One parallel RCT found no statistically significant difference in incidence of spasms (as reported by the child or parent) when children with moderate to severe spasticity were treated with dantrolene compared to placebo. (MODERATE)

With regard to optimisation of movement, one cross-over RCT found no statistically significant difference in PROM or Spontaneous ROM when children with spasticity and learning disabilities were given dantrolene compared with placebo. (Both LOW)

With regard to optimisation of functioning, one cross-over RCT found no statistically significant difference in motor function when children with mild to severe spasticity were given dantrolene compared with placebo. (LOW) However, statistically significantly more children with mild to severe spasticity showed improvement in activities of daily living and behaviour assessed by staff and parents when given dantrolene compared with placebo (VERY LOW and LOW). One cross-over RCT found that for between 8 and 13 of 28 participants no discernable differences in function could be found between the drug and placebo treatment periods. (LOW) One parallel RCT found no significant differences in multiple performance tests to assess activities of daily living when children with moderate to severe spasticity were treated with dantrolene or 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 found that statistically significantly more children with mild to severe spasticity experienced side effects when they were receiving dantrolene compared with placebo although these were generally transient. (LOW)

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 no statistically significant difference in BAD scores in children with dystonia (and spasticity) when they were given trihexyphenidol compared to placebo. (LOW)

With regard to optimisation of functioning, one cross-over RCT found that there were no statistically significant differences in QUEST scores, GAS (Goal Attainment Scale) T scores and COPM - performance (Canadian Occupational Performance Measure QUEST scores when children with dystonia (and spasticity) were given trihexyphenidol compared to placebo. (LOW; VERY LOW: 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 found that sixteen children (100%) experienced side effects when they were given trihexyphenidol, with one child requiring brief hospitalisation for multiple side effects. By comparison, six (38%) of children experienced side effects during the placebo phase. (LOW)

With regard to acceptability and tolerability, one cross-over RCT found that there were no statistically significant differences in COPM-satisfaction scores when in children with dystonia (and spasticity) were given trihexyphenidol compared to placebo. (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
- levadopa 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.

Evidence to recommendations

The GDG consensus was that reduction in spasticity, improvements in mobility and other physical outcomes were the most important outcomes for oral medication. 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 side-effects affect long term acceptability and tolerability of drugs, both to the child themselves but also to the parents and carers who look after them. These outcomes were also reported in the review of the literature.

Evidence was identified for diazepam, baclofen and dantrolene only.

Oral diazepam

Evidence was only identified from one trial of bedtime administration of diazepam. There was no evidence that it significantly reduced spasticity. The study reported a significant difference in muscle tone but no evidence was identified of an improvement in movement or function, pain (reduction of pain) or quality of life, or parental acceptability. The study did report that bedtime administration improved the child's disposition, and improved the reported "burden of care" and child's behaviour. Bedtime administration was not associated with daytime drowsiness. However, the GDG noted that the dose of diazepam employed in this trial was less than that usually employed in UK practice currently and compared with recommendations (BNF-c). The trials did not examine the potential effectiveness of daytime treatment with diazepam. It was also observed that children with painful muscle spasms were specifically excluded from the trial. The GDG considered that with higher doses the outcomes might have been different, and the likelihood of sedation and increased oral secretions (a recognized side effect of diazepam therapy in these children) might have been greater.

Baclofen

Three studies were identified in the review. Evidence from one study reported that patients taking baclofen experienced a small reduction (one level improvement on the Ashworth scale) in level of spasticity but this was not consistently observed in the other trials. It was not clear from the study whether this benefit was more likely with mild or more severe spasticity. There was no evidence of any larger benefit (more than one level improvement on the Ashworth scale). The evidence did not demonstrate benefit in mobility and function, or an improvement in muscle tone. There was no reported improvement in Tardieu 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". Some adverse side-effects of treatment were reported in all studies. Drowsiness was reported as a specific side-effect, and this appeared to be dose related. One trial reported that more parents of children who received baclofen (versus placebo) would have chosen to continue the treatment.

Dantrolene

Three studies reported evidence of outcomes. One reported that scissoring was significantly reduced but otherwise there was no evidence that spasticity was reduced by this agent. One study reported improved performance with daily activities and behaviour but the others did not report this benefit. Its

use was associated with increase drowsiness, lethargy and malaise although these symptoms were reportedly transient.

Baclofen, diazepam and dantrolene are inexpensive drugs, and if clinically effective the GDG considered that they would be cost effective. Oral diazepam is inexpensive, (current cost of 28 diazepam tablets, 2mg tablets £0.98), 5 mg tablets £1.01, 10 mg tablets £1.02). The maximum daily dose recommended (BNF-c) is 40mg daily £53.19 if given as 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 100-mL pack = £6.38. Oral baclofen is inexpensive treatment (current information (BNF=C) £0.02 per tablet and between £8.95 and £10.00 for 300ml of oral solution (5 mg/5 ml). Given that the maximum dose of baclofen recommended (BNF-C) is 100mg daily, this amounts to an annual cost of no more than £69.09.

The GDG noted that evidence regarding the effectiveness of oral medications in managing spasticity and associated motor problems was limited, inconsistent and often of low quality. The GDG noted that there were no trials in which oral drugs were directly compared. The GDG therefore relied on the group's expertise and on consensus in their deliberations on the choice of oral drugs. The reported trials did not provide evidence to guide optimal dosage. The reported trials were of short duration, and the GDG considered that with time, increased tolerance might have developed. Despite the deficiencies and inconsistencies in the evidence the GDG believed that oral medications do have a potentially important role in the care of some children 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 GDG members, benefit was regularly observed or reported by individual patients and carers.

The GDG recognized that oral medication as a non-invasive form of therapy would be of great value if successful in alleviating spasticity and relieving associated conditions such as pain, muscle spasms and functional disability. The GDG believed that the individual response to oral medication was unpredictable and that the benefits achieved and the adverse effects experienced might vary from one person to the next. Any likely side effects would usually be reversible either by dosage alteration or discontinuation if necessary. Daytime drowsiness might be a significant problem and might disturb a child'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 through a judicious trial of therapy in selected children.

The GDG noted that oral benzodiazepines especially diazepam are frequently used in the management of children with spasticity. Given that the available trial evidence was in relation to diazepam the GDG believed that this should be the benzodiazepine of choice.

The GDG considered that diazepam should be the first choice of oral medication if the goal was to alleviate troublesome night-time muscle spasms or if there was a severe pain crisis. This was because diazepam was likely to have a more rapid onset of action than baclofen. However, if the goal was to achieve a sustained long-term effect from oral therapy oral baclofen was to be preferred. This was because the GDG was concerned about the possibility of adverse consequences from long-term administration of a benzodiazepine drug.

The GDG consensus is that a rational approach to the use of oral medications is 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 reported benefit associated with this approach. The GDG view is that if oral diazepam is offered as treatment, this should begin as a single bed-time dose. If necessary the dose may be increased stepwise and/or a daytime dose added. When using oral baclofen, again it was advisable to begin with a low dose and increased stepwise over 4 weeks. The GDG view was that this was the appropriate time period to achieve the intended therapeutic goal with minimal side-effects.

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

The GDG view is that if oral medication is found to have a useful affect in an individual child, that is it achieves the 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 medication is still necessary on each occasion when a child is reviewed. Such a review of treatment should take place at least six-monthly.

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

The GDG considered that there were potential adverse effects associated with withdrawal of these medications after a long period of therapy. They therefore recommended that discontinuation after a long period of usage should be gradual with stepwise dose reduction.

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

The GDG considered that neither the evidence of the efficacy 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 on tizanidine and trihexylphenidyl and the limited experience in their usage the GDG made no recommendation regarding these drugs.

Recommendations

Number	Recommendation
	Oral drugs
57	Consider oral diazepam if spasticity is contributing to: • discomfort or pain • muscle spasms (for example night-time muscle spasms) • functional disability and • a rapid effect is desirable (for example, in pain crisis).
58	Consider oral baclofen if spasticity is contributing to: • discomfort or pain • muscle spasms • functional disability and • a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).
59	Start oral diazepam treatment with a single dose at bedtime. If the clinical response is unsatisfactory consider: • increasing the dose or • adding a daytime dose.
60	Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect.
61	If oral diazepam is used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.
62	Continue using oral diazepam or oral baclofen if they have a clinical benefit and are well tolerated, but consider whether to stop treatment every time the child or

Number	Recommendation
	young person's management programme is reviewed and at least every 6 months.
63	If adverse effects (such as drowsiness) occur with oral diazepam or oral baclofen consider reducing the dose or stopping treatment.
64	If the clinical response to oral diazepam or oral baclofen used alone is unsatisfactory within 4–6 weeks, stop using the drug or consider a trial of combination treatment with both oral diazepam and oral baclofen.

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Number	Research recommendation
12	What is the 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 in GMFCS levels 1 to 5?
13	What is the 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 in GMFCS levels 1 to 5?

7 Botulinum toxin

Introduction

Botulinum toxin (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 can not be triggered to contract and flaccid paralysis is produced. In spastic muscles this relaxation is the desired effect and can help alleviate some of the problems associated with upper motor neurone (UMN) 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 three 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 from assessment of patients, administration and follow up pathways. For this reason the GDG wanted to review available evidence and formulate a consensus of recommendations to help inform practice.

BoNT is one of a number of strategies available for the management of spasticity in children and young people with a non-progressive brain disorder and 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 that is used across the UK although some centres are turning to type B when response to A is inadequate.

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

- The effectiveness of a single dose of BoNT A given in combination with a program of therapy appropriate to the child's or young person's needs compared to:
    - therapy alone
    - oral antispasmodic medication and therapy.
- The effectiveness of BoNT A treatment repeated every four months compared to every 12 months.
- The comparative effectiveness of BoNT A treatment when administered using the following location 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 was identified for this review question.

Review question

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

Description of included studies

In total there were eight publications addressing four comparisons as follows:

- BoNT A and physical therapy versus physical therapy alone (one Cochrane systematic review (Hoare 2010; data from several of the trials included in the systematic review are presented in the evidence profiles below), one RCT for upper limb (Olesch 2010), and three RCTs for lower limb (Ackman 2005; Kay 2004; Reddishough 2002))
- BoNT A every 4 months versus BoNT A every 12 months (one RCT; Kanovsky 2009)
- electrical stimulation versus palpation (one RCT; Xu 2009)
- ultrasound versus electrical stimulation (one RCT; Kwon 2010).

Evidence profiles

Botulinum toxin type A and physical therapy versus physical therapy alone

The eight RCTs identified for inclusion compared BoNT A and occupational therapy to occupational therapy alone.

One systematic review and one RCT reported outcomes relevant to reduction of spasticity and optimisation of movement in the upper limb (Hoare 2010; Olesch 2010).

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	OT only all outcomes	Relative (95% CI)	Absolute (95% CI)	
Modified Ashworth scale - shoulder adductors - 4 months					
1 study (Greaves 2004)	9	9	OR 0.20 (0.03, 1.15) †	-	LOW
Modified Ashworth scale - elbow flexors - 3 months					
2 studies (Russo 2007; Wallen 2007)	41	39	OR 0.16 (0.06 to 0.43) †	-	MODERATE
Modified Ashworth scale - elbow flexors - 6 months					
2 studies (Russo 2007; Wallen 2007)	41	39	OR 0.33 (0.13 to 0.86) †	-	LOW
Modified Tardieu scale - elbow flexors (change from baseline R2-R1) - 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
Modified Tardieu scale - elbow flexors - Four months (cycle 1) final score (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 34.3 lower (70.67 lower to 2.07 higher)*	MODERATE
Modified Tardieu elbow flexors cycle 2 final score (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 36 lower (71.3 to 0.7 lower)*	MODERATE
Modified Tardieu elbow flexors cycle 3 final score (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 42.8 lower (86.48 lower to 0.88 higher)*	MODERATE
Elbow extension passive range of motion (PROM) (change from baseline) - 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
Elbow extension PROM (change from baseline) - 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
Modified Ashworth scale - pronators - 3 Months					
1 study (Wallen 2007)	20	17	OR 1.58 (0.45 to 5.52) †	-	MODERATE
Modified Ashworth scale - pronators - 4 Months					
1 study (Greaves 2004)	9	9	OR 0.13 (0.02 to 0.97) †	-	LOW
Modified Ashworth scale - pronators - 6 Months					
1 study (Wallen 2007)	20	17	OR 1.5 (0.22 to 10.16) †	-	LOW
Modified Tardieu scale - forearm pronators - 4 months (cycle 1) mean change (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 4 higher*	LOW
Modified Tardieu forearm pronators Cycle 2 mean change (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 5.8 lower*	LOW

Modified Tardieu Forearm pronators cycle 3 mean change (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 18.5 lower*	LOW
Supination active range of motion (AROM) (change from baseline) - 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
Supination AROM (change from baseline) - 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
Forearm supination PROM (change from baseline) - 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
Forearm supination PROM (change from baseline) - 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
Modified Ashworth scale - wrist flexors - 3 Months					
2 studies (Russo 2007, Wallen 2007)	0/0 (0%)	0/0 (0%)	OR 0.1 (0.03 to 0.29) †	-	MODERATE
Modified Ashworth scale - wrist flexors - 4 Months					
1 study (Greaves 2004)	0/0 (0%)	0/0 (0%)	OR 0.36 (0.07 to 1.87) †	-	LOW
Modified Ashworth scale - wrist flexors - 6 Months					
2 studies (Russo 2007, Wallen 2007)	0/0 (0%)	0/0 (0%)	OR 0.2 (0.08 to 0.51) †	-	LOW
Modified Tardieu scale - wrist flexors (change from baseline R2-R1) - Four months (Better indicated by lower values)					
1 study (Greaves 2004)	10	10	-	MD 10.56 lower (30.83 lower to 9.71 higher) †	LOW
Modified Tardieu scale - wrist flexors - 4 months (cycle 1) final score (Better indicated by lower values)					
1 study (Olesch 2010)	11	11	-	MD 18.5 lower (37.78 lower to 0.78 higher)*	MODERATE
Modified Tardieu (final score comparison) Wrist flexors Cycle 2 (Better indicated by lower values)					
1 study	11	11	-	MD 18.5 lower (37.78 lower to	MODERATE

(Olesch 2010)				0.78 higher)*	
Modified Tardieu(final score comparison) Wrist flexors Cycle 3 (Better indicated by lower values)					
1 study (Olesch 2010)	1129	1130	-	MD 20.9 lower (38.27 to 3.53 lower)*	HIGH
Wrist extension AROM (change from baseline) - 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
Wrist extension AROM (change from baseline) - 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
Wrist extension PROM (change from baseline) - 3 months (Better indicated by higher values)					
1 study (Fehlgins 2000)	14	15	-	MD 3.31 higher (4.7 lower to 11.32 higher †)	LOW
Wrist extension PROM (change from baseline) - 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
Palmar thumb abduction PROM (change from baseline) - 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
Palmar thumb abduction PROM (change from baseline) - 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

* Calculated by the NCC-WCH

† Data from Hoare 2010 Cochrane systematic review

Three RCTs reported outcomes relevant to reduction of spasticity and optimisation of movement in the lower limb (Ackman 2005, Kay 2004, Reddishough 2002).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin (BoNT) + physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
Modified Ashworth score (MAS) Plantar flexor spasticity (reduction in spasticity) mean change 3 months Better indicated by higher values)					
1 study (Kay 2004)	16 limbs	20 limbs	-	MD 0.2 higher (0.52 lower to 0.92 higher)*	LOW
MAS Plantar flexor spasticity (reduction in spasticity)mean change 6 months (Better indicated by					

higher values)					
1 study (Kay 2004)	16 limbs	20 limbs	-	MD 0.94 higher (0.14 to 1.74 higher)*	LOW
Ashworth score at ankle (reduction in spasticity) – mean change 3 months (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 0.3 higher	LOW
Ashworth score at ankle (reduction in spasticity) – mean change 6 months (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 0.0 lower/higher	LOW
Active dorsiflexion at ankle – mean change at 3 months (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	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	13	-	MD 3 higher	LOW
Ankle dorsiflexion (knee flexion) passive range of motion (PROM) at 3 months (mean change from baseline) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 0.5 lower	LOW
Ankle dorsiflexion (knee flexion) PROM at 6 months (mean change from baseline) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 1.5 higher	LOW
Ankle dorsiflexion (knee extension) PROM at 3 months (mean change from baseline) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 1 higher	LOW
Ankle dorsiflexion (knee extension) PROM at 6 months (mean change from baseline) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13	-	MD 1.5 higher*	LOW
Ankle dorsiflexion PROM at 3 months (mean change from baseline) (Better indicated by higher values)					
1 study (Kay 2004)	16	20	-	MD 4.5 higher (3.22 lower to 12.22 higher)*	LOW

Ankle dorsiflexion PROM at 6 months (mean change from baseline) read from graph (Better indicated by higher values)					
1 study (Kay 2004)	16	20	-	MD 1.5 lower	LOW
Right ankle dorsiflexion (knee extension) PROM at 3 months (mean change from baseline) (Better indicated by higher values)					
1 study Reddishough 2002)	11	11	-	MD 8.63 higher (2.23 to 15.03 higher)*	LOW
Right ankle dorsiflexion (knee flexion) PROM at 6 months (mean change from baseline) (Better indicated by higher values)					
1 study Reddishough 2002)	34	34	-	MD 8.53 higher (0.27 lower to 17.33 higher)*	VERY LOW
MAS Left calf mean change 6 months (Better indicated by lower values)					
1 study Reddishough 2002)	35	35	-	0.52 lower (0.89 to 0.15 lower)*	VERY LOW
MAS Left adductor mean change 6 months (Better indicated by higher values)					
1 study Reddishough 2002)	8	8	-	1.63 lower (2.53 to 0.71 lower)*	VERY LOW
MAS Right adductor mean change 6 months (Better indicated by lower values)					
1 study Reddishough 2002)	N=?44	N=?45	-	-	MODERATE
MAS Total score mean change 3 months (Better indicated by higher values)					
1 study Reddishough 2002)	18	18	-	2.51 lower (3.22 to 1.8 lower)	MODERATE

* Calculated by the NCC-WCH

One systematic review and one RCT reported outcomes relevant to optimisation of function in the upper limb (Hoare 2010; Olesch 2010).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	**OT only all outcomes**	**Relative (95% CI)**	**Absolute (95% CI)**	
Goal Attainment Scaling (GAS) (change from baseline) - Parent - Three 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 (change from baseline) - Parent - Four months (Better indicated by higher values)					
1 study (Greaves 2004)	10	10	-	MD 9.21 higher (1.06 to 17.36 higher) †	LOW
GAS (change from baseline) - Parent - Six 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	11	-	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	11	-	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	11	-	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	11	-	MD 7 higher (0.59 to 13.41 higher)*	MODERATE
Canadian occupational performance measure (COPM) performance (change from baseline) - Three 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 Performance (change from baseline) - Four 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 Performance (change from baseline) - Four months (cycle 1) change score (Better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 0.7 higher (0.32 lower to 1.72 higher) *	MODERATE
COPM Performance(change from baseline) Cycle 2 (Better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 0.9 higher (0.1 to 1.7 higher)*	MODERATE
COPM Performance (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 Performance(change from baseline) over whole year (Better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 0.8 higher (0.04 lower to 1.64 higher)*	MODERATE
COPM Performance (change from baseline) - Six 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
Paediatric evaluation of disability inventory (PEDI) scaled score - Functional Skills (change from baseline) - Three 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
Paediatric evaluation of disability inventory (PEDI) scaled score - Functional Skills (change from baseline) - Three months (Better indicated by higher values)					
3 studies Boyd 2004; Fehlings; Wallen 2007)	49	47	-	MD 0.6 higher (1.44 lower to 2.63 higher) †	LOW
PEDI scaled score - Functional Skills (change from baseline) - Six 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 scaled score - Caregiver assistance (change from baseline) - Three 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 scaled score - Caregiver assistance (change from baseline) - Six months (Better indicated by higher values)					
1 study (Wallen 2007)	20	17	-	MD 4.4 lower (13.38 lower to 4.58 higher) †	MODERATE
Quality of Upper Extremity Skills Test (QUEST) (change from baseline) - Parent - Three 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 (change from baseline) - Parent - Four months (Better indicated by higher values)					
1 study (Greaves	10	10	-	MD 4,42 lower (9.98 lower to	LOW

2004)				1.14 higher) †	
QUEST (change from baseline) - Parent - Six 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	11	-	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	11	-	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	11	-	MD 6.70 higher (1.58 lower to 14.98 higher) *	MODERATE

* Calculated by the NCC-WCH

† Data from Hoare 2010 Cochrane systematic review

Two studies reported outcomes relevant to optimisation of function in the lower limb (Kay 2004, Reddishough 2002).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin (BoNT) + physical therapy	**Physical therapy only**	**Relative (95% CI)**	**Absolute (95% CI)**	
Gross Motor Function Measure (GMFM) –C, D, E. Percent score mean change 3 months (Better indicated by higher values)					
1 study (Kay 2004)	16 limbs	20 limbs		MD 3.8 higher (0.5 lower to 8.1 higher)*	LOW
GMFM –C, D, E. Percent score mean change 6 months (Better indicated by higher values)					
1 study (Kay 2004)	16 limbs	20 limbs		MD 1.01 higher (1.13 lower to 3.15 higher)*	LOW
GMFM Total score mean change 3 months (Better indicated by higher values)					
1 study (Reddishough 2002)	19	19		MD 1.33 lower (5.12 lower to 2.46 higher)*	LOW
GMFM Total score mean change 6 months (Better indicated by higher values)					
1 study (Reddishough 2002	19	19		MD 0.16 higher (4.37 lower to 4.69 higher)*	LOW

GMFM Total score with aids mean change 3 months (Better indicated by higher values)					
1 study (Reddishough 2002)	7	7		MD 3.72 higher (7.56 lower to 15 higher)	LOW
GMFM Total score with aids mean change 6 months (Better indicated by higher values)					
1 study (Reddishough 2002)	24	24		MD 7.19 lower (13.64 to 0.74 lower)	LOW
Velocity (m/s) mean change 3 months (as reported, read from graph) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13		MD 0.2 higher*	LOW
Velocity (m/s) mean change 6 months (as reported, read from graph) (Better indicated by higher values)					
1 study (Ackman 2005)	12	13		MD 0.05 higher*	LOW

1 * Calculated by the NCC-WCH

2 One systematic review reported outcomes relevant to quality of life pertaining to the upper limb
3 (Hoare 2010).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	**OT only all outcomes**	**Relative (95% CI)**	**Absolute (95% CI)**	
Child health questionnaire (CHQ) - physical functioning - 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 - 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 - 3 months (Better indicated by higher values)					
3 studies (Boyd 2004; Russo 2007; Wallen 2007)	56	54	-	MD 12.98 higher (1.37 to 24.60 higher)*	MODERATE
CHQ - role emotional - 6 months (Better indicated by higher values)					
2 studies (Russo 2007; Wallen 2007)	41	39	-	MD 7.28 higher (7.73 lower to 22.29 higher)	MODERATE
CHQ - role physical - 3 months (Better indicated by higher values)					
3 studies (Boyd 2004;	56	54	-	MD 8.76 higher (3.08 lower to	MODERATE

Russo 2007; Wallen 2007)				20.61 higher)	
CHQ - role physical - 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

* Calculated by the NCC-WCH from data in Hoare 2010 Cochrane systematic review

None of the included studies reported outcomes relevant to quality of life pertaining to the lower limb.

One RCT reported outcomes relevant to acceptability and tolerability pertaining to the upper limb (Olesch 2010).

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	**OT only all outcomes**	**Relative (95% CI)**	**Absolute (95% CI)**	
Canadian occupational performance measure (COPM)Satisfaction (change from baseline) Three 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 Satisfaction (change from baseline) Four 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 Satisfaction (change from baseline) Six 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 Satisfaction (change from baseline) Cycle 1 (Better indicated by higher values)					
1 study (Olesch 2010)	11	11	-	MD 1.2 higher (0.15 to 2.25 higher)*	MODERATE
COPM Satisfaction (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 Satisfaction (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 Satisfaction(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	MODERATE

				higher)*	

* Calculated by the NCC-WCH

† Data from Hoare 2010 Cochrane systematic review

One study reported outcomes relevant to acceptability and tolerability pertaining to the lower limb (Reddishough 2002).

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	OT only all outcomes	Relative (95% CI)	Absolute (95% CI)	
Parental perception "did the parent feel that the BoNT injection had been of benefit to the child?" Three months					
1 study (Reddishough 2002)	-	-	-	-	LOW
Parental perception "did the parent feel that the BoNT injection had been of benefit to the child?" Six months					
1 study (Reddishough 2002)	-	-	-	-	LOW

None of the included studies reported outcomes relevant to adverse effects pertaining to the upper limb.

One systematic review and one RCT reported outcomes relevant to quality of life pertaining to the upper limb (Hoare 2010; Olesch 2010)

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	OT only all outcomes	Relative (95% CI)	Absolute (95% CI)	
Adverse effects					
1 study (Hoare 2010)	-	-	-	-	LOW
1 study (Olesch 2010)	11	11	-	-	LOW

Two studies reported outcomes relevant to adverse effects pertaining to the lower limb (Reddishough 2002; Ackman 2005)

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin A (BoNT A)/ Occupational therapy (OT)	OT only all outcomes	Relative (95% CI)	Absolute (95% CI)	

Parental response "did the child experience some form of complication or side effect from the BoNT?" Three months					
1 study (Reddishough 2002)	-	-	-	-	LOW
Parental response "did the child experience some form of complication or side effect from the BoNT?" Six months					
1 study (Reddishough 2002)	-	-	-	-	LOW
Parental response "did the child experience any pain in their legs following injection?" Three months					
1 study (Reddishough 2002)	-	-	-	-	LOW
Adverse effects: reported by parent					
1 study (Ackman 2005)	1/12	0/13	-	-	LOW

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 RCT identified for inclusion compared BoNT A injected into the gastrocnemius muscles every 4 months to BoNT A every 12 months to treat lower limb spasticity (Kanovsky 2009).

The study did not report any relevant outcomes pertaining to the upper limb.

Reduction of spasticity and optimisation of movement in the lower limb

Number of studies	**Number of patients**		**Effect**		**Quality**
	Botulinum neurotoxin (BoNT) / Occupational therapy (OT) every 4 months	**BoNT /OT every 12 months**	**Relative (95% CI)**	**Absolute (95% CI)**	
Worse leg ankle dorsiflexion (knee extension) PROM at 12 months (mean change from baseline) (Better indicated by lower values)					
1 study (Kanovsky 2009)	110	104	-	MD 2 higher*	LOW
Worse leg ankle dorsiflexion (knee extension) PROM at 28 months (mean change from baseline) (Better indicated by lower values)					
1 study (Kanovsky 2009)	110	104	-	MD 2.5 higher*	LOW

* Calculated by the NCC-WCH

Optimisation of function in the lower limb

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin (BoNT) 4 months	BoNT yearly	Relative (95% CI)	Absolute (95% CI)	
Gross motor function measure (GMFM)Overall score - Median change from baseline at month 28 (Better indicated by higher score)					
1 study (Kanovsky 2009)	110	104		2.7 higher	LOW
GMFM Goal total score - Median change from baseline at month 28 (Better indicated by higher score)					
1 study (Kanovsky 2009)	11	104		2.4 higher	LOW

The study did not report any relevant outcomes for quality of life or acceptability and tolerability pertaining to the lower limb.

Adverse events relating to the lower limb

Number of studies	Number of patients		Effect		Quality
	Botulinum neurotoxin (BoNT) 4 months	BoNT yearly	Relative (95% CI)	Absolute (95% CI)	
Proportion of children experiencing adverse effects at month 28					
1 study (Kanovsky 2009)	89/110 (81%)	88/104 (85%)	-	3 fewer per 100 (from 14 fewer to 6 more)*	LOW
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	4/109 (3.7%	1/103 (1%)	-	3 more per 100*	LOW

2009)					
Proportion of children experiencing pain at month 28					
1 study (Kanovsky 2009)	19/110 (17%)	22/104 (21%)	-	4 fewer per 100*	LOW

* Calculated by the NCC-WCH

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

Electrical stimulation versus palpation

One RCT (Xu 2009) that included 65 children aged 2-10 years compared the efficacy of BoNT A treatment of ankle plantar flexor spasticity administered using electrical stimulation-guided injection compared to injection guided by palpation of the spastic muscle group.

Reduction of spasticity and optimisation of movement

Number of studies	Number of patients		Effect		Quality
	Electrical stimulation (ES) and physiotherapy	Palpation and physiotherapy	Relative (95% CI)	Absolute (95% CI)	
Change in Modified Ashworth Scale at 3 months from baseline (Better indicated by lower values)					
1 study (Xu 2009)	23	22	-	MD = 0.5 (0.74 to 0.26) lower*	MODERATE
Change in passive range of movement at 3 months from baseline, degrees (Better indicated by higher values)					
1 study (Xu 2009)	23	22	-	MD = 3.8 (0.79 to 6.81) higher*	MODERATE

* Calculated by the NCC-WCH

Optimisation of movement and function

Number of studies	Number of patients		Effect		Quality
	Electrical stimulation (ES) and physiotherapy	Palpation and physiotherapy	Relative (95% CI)	Absolute (95% CI)	
Change in Gross Motor Function Measure (D and E) at 3 months from baseline (Better indicated by higher values)					
1 study (Xu 2009)	23	22	-	MD = 7.3 (5.5 to 9.10) higher*	HIGH
Change in walking velocity at 3 months from baseline, m/s (Better indicated by higher values)					
1 study (Xu 2009)	23	22	-	MD = 0.07 (0.04 to 0.10) higher*	HIGH

* Calculated by the NCC-WCH

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

Ultrasound versus electrical stimulation

One quasi-randomised controlled trial (Kwon 2010) conducted among 30 children with cerebral palsy compared the efficacy of BoNT A treatment into calf muscles administered using ultrasound-guided injection compared to electrical stimulation-guided injection.

Reduction of spasticity

Number of studies	Number of patients		Effect		Quality
	Ultrasound (US) group	Electrical simulation (ES) group	Relative (95% CI)	Absolute (95% CI)	
Change in Modified Ashworth Scale (with knee extended) at 3 months from baseline (Better indicated by lower values)					
1 study (Kwon 2010)	14	16	-	-	LOW
1 study (Kwon 2010)	14	16	-	-	LOW

Optimisation of movement and function

Number of studies	Number of patients		Effect		Quality
	Ultrasound (US) group	Electrical simulation (ES) group	Relative (95% CI)	Absolute (95% CI)	
Change in physician's rating scale (speed of gait) at 3 months from baseline, m/s (Better indicated by higher values)					
1 study (Kwon 2010)	14	16	-	-	LOW

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

Evidence statement

Botulinum toxin type A and therapy versus therapy alone

Regarding reduction of spasticity and optimisation of movement, one RCT found no significant difference between children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding reduction of spasticity in shoulder adductor muscles (modified Ashworth) at four months. (LOW) Pooled results of two RCTs found a statistically significant improvement between the children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding reduction in spasticity in the elbow flexor muscles (modified Ashworth) at 3 months (MODERATE) and 6 months (LOW). A third RCT reported no statistically significant difference in elbow flexor muscle tone (modified Tardieu) when groups were compared at 4 months. (LOW) Another RCT reported that there was no significant difference in elbow flexor tone at 4 and 12 months (after 1 and 3 cycles of treatment) although a statistically significant greater reduction was found at 9 months (after 2 cycles of treatment) in the group receiving BoNT A and therapy as compared to children who received therapy alone. (MODERATE) Pooled results of two RCTs found no statistically significant improvement between the children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding elbow extension PROM at 3 or 6 months. (LOW) Three RCTs reported outcomes for forearm pronator tone.

No significant differences between children who received treatment with BoNT A and therapy as compared to children who received therapy alone were reported at 3 months (one RCT; MODERATE) or 6 months. (one RCT; LOW). Although statistically significant greater reduction in pronator tone at 4 months was reported in the third RCT in children who received treatment with BoNT A and therapy as compared to children who received therapy alone. (LOW) Another RCT reported that there was a increase in elbow flexor tone (modified Tardieu) at 4 months (after 1 cycle of treatment) and a reduction of tone 8 months and 12 months (after 2 and 3 cycles of treatment) in the group receiving BoNT A and therapy as compared to children who received therapy alone, although the statistical significance of these findings is not clear. (LOW) One RCT found no significant difference between children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding improvement in supination active range of movement in the forearm pronators at three or six months.(MODERATE) Pooled results from two RCTs found no significant difference between children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding improvement in forearm supination passive range of movement at three or six months. (LOW) Pooled results from two RCTs found a significant difference between children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding reduction of spasticity in the wrist flexor muscle (modified Ashworth) at 3 months (MODERATE) and 6 months (LOW) favouring the group receiving BoNT A and occupational therapy. However another RCT found no significant difference between children who received treatment with BoNT A and therapy as compared to children who received therapy alone regarding reduction of spasticity in the wrist flexor muscle (modified Ashworth) at 4 months. (LOW) Two RCTs assessed wrist flexor tone using the modified Tardieu scale. Both studies found no significant differences in effect at 4 months. (LOW to MODERATE) One of the RCTs found no significant differences in wrist flexor tone at 8 months (after 2 cycles of treatment). (MODERATE) However, at 12 months (after 3 cycles of treatment) tone in wrist flexors was statistically significantly reduced in the children who received treatment with BoNT A and therapy as compared to children who received therapy alone (HIGH) One RCT found no significant difference between children who received treatment with BoNT A and therapy as compared to children who received occupational therapy alone regarding improvement in wrist extension active range of movement at either three or six months. (MODERATE) One RCT found no significant difference between children who received treatment with BoNT A and occupational therapy as compared to children who received occupational therapy alone regarding improvement in wrist extension passive range of movement at either three or six months. (LOW) One RCT found no significant difference between children who received treatment with BoNT A and occupational therapy as compared to children who received occupational therapy alone regarding improvement in palmar thumb abduction passive range of movement at three or six months. (LOW)

One RCT found there was no significant difference at 3 months in plantar flexor spasticity (mean modified Ashworth) between children who received treatment with BoNT A and serial casting as compared to children who received serial casting alone, (LOW) althougha statistically significant reduction in plantar flexor spasticity was reported at 6 months in children who received serial casting alone compared to children who received treatment with BoNT A and serial casting. (LOW) One RCT did not provide sufficient information to determine whether there was a statistically significant difference at 3 or 6 months in tone at the ankle (modified Ashworth score) between children who received placebo with physical therapy and to children who received treatment with BoNT A and therapy. The same RCT did not provide sufficient information to determine whether there were statistically significant differences between children who received treatment with BoNT A and therapy as compared to children who received placebo and therapy in active ankle dorsiflexion, or in passive ankle dorsiflexion with knee extended or flexed at 3 or 6 months. (LOW)

One RCT found a significant improvement in right ankle dorsiflexion (knee extension) passive range of movement at 3 months (LOW) and right ankle dorsiflexion (knee flexion) passive range of movement at 6 months (VERY LOW) favouring children who received BoNT A and therapy as compared to children who received therapy alone. The same RCT reported a statistically significant reduction in tone in the left calf (modified Ashworth) and in adductors in both legs at six months favouring the children who received treatment with BoNT A and therapy as compared to children who received therapy alone. (VERY LOW) There were no significant differences in total reduction of

spasticity (modified Ashworth) at three months between children who received treatment with BoNT A and therapy as compared to children who received therapy alone. (MODERATE)

Regarding optimisation of function, pooled data from four RCTs found a statistically significant improvement in upper limb function (Goal Attainment Scaling-parent) in children who received BoNT A and therapy as compared to the therapy group only at 3 months. (HIGH) A statistically significant improvement in upper limb function (Goal Attainment Scaling-parent) at 4 months was also reported in one RCT in children who received BoNT A and therapy compared to the therapy group only. (LOW) Pooled data from three RCTs found no significant difference in upper limb function (Goal Attainment Scaling-parent) at 6 months between children who received BoNT A and therapy as compared to the therapy group only. (MODERATE) One further RCT reported no significant differences between treatment groups in upper limb functioning (GAS-T scores) at 4, 8 or 12 months (after 1, 2 or 3 treatment cycles). A further analysis of GAS-T scores made over the whole study period of 1 year found a statistically significant improvement in children receiving BoNT and therapy compared to those receiving therapy alone. Pooled data from three RCTs found a statistically significant benefit in upper limb function (COPM Performance) at 3 months in children who received BoNT A and therapy as compared to the therapy group only. However, no significant differences in upper limb function (COPM Performance) were found between treatment groups at 4 months (one RCT; LOW) or at 6 months (pooled data from two RCTs; MODERATE). One further RCT reported a statistically significant improvement in COPM Performance scores at 8 and 12 months (after two and three treatment cycles) favouring the BoNT and therapy group compared to the therapy only group, but no significant differences between treatment groups were reported at 4 months or over the entire year-long study period (after 1 and 3 treatment cycles). (MODERATE) No significant differences were found between the BoNT and therapy group compared to the therapy only group in functional skills (PEDI scaled scores) at 3 months (three RCTs; MODERATE) or at 6 months (two RCTS). One RCT reported no significant differences in caregiver assistance (PEDI scaled score) at 3 and 6 months. (MODERATE)

One RCT found no significant differences in lower limb function (GMFM C, D, E percentage score) in children who received BoNT A and serial casting compared to children who received serial casting alone at 3 months (LOW) or at 6 months (LOW). One RCT found no significant differences in lower limb function (GMFM Total Score at 3 or 6 months when children who received treatment with BoNT A and therapy were compared to children who received therapy alone. Although GMFM Total Score (with aids) at 3 months was not significantly different between the treatment groups, there was a statistically significant improvement in the therapy only group comared to the children who also received BoNT. (LOW) One RCT provided insufficient data to establish whether then were any significant differences in walking velocity in children who received treatment with BoNT A and therapy and those who received placebo and therapy at 3 or 6 months. (LOW)

Outcomes were available for CHQ (physical, functioning and emotional roles) at 3 months (three studies; pooled data) and 6 months (two studies; pooled data). No significant differences in treatment effect were noted in any study (or for pooled results) at either time period, except in the CHQ emotional role estimation at 3 months.

Acceptability and tolerability

Upper limb

Pooled data from three RCTs found a statistically significant benefit in COPM Satisfaction scores at 3 months in children who received BoNT A and therapy as compared to the therapy group only. However, no significant differences in COPM Satisfaction scores were found between treatment groups at 4 months (one RCT; MODERATE) or at 6 months (pooled data from two RCTs; MODERATE). One further RCT reported statistically significant improvements in COPM Performance scores at 4, 8, 12 months and a full year (after one, two and three treatment cycles) favouring the BoNT and therapy group compared to the therapy only group. (MODERATE)

Lower limb

In one cross-over RCT a significant number of parents reported benefit of BoNT at both 3 and 6 months post-injection. 75.6% of parents at 3 months and 81.4% of parents at 6 months rated the benefit as good, very good or excellent (LOW). 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)

Adverse effects

Upper limb

Four children were reported to have experienced a serious adverse event requiring hospitalisation (Russo 2007). 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 injection site, respiratory infections, headache, fainting episodes (on a hot day), anxiety, depression (past history), alopecia and fatigue. (LOW)

Lower limb

In one cross-over RCT there were 10 reports of adverse affects in total over the 6 month periods which occurred following BoNT treatment. These included a degree of incontinence, short term muscle weakness and less specific complaints. 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. In one cross-over RCT there were 11 reports of leg pain following BoNT injection in total over the 6 month treatment periods. (LOW)

No evidence was identified for reduction of pain.

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

Regarding reduction of spasticity and optimisation of movement, one RCT found no statistically significant differences in ankle dorsiflexion (knee extension) PROM at 12 or 28 months when four monthly BoNT A treatment was compared to annual BoNT A treatment (LOW)

Regarding optimisation of function, one RCT found no statistically significant differences in GMFM overall scores or GMFM goal total scores when four monthly BoNT treatment was compared to annual BoNT treatment (LOW)

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

Adverse events were reported in 81% of the four monthly treatment group and in 85% of the yearly group (LOW). There were no significant differences for any adverse event occurrences when the groups were compared (LOW) except for convulsions (LOW) where significantly more convulsions were experienced in the annually treated group than the 4 monthly treated group. However, this was not considered to be relevant to treatment by the authors. Neutralising antibodies were present in two patients at baseline and developed in a further five patients by the end of the 28month follow up. Four of these patients were in the 4 monthly treatment group (not statistically significant). (LOW) There were no significant differences in the number of children reporting pain as an adverse effect when 4 monthly treatments were compared to annual treatment. (LOW)

No evidence was found for reduction of pain.

Electrical stimulation versus palpation

Regarding reduction of spasticity, there was evidence from one randomised controlled trial of a statistically significant reduction in spasticity (modified Ashworth scale) 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) There was also a statistically significant improvement in passive range of movement 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 movement and function, there was evidence from one randomised controlled trial of a statistically significant increase in, gross motor function and walking velocity 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 found for quality of life, acceptability and tolerability, adverse events or reduction of pain.

Ultrasound versus electrical stimulation

Regarding reduction of spasticity, there was evidence from one quasi-randomised controlled trial of no significant difference reduction in spasticity with knee flexed or extended (modified Ashworth scale) in children who received BoNT A administered using ultrasound-guided injection and physical therapy as compared to children who received BoNT A administered using electrical stimulation-guided injection and physical therapy. (LOW)

Regarding optimisation of movement and function, there was evidence from one quasi-randomised controlled trial of significant improvement in gait speed (m/s) in children who received BoNT A administered using ultrasound-guided injection and physical therapy as compared to children who received BoNT A administered using electrical stimulation-guided injection and physical therapy. (LOW)

No evidence was found 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

A cost analysis was carried out based on descriptions of the BoNT services at Leeds and GOSH (see appendix). The initial analysis showed assessment of the patient by a multidisciplinary team, after presentation to the GDG they agreed this would not happen and assessment would be carried out by a consultant. An NHS reference cost was used for the actual injection as BoNT is a high cost drug. The reference cost for 2008-9 was £417. There is also a specialist uplift to tariffs for children of 78%, if this is applied then the cost increases to £742. This reference cost will include all costs related to the procedure, the day case admission, drug costs, and staff. It was assumed that the assessment and follow-up would be an additional cost.

The analysis presented a baseline cost for a patient having two sets of injections in a year with only one follow-up assessment, £1,860 per patient. The costs would increase if more repeat injections were given in a year, and with the increased likelihood of adverse events.

Of course it is important to consider the costs alongside the benefits of treatment. The evidence for this 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 by using the NICE cost-effectiveness threshold to show what levels of effectiveness a group of patients would need to see in terms of pain or discomfort, improvements with self care, improvements performing their usual activities, or conversely prevention of deterioration with self care or usual activities. Although no cost-effectiveness results could be reported for this question the analysis presented a framework to allow the GDG to make decisions on when they should consider BoNT injections were beneficial enough to recommend.

Casting after BoNT injections

The GDG commented on casting after BoNT injections, which was reviewed as part of the therapy question (question 1). There was limited evidence of low quality which reported a statistically significant reduction in spasticity in children who received casting immediately after BoNT injections as opposed to those who received casting 4 weeks after BoNT injection. Although, 50% of children who had the cast immediately after injection complained of pain and required a change of cast within 48 hours.

The evidence for casting compared to no casting reported no statistically significant difference in walking speed between groups. A statistically significant improvement in passive range of motion 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 based on the evidence available. There is considerable uncertainty around its effectiveness compared to no casting. If casting is found to be effective, then timing of casting is another question which has resource implications. If an additional appointment is needed for a cast done at a later date than the injections, but also if casts done immediately after injection frequently need to be replaced due to pain. Further research on these questions is needed which also consider resource use.

Evidence to recommendations

Relative value placed on the outcomes considered

The GDG believed that the pharmacological activity of botulinum toxin was unlikely to extend beyond 4 months, and for that reason they were primarily interested in examining outcomes measured within that time interval. Outcomes beyond this time were also investigated however, to examine any potential carryover effect.

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

Patient important outcomes including estimates of acceptability/tolerability and pain reduction were prioritised as the invasive nature of BoNT treatment may not be acceptable for all CYP if functional gains are not significant. This in turn can lead to lack of motivation to participate in treatment and therapy.

Goal attainment scales which are individual to the circumstance of individual child are more likely to detect a significant effect than other scores and thus were prioritized by the GDG.

There are some adverse effects that particularly pertain to BoNT treatment and a few deaths after treatment have been reported. Therefore the GDG were particularly interested in breathing and swallowing difficulties when injections are given in the shoulder or neck. Despite these being rare, with none reported in the evidence reviewed, the GDG felt it important to highlight these potentially life-threatening adverse effects in the recommendations. Great care needs to be taken with any treatment in a child where that child needs some spasticity to function as too much weakness can result (too big an effect) leading 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 considered that the potential positive benefits of a reduction of spasticity, optimisation of movement and function, improved ease of care, reduction in pain and improvement in quality of life would only render treatment appropriate if side effects were not serious and rarely encountered, and if treatment was acceptable to the child and caregivers.

BoNT should not be given in isolation but should be given along with either physical or occupational therapy as it has been demonstrated that it can reduce spasticity and therefore physical therapy may be facilitated

The GDG took account of the complexities of evidence and interpretation when considering the clinical significance of trial results. It was noted that no significant benefit was observed in relation to various outcomes in many of the studies. Nevertheless, there were several reports of potential significance supporting the efficacy 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 botulinum toxin can reduce spasticity in the elbow and wrist flexor muscles, and in the forearm pronators. Most of the trials excluded children with significant contractures. That is, they 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 therapy alone. One of the RCTs included in the Hoare 2010 review did examine supination and wrist AROM but there were no significant differences between the treatment groups at either 3 or 6 months.

Lower limb

Regarding the trials of, The quality of the evidence from the three trials examining botulinum toxin for the lower limb was low or very low. One trial reported an greater improvement in plantar flexor tone at 6 months with serial casting when compared to the combination of serial casting and BoNT. One small crossover 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 is likely to be selective reporting of outcomes with these results. The available trials did not therefore provide compelling evidence for a reduction in muscle tone with BoNT.

Optimisation of function

Upper Limb

There was evidence of functional benefit associated with botulinum toxin treatment for the upper limb, from a meta-analysis of four trials and from 2 separate trials reporting statistically significant improvement in Goal Assessment Scaling at 3 and 4 months (following one BoNT treatment), as expected, but no carryover effect was seen at 6 months when the pharmacological effect of the toxin has ceased. Improvement with addition of BoNT was also seen in one RCT at one year (following 3 cycles of treatment with BoNT) compared to therapy alone. A meta-analysis of three trials reported significant improvement (compared to therapy alone) in COPM Performance at 3 months and one trial reported this benefit at 8 and 12 months (following 2 and 3 cycles of treatment). However, there were no significant differences between the treatment groups in meta-analysis and single trial analysis of PEDI scores, although a meta analysis of QUEST scores showed significant improvement with BoNT treatment at 3 months only.

Lower limb

Evidence in the lower limb is of low quality and is based on GMFM scores and walking speed. There was little evidence from 2 trials of improved functioning (higher GMFM score) when BoNT was administered in addition to therapy or serial casting. The GDG believe that the varied approaches adopted to reporting of the GMFM (for example varied subscore,) 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 a clinically important significant difference to the child

Quality of Life

There is little evidence that injections have a significant effect on QoL. 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 tool that were examined. The only supportive evidence for benefit from botulinum toxin therapy in the lower limb comes from a single cross-over randomised control trial, 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 botulinum toxin treatment for the upper limb measured using the COPM Satisfaction assessment tool, This was from a meta-analysis of 3 trials (at 3 months, although no carryover effect was seen at 4 or 6 months when the pharmacological effect of the toxin has ceased) and from another trial that reported statistically significant improvement in Goal Assessment Scaling at 4, 8 and 12 months and one year (following 1,2 and 3 cycles of BoNT treatment), These findings were the most consistent evidence of benefit of additional BoNT use of all the outcomes examined in this review and may suggest that sustained improvement requires a repeated cycles of a programme of combining toxin and therapy

Lower limb

In one RCT examining the lower limb, parents felt that botulinum toxin was of benefit 3 and 6 months after injection therapy. No other evidence was available

Adverse effects

There were 4 serious adverse events (requiring hospitalisation) reported in one upper limb RCT within the Hoare 2010 meta-analysis. These were all in children who were known to have other co-existing medical conditions. Severe adverse events of concern, but not reported in the evidence reviewed, include swallowing and breathing difficulties following injection around the shoulder, neck and thorax. The GDG considered that children and young people and their parents and carers should be informed of these serious side-effects, how to recognise them, and what action to take should complications occur. Other reported adverse effects included short term muscle weakness and less specific complaints.

In the lower limb, adverse events were reported in 2 studies These included pain post injection, increased frequency of falls, incontinence, short term muscle weakness and less specific complaints. The GDG felt that these side effects are important to note when taking consent for the procedure, but are infrequently reported and usually short lived.

On balance, the GDG believed that the positive effects of BoNT A do outweigh the possible side effects as long as careful multidisciplinary individualised assessment is carried out and close monitoring of outcomes is maintained. The GDG felt that it was important for careful assessment of the effects of injections to be performed, especially into new muscle groups, which would be best carried out during the peak pharmacological effect at six to 12 weeks post injection. In light of the variable assessment techniques and their interpretations the GDG felt that reassessment should be carried out by the same clinician who initially assessed the individual. However, the group appreciated that this is not always possible due to service constraints but advocated careful documentation of assessment findings to allow comparison where possible. It is at this point that a decision on effectiveness may be made and future management plans formulated. For repeat injections it may be more practical to reassess at the point of reinjection providing subjective reports from parents are deemed reliable and the subjective and objective opinion of the child's lead therapist is provided.

From their experience the GDG considered that BoNT A was more likely to be beneficial if there was careful consideration given to patient selection. They believed that its use should be considered in children and young people in whom 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. It was felt that alleviation of spasticity could potentially assist in the application of other treatments, including physiotherapy, occupational therapy and the use of orthoses. The GDG was aware that none of the available trials had found evidence that BoNT A therapy could alleviate the pain associated with spasticity. Nevertheless, the GDG believed that a trial of BoNT A should be considered where focal spasticity was associated with significant pain, discomfort or abnormal postures. In some children the restrictions of movement and abnormal postures associated with spasticity can compromise care and lead to difficulties with skin hygiene. In selected cases BoNT A might potentially alleviate these difficulties. Postural difficulties associated with spasticity are sometimes a source of upset and embarrassment to children and young people, and in such cases alleviation of these cosmetic concerns could be an indication for BoNT A therapy.

Due to the invasive nature of treatment and the potential side effects it is important that the assessment, decision to treat and the administration of the BoNT A should be performed by a team with experience in child neurology, development and musculoskeletal assessment. The key components of a successful BoNT A programme are choosing the right child, choosing the right muscle, accurate placement of injection, and choosing the right concomitant therapy. The line between positive and negative effects with treatment is very fine and careful consideration of all influencing variables is essential.

Frequency of injections

With regard to frequency of injections, the evidence was limited to two studies and demonstrated a significant improvement in upper limb tone after four monthly injections with OT compared to OT alone but this did not continue after the next treatment cycle at 12 months. The six monthly injection cycles showed a significant improvement across a number of measures at both six months and 12 months. Neither group reported serious side effects related to treatment. In the lower limb studies neither four monthly or 12 monthly treatment cycles resulted in significant improvement in the outcome measures used and side effect frequency was similar for both groups. However, the identification of neutralising antibodies in four children in the four monthly injection cycle group may be worth consideration when planning treatment cycles and care pathways for BoNT services.

In the GDG's experience, careful reassessment after injections is essential regarding decision-making for ongoing BoNT therapy. It is the GDG's opinion that children should be reassessed and reinjected if possible at the same visit to hospital to reduce the frequency of hospital visits. The evidence does not give strong recommendations on whether to reinject at four, six, or 12 months. However, the risk of developing neutralising antibodies is likely to be higher with early and frequent injections. Conversely, if the gap between reassessment and injections is 12 months, the opportunity for maintaining ROM and improving function may be diminished or lost.

Once reassessment has taken place a decision must be made as to the effect of injections. If the response was good and continues to provide benefit for the child it is the GDG's opinion that repeat injections should not be given thus reducing the risk of side effects. If the response was poor more careful consideration must be given to the reasons for this. An unsatisfactory response may be due to poor muscle identification, insufficient dose, misinterpretation of assessment at initial visit, or poor adherence to adjunctive therapies. Careful reassessment and identification of the root cause is important and careful goal planning for future BoNT is essential to ensure any repeat injections are likely to help.

Botulinum toxin type A versus botulinum toxin type B

No evidence was found in the literature to support or refute the use of BoNT A against BoNT B. With no evidence to consider 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 who received BoNT A administered using electrical muscular stimulation-guided injection as compared to children who received BoNT A administered using injection guided by palpation of the spastic muscle group. The GDG noted, however, that there was no evidence reported regarding acceptability and tolerability of the procedure. In addition, there was evidence from one quasi-randomised controlled trial of a significant improvement in walking speed in children who received BoNT A administered using ultrasound-guided injection as compared to children who received BoNT A administered using electrical muscular stimulation-guided injection. Again no evidence was reported for acceptability and tolerability of the procedure. In addition to the modest benefits reported, the GDG felt that improvements in injection site identification with use of ultrasound guidance and electrical muscular stimulation guidance may help reduce the possible systemic effects of BoNT and therefore reduce adverse effects.

Trade-off between net health benefits and resource use

Upper limb

The alternatives to BoNT A in children and young people with upper arm spasticity are continuation of therapy and intermittent use of casting and splinting. The cost-effectiveness of this will be reviewed

elsewhere in this guideline. The use of BoNT A does not necessarily diminish the need for therapy. The studies do provide an accompanying programme of tailored therapy which may be more than what the child received pre-study. The ideal situation is where the child or young person received significant long term functional benefit to diminish the need for therapy or assistance with task of daily life i.e. independence.

Net health benefits were identified in only two areas, reducing spasticity for elbow and wrist flexors and improving function as measured by GAS. The reduction in spasticity for elbow and wrist flexors lasted beyond the pharmacological activity for BoNT when combined with therapy however this combined approach has significant resource implications. The reported functional improvements were only noted at the 3 month stage and did not continue to 6 months. it may be interpreted that regular reinjection with BoNT, every 3-4 months combined with therapy would be beneficial, however the incidence of adverse effects must be carefully considered as grip weakness was often reported and may play a significant role in causing an increase in disability.

Lower limb

Net 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 six month period, which is beyond the pharmacological activity for BoNT A. Both BoNT A combined with PT and PT alone demonstrated significant improvements in function at a six month period, which may indicate the value of targeted PT with or without BoNT to improve a child's function. The GDG felt that the reduced spasticity reported and observed in clinical practice may have an impact on improving a child's activity levels and participation which is not picked up on in the available literature. When the cost analysis is taken into consideration it is felt that the use of BoNT in line with our recommendations would be cost effective and help improve a child's life significantly enough to warrant its use.

Quality of evidence

The GDG recognised that the available evidence regarding the use of BoNT A in children with spasticity was of moderate or low quality and, in many respects, complex to interpret from a clinical perspective. There was much variation in the patients studied, the goals of therapy, the mode of botulinum toxin administration and especially in the wide range of specific outcomes reported. Inevitably the outcomes between trials varied considerably.

Assessors (and in one lower limb placebo controlled study, parents) were blinded to the treatment allocation for some but not always all outcomes reported. 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 injection. However, two trials were small including 20 children or fewer, three trials included 22 – 30 children and only three trials included over 40 children. The studies of botulinum toxin for upper limb spasticity included children with hemiplegia predominantly, although other distributions were sometimes included. For use of BoNT A in lower limb spasticity five trials were available to inform the review, all of which had limitations. Two trials were small, including fewer than 40 children; two included fewer than 60 children and one included 214 children. The predominant characteristic of all the study participants was diplegia (approximately 88%) although two also included hemiplegia (8%) and two included quadriplegia (<1%). The GDG was aware that variation in response might well be observed in such diverse groups. The effectiveness of botulinum toxin might well vary in different muscle groups, and depending on the intended goal of therapy. Such individual variation might not be recognized in groups of patients with differing degrees of spasticity and patterns of involvement.

In each of the trials of treatment for the upper limb botulinum toxin was administered by multilevel injections into various muscle groups during a single therapeutic session. The GDG was concerned that if botulinum toxin was administered into relatively mildly affected muscle groups it might not be possible to detect a measurable reduction in spasticity, but this might not reflect any inherent lack of effectiveness for that muscle group. It was therefore important to be cautious in interpreting negative results for specific treatment sites. The GDG recognised the potential benefits of injection into more than one muscle but felt this was only appropriate where a clear functional goal has been identified. It

was also highlighted that it is important that maximum doses are not exceeded and that the child, young person, parent or carer understand the possible side-effects of the treatment.

The GDG noted that there was variation between trials in the dilution of botulinum toxin 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 nature, intensity and duration of physiotherapy and/or occupational therapy provided in both the treatment and comparison groups.

The included trials reported a very varied range of outcome measures – including measures of spasticity, passive and active range of movement, 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 repeated doses of BoNT A was of low quality. One RCT compared injection frequency of 4 monthly with annually for 2 years. The main outcome prioritised for this area was adverse effects, which were reported in 81% and 85% of participants respectively. These figures were felt to be very high by the GDG when compared to clinical experience in the UK and thus were not felt to represent a reason for not recommending repeated injections where clinical circumstances indicated these may be appropriate. For example if the problem that prompted original treatment returns after the original effect of therapy has worn off, or where new treatment goals are identified.

Other considerations

Epilepsy

Many children with cerebral palsy and acquired brain injuries have co-existing epilepsy which may vary in severity. Although the evidence does not suggest an adverse effect on epilepsy control with BoNT A, care should be taken, particularly if general anaesthesia or sedation is used as part of the injection process.

Disorders of nutrition and growth

Doses of BoNT A should be calculated on the child's body weight to prevent overdosage. Undernourished children may have thin muscles and so localisation techniques should be used.

Pressure sores

Skin integrity of injection sites must be assessed prior to injection and injection in close proximity to pressure sores should be avoided.

Respiratory disorders (including apnoea, airway obstruction and chronic aspiration)

BoNT A will adversely affect breathing, swallowing and speech if it spread to the muscles of the neck and diaphragm. Good injection technique is paramount particularly the closer the injection site is to the neck. Careful explanation of BoNT side effects in particular respiratory compromise must be given prior to gaining consent for the procedure. Instruction on management should such an event occur should also be given.

Feeding difficulties (including enteral tube feeding)

Careful consideration of adverse effects of shoulder muscle injections should be given to patients with swallowing difficulties.

Gastrointestinal disorders (including gastro-oesophageal reflux and constipation)

BoNT A can affect smooth muscle of the GI tract and adversely affect gut motility

Obesity

There may be difficulties in correctly injecting muscles in children and young people who are significantly overweight.

Cognitive and learning ability

Consideration should be given to administration techniques used for children with impaired cognition or those of a young age and learning ability. Methods to reduce stress and improve tolerance should

always be used. These may include the use of topical anaesthesia in most cases with additional sedation, systemic analgesia or anaesthesia for children unable or unlikely to cooperate.

Visual, hearing and speech impairments or other communication disability

Clear concise discussions utilising appropriate communication aids, regarding the purpose of treatment and expectations of the child (where applicable) should be made.

Allergies

An allergic response may cause serious harm to the individual and repeated injections should not be given when allergies to BoNT are reported.

Aminoglycosides

Aminoglycoside antibiotics may affect the function of the neuromuscular junction and the effect of BoNT may be enhanced causing greater risk of weakness of muscles involved in breathing and swallowing

Bleeding disorder or anti-coagulation

Due to the invasive nature of injections, great care must be taken if a child is known to suffer from a bleeding disorder.

Generalised spasticity

As BoNT injections are considered to be a focal treatment for spasticity, children with generalised spasticity may not benefit from its use. Care should be taken when injecting single over active muscle groups as the antagonist muscle group may be allowed to dominate and cause further abnormal posturing.

Fixed muscle contractures

BoNT does not directly affect the length of soft tissues. If contractures are present relaxation of a spastic muscle may allow adjunctive therapies to better effect muscle length i.e. serial casting and tolerance of orthoses.

Marked bony deformity

Bony deformity, especially of the lower limbs, is not directly affected by BoNT. If established, that bony deformity is negatively affecting gait and posture this is unlikely to improve with BoNT injections. Careful assessment of a child's musculoskeletal system as well as their gait is essential in determining the degree of bony deformity.

Weakness

Caution should be considered when injecting more than one muscle group for the first time in children and young people as underlying weakness may be unmasked. Careful assessment of selective muscle control and strength should be made to establish if a child is able to maintain antigravity postures once spasticity has been eliminated.

Acquired brain injury

The GDG from their own experience recognised the early onset of spasticity and dystonia following an acute head injury which often causes discomfort, abnormal postures, and difficulty with positioning and rehabilitation. The GDG believes that BoNT used early in this situation can assist in the rehabilitation process.

Recommendations

Number	Recommendation
	Botulinum toxin type A
	When to use botulinum toxin type A
65	Consider botulinum toxin type A where focal spasticity of the upper limb is: • impeding fine motor function

Number	Recommendation
	• compromising care and hygiene • causing pain • impeding tolerance of other treatments, such as orthoses • causing concerns about appearance to the child or young person.[25]
66	Consider botulinum toxin type A where focal spasticity of the lower limb is: • impeding gross motor function • compromising care and hygiene • causing pain • disturbing sleeping patterns • impeding tolerance of other treatments, such as orthoses and use of equipment to support posture • causing cosmetic concerns to the child or young person.[26]
67	Do not offer botulinum toxin type A in children and young people: • with severe muscle weakness • with a previous adverse reaction or allergy • who are currently taking aminoglycosides.

68	Consider botulinum toxin type A with caution if:
	• the child or young person has any of the following
	  ○ a bleeding disorder or is receiving anti-coagulation therapy
	  ○ generalised spasticity
	  ○ fixed muscle contractures
	  ○ marked bony deformity **or**
	• where there are concerns about the child or young person engaging with post-treatment adjunctive therapy.[27]

69	Consider using botulinum toxin type A to treat rapid-onset spasticity causing abnormal postures and soft-tissue shortening after acquired brain injury.[28]
	### Assessment
70	Local multidisciplinary child development teams and regional specialist centres involved in the assessment and administration of botulinum toxin type A should have expertise in child neurology, child development and musculoskeletal assessment in order to decide on: • the need for botulinum toxin type A • administration of botulinum toxin type A

[25] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

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Number	Recommendation
	• offering repeat injections.
71	Include movement and motor function in assessments for treatment with botulinum toxin type A and involve a paediatric physiotherapist or paediatric occupational therapist.
72	Ensure that children and young people who receive treatment with botulinum toxin type A are offered timely access to orthotic services (see recommendation 44).
	Treatment
73	Consider using ultrasound-guided injection or electrical muscular stimulation when injecting botulinum toxin type A into muscles.[29]
74	Minimise distress to the child or young person undergoing treatment with botulinum toxin type A by considering the need for the: • topical or systemic analgesia or anaesthesia • sedation.
75	Local multidisciplinary child development teams and regional specialist centres involved in the assessment and administration of botulinum toxin type A should: • monitor effectiveness of the first botulinum toxin type A injection by repeating pre-injection assessment 6-12 weeks after the injection (both assessments should preferably be performed by the same healthcare professionals) • monitor effectiveness of subsequent botulinum toxin type A injections and the need for further injections at 3–6 months.
76	If the clinical response to treatment is satisfactory review the child or young person's goals and consider repeat injections if: • the problem that prompted initial treatment returns after treatment wears off • new goals are identified.[30]
77	Inform children and young people and their parents and carers: • how to recognise serious but rare complications associated with botulinum toxin type A (swallowing difficulties and breathing difficulties) • that these complications may arise during the first week after botulinum toxin type A treatment, and • that the child or young person should return to hospital immediately if they occur.
78	Consider injecting botulinum toxin type A into more than one muscle, but ensure that: • maximum doses are not exceeded • a clear functional goal is identified • the child or young person and their parents or carers understand the

[29] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

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Number	Recommendation
	possible side effects.[31]

1

Number	Research recommendation
14 (KRR)	What is the effectiveness of botulinum toxic type A when used routinely or according to clinical need in children and young people who are in GMFCS levels 1 to 3? **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 functional 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 improving 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 in GMFCS levels 1 to 3. Further research is needed to evaluate the effectiveness of botulinum toxin type A, 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.
15	What is the 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 in GMFCS levels 1 to 3?
16	What is the effectiveness of BonT A for reducing muscle pain?
17	What is the effectiveness of BoNT A compared to BoNT B for reducing spasticity while minimising side effects?

2

[31] At the time of publication (October 2011), some botulinum toxin type A products were licensed 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, two years of age or older. Other products were licensed only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Prescribers should refer to the summaries of product characteristics when considering or offering botulinum toxin type A and, where appropriate, informed consent should be obtained and documented.

8 Intrathecal baclofen

Introduction

For many children and young people with severe spasticity, measures such as physiotherapy and oral medications may not prove adequate to alleviate their difficulties. In such circumstances treatment using a continuous infusion of intrathecal baclofen (ITB) may be a useful treatment strategy.

A natural inhibitory neurotransmitter known as gamma-aminobutyric acid (GABA) is present in the nervous system, primarily in laminae 1 to 3 of the spinal cord dorsal horn. Baclofen is a GABA agonist. Because baclofen crosses the blood–brain barrier poorly oral administration cannot readily achieve therapeutic concentration in the cerebrospinal fluid. However, administration of intrathecal baclofen 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 side effects. ITB is infused continuously using a programmable pump implanted in a subcutaneous or subfascial pocket in the abdominal wall. The pump delivers the baclofen via a catheter inserted into the intrathecal space. Before proceeding with pump implantation it is common practice to carry out an ITB test administration 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 an intrathecal baclofen test (ITB-T) help to identify those likely to benefit from continuous pump-administered intrathecal baclofen (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

In total there were 9 publications addressing one or both of the questions:

- ITB-T (two RCTs: Hoving 2007; Gilmartin 2000; two case series: Awaad 2003; Hoving 2009b)
- CITB (eight publications: Hoving 2009a, Hoving 2009b, Gilmartin 2000, Awaad 2003, Krach 2004, Motta 2008, Shilt 2008, Senaran 2007)

Evidence profiles

Intrathecal baclofen testing

Two cross-over RCTs were identified that compared Intrathecal baclofen testing (ITB-T) with placebo (Hoving 2007; Gilmartin 2000) and two case series reports were identified that reported outcomes for children who had received ITB-T (Hoving 2009b; Awaad 2003)

Three studies (Gilmartin 2000; Hoving 2007; Hoving 2009b) evaluated reduction of spasticity in the lower limb.

Number of	Number of patients	Effect	Quality

studies	Intrathecal baclofen testing (ITB-T)	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	17	-	-	VERY LOW
Ashworth scores 12 months after continuous pump-administered intrathecal baclofen (CITB) pump implantation (Better indicated by lower values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
Ashworth scores when receiving test treatment with baclofen 50 µg dose (Better indicated by lower values)					
1 study (Gilmartin 2000)	5	5	-	-	LOW
Ashworth scores when receiving test treatment with baclofen 75 µg dose					
1 study (Gilmartin 2000)	10	0	-	-	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin 2000)	42	0	-	-	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40	0	-	-	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33	0	-	-	VERY LOW

One study (Gilmartin 2000) evaluated reduction of spasticity in the upper limb.

Number of studies	Number of patients		Effect		Quality
	Intrathecal baclofen testing (ITB-T)	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)	5	0	-	-	VERY LOW
Ashworth scores 6 months after continuous pump-administered intrathecal baclofen CITB pump implantation					

1 study (Gilmartin 2000)	42	0	-	-	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40	0	-	-	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33	0	-	-	VERY LOW

One study (Awaad 2003) evaluated reduction of spasticity in the upper and lower limbs combined.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Intrathecal baclofen testing (ITB-T)	**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	0	-[5]	-	VERY LOW
Ashworth scores 12 months after CITB pump implantation					
1 study (Awaad 2003)	7	0	-	-	VERY LOW

Two studies (Hoving 2007; Hoving 2009b) reported ease of care as a component of optimisation of movement and functioning.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Intrathecal baclofen testing (ITB-T)	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Ease of care: Mean Visual Analogue Scale (VAS) 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	13	-	MD 4.20 (2.68 higher to 5.72 higher)*	HIGH
Ease of care: Mean Visual Analogue Scale (VAS) at 6 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
Ease of care: Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving	17	0	-	-	VERY LOW

2009b)					

* Calculated by the NCC-WCH

One study (Hoving 2009b) reported individually formulated problems as a component of optimisation of movement and functioning.

Number of studies	Number of patients		Effect		Quality
	Intrathecal baclofen testing (ITB-T)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Visual Analogue Scale (VAS) at 6 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW

Two studies (Hoving 2007; Hoving 2009b) reported outcomes relevant to pain.

Number of studies	Number of patients		Effect		Quality
	Intrathecal baclofen testing (ITB-T)	Placebo	Relative (95% CI)	Absolute (95% CI)	
Mean Visual Analogue Scale (VAS) 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	10	-	MD 2.2 (0.72 lower to 5.12 higher)*	LOW
Mean Visual Analogue Scale (VAS) at 6 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW

* Calculated by the NCC-WCH

Three studies (Hoving 2007; Gilmartin 2000; Awaad 2003) reported outcomes related to adverse effects and complications.

Number of studies	Number of patients		Effect		Quality
	Intrathecal baclofen	Placebo	Relative	Absolute	

	testing (ITB-T)		(95% CI)	(95% CI)	
Drug related adverse effects during ITB-T					
1 study (Hoving 2007)	8/17	0/17	-	-	MODERATE
Procedure related adverse effects during ITB-T					
1 study (Hoving 2007)	-	-	-	-	LOW
Adverse events during ITB-T					
1 study (Gilmartin 2000)	-	-	-	-	VERY LOW
1 study (Awaad 2003)	-	-	-	-	VERY LOW

Continuous pump-administered intrathecal baclofen

Only one RCT (parallel) was identified that addressed the comparison of continuous pump-administered intrathecal baclofen (CITB) therapy versus conventional care (Hoving 2009a). For this reason the GDG decided to expand their inclusion criteria to include prospective non-comparative studies for data on effectiveness on selected outcomes (ease of care, reduction of pain, need for further orthopaedic surgery, QoL and acceptability and tolerability) where little or no other evidence was available.

In total, seven studies reported in nine articles were included (one RCT (Hoving 2009a), two case-control studies (Senaran 2007; Shilt 2008) and six prospective case series (Awaad 2003; Gilmartin 2000; Hoving 2009b; Krach 2004; Motta 2008; Ramstad 2010)).

Three studies (Gilmartin 2000; Hoving 2009a; Hoving 2009b) evaluated reduction of spasticity in the lower limb.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered intrathecal baclofen therapy (CITB) and standard treatment	**Standard treatment**	**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	-	-	LOW
Ashworth scores 12 months after CITB pump implantation (better indicated by lower values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
Ashworth scores 6 months after CITB pump implantation					
1 study (Gilmartin	42	0	-	-	VERY LOW

2000)					
Ashworth scores 12 months after CITB pump implantation					
1 study (Gilmartin 2000)	40	0	-	-	VERY LOW
Ashworth scores 24 months after CITB pump implantation					
1 study (Gilmartin 2000)	33	0	-	-	VERY LOW

Three studies (Gilmartin 2000; Hoving 2009a; (Hoving 2009b) evaluated reduction of spasticity in the upper limb.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered intrathecal baclofen therapy (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	-	-	VERY LOW
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
1 study (Gilmartin 2000)	41	0	-	-	VERY LOW
1 study (Gilmartin 2000)	40	0	-	-	VERY LOW
1 study (Gilmartin 2000)	32	0	-	-	VERY LOW

One study (Awaad 2003) evaluated reduction of spasticity in the upper and lower limbs combined.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Intrathecal baclofen therapy (CITB)	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	

Ashworth scores 12 months after CITB pump implantation					
1 study (Awaad 2003)	-	0	-	-	VERY LOW

1

2 One study reported outcomes relevant to reduction of dystonia and spasms.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Overall Barry-Albright dsytonia scale (BAD) scores 12 months after CITB pump implantation (Better indicated by lower values)					
1 study (Motta 2008)	19		-	-	VERY LOW
Overall Burke-Fahn-Marsden scores 12 months after CITB pump implantation (Better indicated by lower values)					
1 study (Motta 2008)	19	0	-	-	VERY LOW

3

4 Two studies (Hoving 2009a; Hoving 2009b) reported individually formulated problems as a
5 component of optimisation of movement and functioning.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**	
Mean Visual Analogue Scale (VAS) at 6 months after pump implantation (better indicated by higher values)					
1 study Hoving 2009a)	9	8	-	-	MODERATE
Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW

6

7 Four studies (Hoving 2009a; Hoving 2009b; Awaad 2003; Ramstad 2010) reported outcomes relevant
8 to optimisation of function.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered	**Usual care**	**Relative (95% CI)**	**Absolute (95% CI)**	

	intrathecal baclofen therapy (CITB)				
Gross motor function measure (GMFM)-66 overall at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	7	5	-	-	MODERATE
GMFM-66 total score at 6 months (Ramstad 2010) (better indicated by higher values)					
1 study (Ramstad 2010)	32	0	-	-	VERY LOW
GMFM-66 general score at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12	0	-	-	VERY LOW
GMFM-66 total score at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	31	0	-	-	VERY LOW
GMFM-88 (lying and rolling) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	7	5	-	-	MODERATE
GMFM 88 (lying and rolling) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12	0	-	-[4]	VERY LOW
GMFM-88 (sitting) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	7	5	-	-	MODERATE
GMFM 88 (sitting) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12	0	-	-	VERY LOW
GMFM-88 (goal dimension) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	5	4	-	-	MODERATE
GMFM 88 (goal dimension) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	9	0	-	-	VERY LOW
Paediatric evaluation of disability inventory (PEDI) functional skills (overall score) at 6 months (better indicated by higher values)					

1 study (Hoving 2009a)		8	-	-	MODERATE
PEDI functional skills (overall score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
PEDI Functional Skills (self care score) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	28	0	-	-	VERY LOW
PEDI Functional Skills (self care score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Functional Skills (self care score) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Functional Skills (mobility) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Functional Skills (mobility) at 12 months after pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Functional Skills (mobility) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Functional Skills (social function) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Functional Skills (social function) at 12 months after pump implantation (better indicated by higher values					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Functional Skills (social function) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI caregiver assistance (overall score) at 6 months (better indicated by higher values)					

1 study (Hoving 2009a)	9	8	-	-	MODERATE
PEDI caregiver assistance (overall score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	17	0	-	-	VERY LOW
PEDI Caregiver assistance (self-care score) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	28	0	-	-	VERY LOW
PEDI (caregiver assistance (self care score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Caregiver assistance (self-care score) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Caregiver assistance (mobility score) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	28	0	-	-	VERY LOW
PEDI caregiver assistance (mobility score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Caregiver assistance (mobility score) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	27	0	-	-	VERY LOW
PEDI Caregiver assistance (social function score) at 6 months (better indicated by higher values)					
1 study (Ramstad 2010)	28	0	-	-	VERY LOW
PEDI caregiver assistance (social function score) at 12 months after pump implantation (better indicated by higher values)					
1 study (Awaad 2003)	28	0	-	-	VERY LOW
PEDI Caregiver assistance (social function score) at 18 months (better indicated by higher values)					
1 study (Ramstad 2010)	26	0	-	-	VERY LOW

1

Two studies (Hoving 2009a; Hoving 2009b) reported ease of care as a component of optimisation of functioning.

Number of studies	Number of patients		Effect		Quality
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	Usual care	Relative (95% CI)	Absolute (95% CI)	
Ease of care Mean Visual Analogue Scale (VAS) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	9	7	-	-	MODERATE
Ease of care Mean Visual Analogue Scale (VAS) at 6 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16	0	-	-	VERY LOW
Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16	0	-	-	VERY LOW

Four studies (Hoving 2009a; Hoving 2009b; Motta 2008; Ramstad 2010) reported outcomes relevant to pain.

Number of studies	Number of patients		Effect		Quality
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	Usual care	Relative (95% CI)	Absolute (95% CI)	
Pain Mean Visual Analogue Scale (VAS) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	6	6	-	-	LOW
Pain Mean Visual Analogue Scale (VAS) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	12	0	-	-	VERY LOW
Sleeping assessed using a non-validated questionnaire					
1 study (Motta 2008)	19	0	-	-	VERY LOW
Pain assessed using a non-validated questionnaire					

1 study (Motta 2008)	19	0	-	-	VERY LOW
Average frequency of awakenings during night in previous 4wks at 6 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	29	0	-	-	VERY LOW
Average frequency of awakenings during night in previous 4wks at 12 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	30	0	-	-	VERY LOW
Pain frequency when not sleeping in previous 4wks at 6 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31	0	-	-	VERY LOW
Pain frequency when not sleeping in previous 4wks at 12 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31	0	-	-	VERY LOW
Pain severity (using a scale 0-4) in previous 4wks at 6 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31	0	-	-	VERY LOW
Pain severity (using a scale 0-4) in previous 4wks at 12 months after pump implantation (better indicated by lower values)					
1 study (Ramstad 2010)	31	0	-	-	VERY LOW

Two studies (Motta 2008 and Hoving 2009b) examined outcomes of relevance to acceptability and tolerability.

Number of studies	**Number of patients**		**Effect**		**Quality**
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**	
Satisfaction with treatment assessed using a non-validated questionnaire					
1 study (Motta 2008)	19	0	-	-	LOW
Acceptability and tolerability assessed at least 12 months post implantation					

1 study (Hoving 2009b)	17	0	-	-	LOW

Two studies (Hoving 2009a; Hoving 2009b) reported outcomes relevant to quality of life.

Number of studies	Number of patients		Effect		Quality
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	Usual care	Relative (95% CI)	Absolute (95% CI)	
Child-Health Questionnaire-Parent Form (CHQ-PF50, physical summary) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	8	8	-	-	MODERATE
Child-Health Questionnaire-Parent Form (CHQ-PF50, psychosocial summary) at 6 months (better indicated by higher values)					
1 study (Hoving 2009a)	8	8	-	-	MODERATE
Child-Health Questionnaire-Parent Form (CHQ-PF50, physical summary) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16	0	-	-	VERY LOW
Child-health questionnaire-parent form (CHQ-PF50, psychosocial summary) at 12 months after pump implantation (better indicated by higher values)					
1 study (Hoving 2009b)	16	0	-	-	VERY LOW

One study (Krach 2004) reported outcomes relevant to need for further orthopaedic surgery.

Number of studies	Number of patients		Effect		Quality
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	Usual care	Relative (95% CI)	Absolute (95% CI)	
Absolute migration percentage at 12 months in children under 8 years old (better indicated by lower values)					
1 study (Krach 2004)	11 (22 hips)	0	-	-	VERY LOW
Absolute migration percentage at 12 months in children 8 to 18 years old (better indicated by lower values)					

1 study (Krach 2004)	17 (34 hips)	0	-	-	VERY LOW

Two studies (Senaran 2007; Shilt 2008) reported outcomes relevant to adverse effects and complications (scoliosis).

Number of studies	Number of patients		Effect		Quality
	Continuous pump-adminstered intrathecal baclofen therapy (CITB)	Usual care	Relative (95% CI)	Absolute (95% CI)	
Final Cobb angles (degrees) at approximately 3 years after pump insertion (better indicated by lower values)					
1 study (Shilt 2008)	50	50	-	-	VERY LOW
Final Cobb angles (degrees) at approximately 3 years after pump insertion (better indicated by lower values)					
1 study (Senaran 2007)	26	25	-	-	VERY LOW
Mean annual progression of Cobb angles (degrees) (better indicated by lower values)					
1 study (Shilt 2008)	50	50	-	-	VERY LOW

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 with CITB in patients undergoing or not undergoing ITB-T.

No clinical studies were identified that determined the accuracy of ITB-T in predicting the outcome with CITB.

Effects of bolus intrathecal baclofen given in the setting of intrathecal baclofen testing

With regards to reduction of spasticity in the lower limb, two placebo-controlled cross-over RCTs and one prospective case series provided evidence that ITB testing can induce a statistically significant reduction in spasticity (VERY LOW and LOW).

With regards to reduction of spasticity in the upper limb, one placebo-controlled cross-over RCT provided evidence that ITB testing can induce a statistically significant reduction in spasticity (VERY LOW).

With regards to reduction of spasticity in the upper and lower limbs combined, one prospective case series provided evidence that ITB testing can induce a statistically significant reduction in spasticity when compared to baseline (VERY LOW).

With regards to ease of care, one placebo-controlled cross-over RCT and one prospective case series provided evidence that ITB testing can lead to a statistically significant improvement (HIGH and VERY LOW).

With regards to individually formulated problems, one prospective case series provided evidence that ITB testing can lead to a statistically significant improvement when compared to baseline (VERY LOW).

With regards to pain, one placebo-controlled cross-over RCT reported no statistically significant difference in pain (measured using visual analogue score) in children receiving ITB-T as compared to children receiving a placebo. (LOW) One prospective case series provided evidence of a statistically significant reduction in pain at 6 and 12 months after pump implantation, when compared to baseline (VERY LOW).

With regards to complications and adverse effects, two placebo-controlled cross-over RCTs and one prospective case series provided evidence that approximately 15% of patients receiving ITB-T experienced complications, and 18% experienced adverse effects presumed to be related to baclofen, particularly lethargy (MOD to VERY LOW).

No evidence was identified in relation to the acceptability and tolerability of ITB-T for children and their families.

No evidence was identified in relation to dystonia,

No evidence was identified in relation to children with special concerns such as hydrocephalus, ventriculoperitoneal shunt or those needing medical devices such as cardiac pacemakers.

Outcome with continuous pump-administered intrathecal baclofen in patients who had a positive response to intrathecal baclofen testing

With regards 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, when compared to baseline. (all VERY LOW) One RCT reported that there was a reduction in spasticity at 6, 12 and 24 months compared to baseline, although statistical significance was not reported. (LOW)

With regards to ease of care, individually formulated problems and pain, one prospective case series provided evidence that CITB implantation can lead to a statistically significant improvement at 6 and 12 months compared to baseline (all VERY LOW).

No evidence was identified in relation to acceptability and tolerability of CITB.

Continuous pump-administered intrathecal baclofen

With regards to reduction of spasticity in the lower extremities, one RCT provided evidence of a statistically significant improvement in the change in Ashworth score at 6 months for the left hip adductors and both hip flexors, in children who received a continuous infusion of intrathecal baclofen and standard treatment, as compared to children who received standard treatment alone. The same RCT reported no statistically significant difference in the change in Ashworth score for other lower extremity muscle groups between children who received a continuous infusion of intrathecal baclofen and children who received standard treatment. (LOW) One prospective case series (follow-up to previous RCT) provided evidence of a statistically significant decrease in bilaterally assessed Ashworth scores in 9 out of 14 lower-extremity muscle groups at 12 months after commencing CITB. (VERY LOW) One other prospective case series provided evidence that, in children and adults with spasticity, average Ashworth scores in lower extremity muscle groups improved over time at 6,12 and 24 months after CITB, when compared to baseline. (VERY LOW)

With regards to reduction of spasticity in the upper extremities, one RCT provided evidence of a statistically significant improvement in the change in Ashworth score at 6 months for the right wrist flexors, in children who received a continuous infusion of intrathecal baclofen and standard treatment, compared with children who received standard treatment. The same RCT reported no statistically significant difference in the change in Ashworth score for other upper extremity muscle groups between children who received a continuous infusion of intrathecal baclofen and children who received standard treatment. (VERY LOW) One prospective case series (follow-up to previous RCT)

provided evidence of a statistically significant decrease in bilaterally assessed Ashworth scores in 5 out of 8 upper-extremity muscle groups at 12 months after commencing CITB. (VERY LOW) One other prospective case series provided evidence that average Ashworth scores in upper extremity muscles groups improved over time at 6, 12 and 24 months after CITB, when compared to baseline (VERY LOW).

With regards to reduction of spasticity in lower and upper extremities combined (average combined score), one prospective cases series provided evidence of a statistically significance decrease in Ashworth score at 12 months after commencing CITB, when compared to baseline. (VERY LOW)

With regards to reduction of dystonia, one prospective case series provided evidence of a positive effect on generalised dystonia in children with cerebral palsy and a severe degree of impairment. The study provided evidence of a statistically significant improvement in overall BAD scores at 12 months post CITB when compared to baseline. (VERY LOW) There was a statistically significant improvement in dystonia in all body regions assessed at 12 months post CITB when compared to baseline. (VERY LOW) The study also provided evidence of a significant improvement in overall BFM scores-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 patients showed a statistically significant in BFM scores regarding everyday activities. (VERY LOW)

With regards to optimisation of movement and functioning measured by individually formulated problems, one RCT provided evidence of a statistically significant improvement in individually formulated problems in children treated with a CITB pump and standard treatment, as compared to children treated with standard treatment alone. (MODERATE) One prospective case series (follow-up to previous RCT) provided evidence of a statistically significant decrease in VAS scores for both assessment points at 12 months after the start of CITB, when compared to baseline (VERY LOW).

With regards to optimisation of movement and functioning measured by GMFM, one RCT provided evidence of a statistically significant improvement in overall function in children treated with CITB pump and standard treatment, as compared to children treated with standard treatment alone. (MODERATE) However, the same study found no statistically significant difference in specific GMFM measurements such as lying and rolling, sitting and goal dimension between children treated with CITB pump and usual care, as compared to children treated with usual care alone. (MODERATE) One prospective case series (follow-up to previous RCT) found no statistically significant difference in overall function or in lying and rolling at 12 months, when compared to baseline. (VERY LOW) However, the same study found a statistically significant improvement in sitting and in goal dimension at 12 months, when compared to baseline. (VERY LOW) Another prospective case series reported a statistically significant improvement in GMFM overall function in children treated with CITB at 6 and 18 months compared to baseline. (VERY LOW)

With regards to optimisation of movement and functioning measured by PEDI functional skills scores, one RCT found no statistically significant difference in functional skills between children treated with CITB and standard treatment, as compared to children treated with standard treatment alone. (MODERATE) One prospective case series (follow-up to previous RCT) found no statistically significant difference in functional skills at 12 months, when compared to baseline. (VERY LOW) Another prospective case series found no statistically significant difference in the mobility and social function dimensions of functional skills at 12 months, when compared to baseline. (VERY LOW) However, the same study provided evidence of a statistically significant improvement in the self care dimension of functional skills at 12 months, when compared to baseline. (VERY LOW) One further prospective case series reported no statistically significant difference in the self-care and mobility dimensions of functional skills PEDI at 6 months compared to baseline, although statistically significant improvements were found at 18 months for these dimensions and for the social function dimension at both 6 and 18 months compared to baseline. (VERY LOW)

With regards to optimisation of movement and functioning measured by PEDI caregiver assistance scores, one RCT found no statistically significant difference in caregiver assistance between children treated with CITB and standard treatment, as compared to children treated with standard treatment alone. (MODERATE) One prospective case series (follow-up to 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 (at 6 and 18 months) and mobility (at 6 months) dimensions 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 20 months compared to baseline. (VERY LOW)

With regards to optimisation of movement and functioning measured by the ease of care, one RCT provided evidence of a statistically significant increase in the improvement in ease of care in children treated with CITB and standard treatment, as compared to children treated with standard treatment alone. (MODERATE) One prospective case series (follow-up to previous RCT) provided evidence of a statistically significant decrease in VAS score at 6 and 12 months, when compared to baseline, indicating improvement in ease of care. (VERY LOW)

With regards to reduction of pain, one RCT provided evidence of a statistically higher decrease in VAS score at 6 months in children treated with CITB and standard treatment, as compared to children treated with standard treatment alone. (LOW) One prospective case series (follow-up to previous RCT) provided evidence of a statistically significant decrease in VAS score at 12 months, when compared to baseline, indicating a reduction in pain. (VERY LOW) Another prospective case series of children affected by cerebral palsy and with a severe degree of impairment reported that 53% of patients/caregivers indicated both decreased pain and improved sleep at follow-up during CITB. (VERY LOW) One further prospective case series provided evidence of statistically significant decreases in the number of night awakenings, frequency of pain and severity of pain at both 6 and 18 months. (VERY LOW)

With regards to acceptability and tolerability, one prospective case series of children receiving CITB reported that 88% of children and/or their parents said that they would participate in the test treatment and implantation procedures again. (VERY LOW) One further prospective case series of children with a severe degree of impairment receiving CITB for generalised dystonia reported that 79% of parents/caregivers were satisfied with the implant and 68% said that they would have the procedure performed again. (VERY LOW)

With regards to quality of life, one RCT provided evidence of a statistically significant improvement in both the physical and psychosocial dimensions of quality of life at 6 months in children receiving CITB and standard treatment, as compared to children receiving standard treatment alone. (MODERATE) One prospective case series (follow-up to previous RCT) reported no statistically significant difference in either the physical or psychosocial dimensions of quality of life at 12 months after the start of CITB, when compared to baseline. (VERY LOW)

With regards to the need for further orthopaedic surgery, one prospective case series reported a significant difference in hip migration percentage after 12 months of CITB, when compared to baseline, in both children younger than 8 years old and in children 8 to 18 years old. (VERY LOW)

With regards to adverse events and complications, two case-control studies did not find a statistically significant effect of using a CITB pump, compared to not using a CITB pump, on the progression of scoliosis in children with spasticity. (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/operator failure (See Appendix M, Table M.2).

Evidence to recommendations

Intrathecal baclofen testing

Relative value of outcomes

In examining the evidence regarding ITB the GDG considered the outcomes that would be most clinically meaningful. The GDG wished to examine evidence that ITB can reduce spasticity. To this end they prioritised papers using Ashworth and modified Ashworth scores as these were more often used in clinical practice. However, if available, they regarded functional benefit as being of greater importance. They considered certain outcomes were likely to be particularly important. These included:

- Alleviation of pain and discomfort - some children with spasticity are prone to muscle spasms that may be distressing or painful.
- Improved mobility and motor function (optimisation of movement and function). This would also include improvement in sitting, range of movement and ease of care. In the UK, ITB is generally offered to children with severe spasticity (GMFCS IV and V) so specific outcomes in this category were prioritised by the GDG.
- Reduction of dystonia was also prioritised, as children with severe spasticity and/or dystonia have been treated with ITB
- Frequency and nature of adverse events were an important consideration both in the cost benefit analysis of the procedure and in obtaining informed consent
- Acceptability and tolerability of ITB testing also needed to be considered.

Trade-off between clinical benefits and harms

The evidence for ITB is very sparse. There is evidence from observational studies that ITB testing administered as one or more boluses can reduce spasticity. In this setting there is also evidence that test doses can reduce pain and possibly improve ‘ease of care’. There was no convincing evidence from these studies of function, or change in dystonia. Nevertheless the GDG believed that it would be important to consider these outcomes when relevant to the individual patient undergoing ITB-T.

The GDG also recognised that on occasion, where there is a high risk of adverse events, ITB-T is contraindicated, including children who have previously undergone spinal infusion although no evidence identified. The evidence from case series of children with a positive ITB-T receiving CITB indicated that sustained reductions in spasticity and in pain could be demonstrated 12 months later and improvements in “ease of care” and in “individually formulated problems” 6-12 months later. While this is not conclusive evidence for the value of ITB-T it supports the assumption that an initial response to ITB-T can be sustained over a long period.

There was no evidence from RCTs evaluating the accuracy of ITB or assessing the effectiveness of ITB-T in predicting response to CITB. However, the GDG view is that it is reasonable, based on physiological principles, to accept that this was likely to be the case. If a child either did not respond to test doses in the intended way (for example, relieving their pain) a response to CITB would be unlikely. Members of the GDG observed that seeing an immediate beneficial response to ITB-T was often helpful to parents in their decision to proceed with pump implantation for CITB. On the other hand some children might not merely fail to respond to IBT but might actually find its effects disadvantageous, and if this occurred with ITB-T it would suggest that CITB would be contra-indicated. The GDG noted that there may be specific circumstances where ITB-T was inappropriate, such as in a child who had undergone spinal fusion or who was allergic to baclofen. They considered

that on occasions ITB-T should be deferred, such as during intercurrent localised or systemic infection or if clotting is deranged.

The ideal study to determine the value of ITB-T in predicting a beneficial outcome with CITB would be a RCT in which subjects would assigned to ITB-T or no testing prior and the decision regarding CITB taken accordingly. No such studies were found on review of the literature. The GDG noted that based on physiological considerations it is believed that failure to respond to ITB-T or experiencing an adverse response would be a contraindication to CITB. Nevertheless, it was considered important to consider the available evidence in relation to ITB-T, in order to determine whether testing can actually provide evidence of responsiveness to ITB, and also to examine the outcomes reported in those receiving CITB following a positive ITB-T. Weighing up the evidence and their own clinical view, the GDG consensus was that there was benefit in children and young people being considered for treatment undergoing ITB to determine therapeutic goals and assess adverse events. However in children with allergies to baclofen, ITB is contraindicated.

Trade-off between net health benefits and resource use

The GDG suggested that provisional funding for the ITB pump should be secured before a test dose is carried out. Delays or refusal of funding for pump insertion after a positive ITB test is likely to result in further deterioration and be distressing for the child and their carers.

The GDG observed that in the studies examined, the majority of children showed a reduction in spasticity with ITB testing but despite this, a small number declined subsequent pump insertion. The group considered that ITB testing may serve a wider purpose than simply confirming responsiveness to baclofen and allows fully informed consent on the part of the child or young person and their carers.

Quality of the evidence

The reported studies frequently did use the Ashworth score as a measure of spasticity. Being an ordinal scale, averaging of scores is not methodologically correct but it was frequently done in the studies examined. Two of the three studies reviewed included adults as well as children and subgroup analysis and group demographics were often not reported. In addition, the GDG noted that studies reported varied outcomes with ITB-T so that synthesis of data was often difficult. It was common to all three studies that all patient groups comprised those with moderate to severe bilateral involvement (GMFCS level 3, 4 or 5).

The GDG noted that in the UK oral medications including baclofen are generally continued during ITB-T. One of the studies from USA reported that the investigators aimed to discontinue oral medications as part of the trial protocol - a potential source of bias in that study.

Other considerations

The GDG considered that when performing ITB-T the assessments used to measure the response need to be individualised, based on the therapeutic goals. Aims in a severely affected child (GMFCS IV and V) will usually differ from those in a more functional child When performing ITB-T formal assessment of function as well as muscle tone was considered important not only to help assess the efficacy of ITB but also to reveal evidence for any loss of function.

The GDG considered that ITB testing should include an expert pre-test assessment including where necessary an assessment of joint range of movement while the child or young person is under general anaesthetic. This is to ensure the patient's comfort and experiences minimal discomfort/distress whilst a thorough assessment of joint range is performed.

The ITB test involves performing a lumbar puncture under general anaesthesia. Patients require a brief inpatient admission to administer test boluses and to assess the response. In general the GDG believed that adverse effects associated with ITB-T would be occasional and usually minor, but nevertheless ITB-T should only be undertaken in those in whom prior assessment identified them as likely candidates to proceed on to CITB. It should first be clarified that the child is a suitable candidate for pump placement, that there is there is a real potential for that individual to benefit from ITB, and that the child, parents and carers are in principle willing to proceed with CITB subject to the ITB-T being positive.

The GDG considered the type of information that should be offered to families when considering ITB testing. Up to date information should be offered on what testing involves, its value in predicting outcomes (positive and adverse), and possible adverse effects of testing. This information should be provided verbally and in writing. Once it has been decided to proceed with CITB, additional information needs to be given to families, providing detailed information on what is involved, the need for follow-up care, pump maintenance and risks associated with the procedure. The GDG considered, given the complexity of the issues and the fact that CITB is an invasive procedure with potential benefits but also significant risks that the information should be provided in written form as well as being discussed verbally.

The GDG view was that assessment of response to testing should be based on standardised outcomes as well as individual goals. Specific observations of changes in muscle tone, muscle pain, posture and function are required, as well as assessment of pain, self care and ease of care from the child and families' point of view. The use of standardised questionnaires and self-assessments can be useful in obtaining responses from families and the children and young people themselves. Specifically the GDG recommended that the response to ITB testing be undertaken using standardised outcome measures and taking account of individualised goals and that the assessment should examine changes in muscle tone (for example, using the Ashworth scale), pain or muscle spasms, posture and function, including head control and the effect on ease of care

The GDG consensus was that ITB testing (including pre-test and post-test assessment) needs to be carried out by an experienced multidisciplinary team in an in-patient setting given the complexity of the decision-making and assessment, and to meet safety requirements. The test itself includes a pre-test assessment which needs to be carried out by a member of the multidisciplinary team. This assessment includes an assessment of joint range movement which needs to be undertaken under general anaesthesia. The test doses of intrathecal baclofen also need to be administered under general anaesthesia. More than one bolus of baclofen can be administered, determined by expert clinical opinion.

Continuous pump-administered intrathecal baclofen

Relative value placed on the outcomes considered

The GDG prioritised those studies that used Ashworth and modified Ashworth scores to assess muscle tone. The following clinical outcomes were considered important: alleviation of pain and discomfort; improved mobility and motor function, including improved sitting, range of movement and ease of care; reduction of dystonia; frequency and nature of adverse events; acceptability and tolerability of CITB. Finally, the GDG wished to consider evidence on the possible effects of CITB on the risk of orthopaedic complications such as hip dislocation, scoliosis and the need for orthopaedic surgery.

Trade-off between clinical benefits and harms

One prospective case series indicated that compared with baseline the hip migration index was improved after 12 months of CIBT.

The GDG noted that there was just one RCT that examined the efficacy of CITB in children and young people with spasticity. This was a small study with just 17 participants with diplegia or tetraplegia. Following ITB-T 8 commenced CITB and they were compared with the remaining 9 who began CITB 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 commencing CITB, reduced muscle tone was documented in muscles affecting hip and wrist but other muscle groups were not significantly altered. The CITB group were 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, reported 'ease of care' and quality of life. It did not show evidence of better functional outcomes based on total PEDI score.

Although this RCT reported various clinically important benefits with CIBT, the GDG noted that the number of subjects in this trial was very small (n=17), the study was inevitably an open-label design (the study investigators and participants were not blinded to which children were in each treatment arm), and the GDG viewed it important to consider outcomes beyond the 6 month time point in the trial. Moreover, they 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 they chose to also consider the reports from non-controlled studies. There were 8 prospective studies, (generally with fewer than 50 subjects) in which change from baseline were reported.

The GDG noted that several prospective case series reported improved muscle tone in the upper and lower limbs at 12 and/or 24 months after commencing CIBT. One of these case series showed that CITB also had a positive effect on generalized dystonia in children with CP. Some prospective case series also found improvement in 'individually formulated problems', GMFM score (overall or in relation to specific motor skills), and reported 'ease of care'. Two reported that at 12 months there was a reduction of pain or discomfort compared with baseline. Almost 90 percent of parents in one series 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 insertion. They further noted that in one small prospective case study of hip migration post CITB pump insertion, there was only a 12 month follow up period. Furthermore a 5% alteration in migration index was reported as significant, which the GDG questioned as clinically meaningful given the method of measurement. The GDG view was 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 there have been technical advances and refinements in surgical techniques and in pump and catheter design, so that the risks described in past series are unlikely to reflect the current experience. They also noted the high level of satisfaction reported by parents even in past studies.

While recognising the limitations of the available evidence, the GDG concluded that CITB had potential to alleviate spasticity and to produce clinically important change. Evidence from the RCT supported by the reports from case series, indicated that CITB could reduce muscle tone and produce clinical benefits with respect to various clinical problems and goals. Members of the GDG with experience of using ITB were also persuaded that in properly selected patients, it could produce important benefits.

The GDG recognised that there were potential risks associated with the ITB pump but that with proper patient selection these risks would be acceptable. They therefore recommended that consideration be given to using CITB if despite the use of appropriate non-invasive treatment, a child or young person had unacceptable difficulties associated with spasticity. In particular it was appropriate to consider CITB in those with pain and/or severe muscle spasms due to spasticity and in those in whom relief of spasticity was expected to significantly improve posture or function including 'ease of care'.

The GDG noted the strongest evidence for improvement in quality of life was in severely limited children (GMFCSV). This observation, in the opinion of the GDG, does not preclude more functional children (GMFCS levels 3, 4 or or 5) from insertion of pump if they have a positive response to an ITB test dose, where benefits should outweigh possible harm.

Trade-off between net health benefits and resource use

No evidence was identified to support an economic analysis of CITB. The GDG concluded that cost-effectiveness evidence is uncertain due to limited evidence of effectiveness and improved quality of life. They questioned whether this may largely be a reflection of the difficulties in capturing meaningful change in this group of children who have not responded to other therapeutic interventions and have moderate to severe symptoms of spasticity. They noted the high degree of child/ caregiver satisfaction with the procedure and evidence of reduced pain, following pump implantation.

The GDG considered whether there successful CITB 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 cost-effectiveness of CITB overall. Need for orthopaedic intervention could also be an indirect measure of improved quality of life.

Other considerations

The GDG considered that CITB was a major intervention that would not be justified in the absence of significant clinical difficulties. Based on the knowledge and experience of GDG members and on the evidence available, the GDG considered that those in whom CITB might be considered would be children with bilateral spasticity, typically affecting both upper and lower limbs and moderate to severe motor functional problems (GMFCS level 3 to 5). Children and young people with moderate to severe motor may also benefit from CITB. They were aware that reducing spasticity could have adverse consequences, in that in some individuals spasticity actually supports function. This needed to be born in mind, and is an important reason for performing ITB-T before proceeding with pump placement.

The GDG considered that it was essential that CITB be commenced only after determining the specific goals of treatment. They recommended that when considering CITB therapy, the intended goals of therapy also be agreed with parents or carers and where appropriate with children and young people. The opinion of the GDG is that treatment should commence within 3 months of satisfactory ITB testing. This should be measured by reduction in spasticity, dystonia, pain, muscle spasms and improved ease of care.

The GDG considered that it would be essential when considering the possibility of CITB, to take account of various factors. The child would need to be large enough so that the CITB pump could be comfortably accommodated. The age at which a pump could be implanted would vary and so the recommendation simply states that the child should not be too small. Intrathecal baclofen does not currently have marketing authorisation for children younger than 4 years of age. Careful consideration should be given to any medical co-existing conditions that might be relative or absolute contraindications to treatment or which might require treatment before proceeding with CITB. For example CITB would generally be contraindicated in children and young people who had undergone a spinal fusion procedure where it is considered that the technical challenges of pump implantation predispose the child to greater postoperative morbidity including infection and cerebrospinal fluid leak. The GDG believed that in addition to spasticity other relevant co-existing functional and medical conditions may influence outcome when CITB insertion is considered. These particularly include epilepsy, malnutrition, impaired bone mineralisation, pressure sores, respiratory disorders, gastrointestinal disorders (including gastro-oesophageal reflux), obesity and coagulation disorders.

The GDG view was that caution should be exercised when considering CITB in children and young people with scoliosis if the child has not yet undergone spinal infusion. In this case, the consensus view of the GDG was that the infusion pump should be inserted before performing spinal infusion. Also, if the child has undergone spinal fusion, the CITB procedure will be more difficult and may not be possible at all.

The risk of infection and delayed wound healing is increased when surgery is carried out in poorly nourished patients and so the GDG considered that where possible, pump insertion should be deferred until nutrition is improved. The GDG considered that patients with severe, chronic respiratory disorders, such as apnoea, airway obstruction and chronic aspiration with reduced lung function, might be at increased risk with CITB and considered these to be possible contra-indications.

When it has been decided to commence treatment, intrathecal baclofen should be titrated to optimise effectiveness. Assessments (both of physical outcomes and self-reported outcomes) should be repeated after changes in titration, preferably by a member of the same team that performed the ITB testing. If treatment is not judged to be working, the team caring for the child or young person should consider a gradual reduction in dose to determine whether spasticity and other symptoms change. Once the lifespan of the pump is complete, a gradual reduction of dose should be considered to allow the child or young person to decide whether to continue based on their own goals and perceived quality of life.

The GDG recognised that successful CITB was dependent on the support of parents or carers. When considering CITB it was essential that careful consideration be give to the family resources in safely supporting a child or young person on CITB. They would need to receive information and support and continuity of care provided by an experienced multi-disciplinary paediatric specialist team. The GDG

considered that support could be provided using both remote contacts (e.g. telephone contact) and face-to-face meetings and assessments.

Follow-up of those on CITB may include both remote and face-to-face meetings and assessments. Parents and carers should have opportunities for direct discussion about CITB supported by written information. They should be given appropriate information about CITB and its safe and effective management tailored to individual needs. The information should state clearly that it is dangerous to stop CITB suddenly and should not be discontinued without seeking advice from a health care professional. They should understand the intended effects of the medication, 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 was either inadequate or excessive. They should be understand the proper management of the pump, the pump settings and the signs and symptoms that might suggest pump related complications or pump failure. They should understand that there are risks associated with sudden discontinuation of CITB. They should be aware that following CITB pump implantation, regular clinic visits will be necessary for pump maintenance and refills as agreed with their specialist team.

The GDG view was that both objective validated assessment out outcome and assessment against individual goals should be undertaken for all children and young people undertaking this procedure.

Finally, the GDG believed that given the risks associated with CITB and the resource implications, the response to CITB should be assessed taking account of the intended goals and that the response should be monitored regularly to ensure that there was sustained benefit to the child. Where possible it was recommended that validated scores and questionnaires be employed to monitor goal attainment – for example regarding assessment of muscle tone, pain and/or muscle spasms, posture and/or function, and 'ease of care'.

Children and young people receiving CITB should have a consistent point of contact within a specialist paediatric multidisciplinary team undertaking the procedure. Where treatment is unsatisfactory, continued support should be offered from the local multidisciplinary team and referral for specialist support considered.

Recommendations

Number	Recommendation
	Intrathecal baclofen
	When to consider intrathecal baclofen
79 (KPI)	Consider treatment with continuous pump-administered intrathecal baclofen if, despite the use of non-invasive treatments, spasticity, with or without dystonia, is causing difficulties with any of the following: • pain or muscle spasms • posture or function • self-care (or ease of care in the case of parents or carers).[32]
80	Be aware that children and young people who benefit from continuous pump-administered intrathecal baclofen typically have: • moderate to severe motor function problems (GMFCS level 3-5) • bilateral spasticity affecting upper and lower limbs.[33]
81	When considering continuous pump-administered intrathecal baclofen, balance the benefits against the risk of reducing spasticity if that spasticity supports function (for example, by compensating for muscle weakness) which may have adverse

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Number	Recommendation
	consequences. Discuss this with the child or young person and their parents and carers.[34]
	Intrathecal baclofen testing
82	In children and young people being considered for treatment with continuous pump-administered intrathecal baclofen perform intrathecal baclofen testing to assess therapeutic effect and to check for adverse effects.[35]
83	Before starting intrathecal baclofen testing inform children and young people and their parents or carers verbally and in writing about: • what the test will entail • how the test might predict successful treatment with continuous pump-administered intrathecal baclofen and achievement of individualised goals • adverse effects of continuous pump-administered intrathecal baclofen that might be predicted by testing • adverse effects that might be associated with intrathecal baclofen testing.[36]
84	Inform children and young people and their parents or carers verbally and in writing about continuous pump-administered intrathecal baclofen. The information should include all of the following: • the surgical procedure used for implantation of the infusion pump • the need for regular hospital follow-up visits • requirements for pump maintenance • risks associated with implantation of the pump, pump-related complications, and adverse effects that might be associated with continuous pump-administered intrathecal baclofen infusion.
85	Intrathecal baclofen testing should be: • performed by a regional specialist centre that is able to carry out the necessary assessments • undertaken in an inpatient setting to ensure safety and to allow a thorough assessment of outcomes.[37]
86	Before intrathecal baclofen testing, a pre-test assessment should be performed, including where necessary, an assessment of joint range of movement while the child or young person is under general anaesthesia.
87	The test dose or doses of intrathecal baclofen should be administered using a catheter inserted under general anaesthesia.[38]
88	Assess the response to intrathecal baclofen testing using standardised outcome measures within 3-5 hours of administration or later if the effects of the general anaesthetic have not worn off.
89	Take account of individualised goals and the following criteria for a satisfactory response to intrathecal baclofen: • reduction in spasticity or dystonia

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Number	Recommendation
	• reduction in pain or muscle spasms • improved posture and function, including head control • improved self-care (or ease of care in the case of parents or carers).
90	Discuss with the child or young person and their parents or carers their subjective assessments of the response to intrathecal baclofen testing. Subjective assessments should include reports on self-care (or ease of care in the case of parents or carers). Consider using a standardised questionnaire to document their assessments.
91	Pre- and post-test assessments should be performed by the same healthcare professionals in the regional specialist centre.
	Continuous pump-administered intrathecal baclofen
92	Perform implantation of 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 89).[39]
93	Be aware of the following potential contraindications to treatment with continuous pump-administered intrathecal baclofen: • the child or young person is too small to accommodate an infusion pump • co-existing medical conditions (for example, uncontrolled epilepsy and coagulation disorders) • intercurrent infections (systemic or around operative sites) which can increase the risks associated with continuous pump-administered intrathecal baclofen temporarily • spinal fusion • malnutrition which increases the risk of post-surgical complications (including infection and delayed healing) • some respiratory conditions.
94	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 regional specialist centre.
95	Monitor the response to continuous pump-administered intrathecal baclofen. Take account of individualised goals and the criteria for a satisfactory response to intrathecal baclofen (see recommendation 89).
96	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 • about the effects of intrathecal baclofen, possible adverse effects, and symptoms and signs suggesting the dose is too low or too high • about safe and effective management of the infusion pump, including correct pump settings and the potential for pump-related complications • that it is dangerous to stop the continuous pump-administered intrathecal baclofen infusion suddenly • that the child or young person will need to attend hospital for follow-up appointments, for example to refill and reprogram the infusion pump • that continuous pump-administered intrathecal baclofen should not be stopped before seeking advice from a healthcare professional.

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Number	Recommendation
97	If the response to continuous pump-administered intrathecal baclofen is unsatisfactory (see recommendation 89) offer continued support from the local multidisciplinary care team and consider referral for specialist support.
98	In children and young people with spasticity and co-existing scoliosis exercise caution and if the child or young person: • has not yet undergone spinal fusion, implant the infusion pump before performing spinal fusion • has undergone spinal fusion be aware that the operative procedure for implantingthe pump will be more difficult technically and may not be possible.[40]
99	Titrate the dose of intrathecal baclofen after continuous pump-administered intrathecal baclofen pump implantation to optimise effectiveness and reassess the child or young person's achievement of their individualised goals.[41]
100	Repeat assessments after titration to determine the response to the new dose. The post-titration assessment should be performed by the same healthcare professionals in the regional specialist centre that performed the pre- and post-implantation assessments.
101	If treatment with continuous pump-administered intrathecal baclofen is judged to be unsatisfactory (see recommendation 89) and the infusion pump system has been confirmed to be working, consider reducing the dose gradually to determine whether spasticity and associated symptoms increase.
102	When the infusion pump is coming to the end of its lifespan, consider reducing the dose gradually to enable the child or young person to decide whether or not to have a new pump.[42]

1

Number	Research recommendation
18	What is the effectiveness of ITB testing in terms of improving functional outcomes in children and young people who are in GMFCS level 2?
19 (KRR)	What is the effectiveness of contimuours pump-administered intrathecal baclofen compared to usual care in children and young people who are in GMFCS level 4 or 5? **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 spasticity (specifically pain or muscle spasms, posture or function, or ease of care). Such children and young people will typically be in GMFCS level 4 or 5. 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,

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	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.
20	What is the effectiveness of gait analysis as an assessment tool in studies to evaluate interventions such as CITB?

1

2

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 botulinum toxin 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 patients. Functional goals for the marginal walker (gross motor function classification system [GMFCS] level 3 or 4) 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 patients in GMFCS level 5 there is a high risk of developing a spinal deformity and a 90% risk of hip displacement defined by a migration percentage of > 30%. Spinal deformity and hip displacement are potentially amenable to orthopaedic surgery. A patient in GMFCS level 5 may have a 20-degree knee contracture that does not require surgery, but correction of the same knee deformity in a GMFCS level 2 patient may be a key factor in improving that patient'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 human body after the face. Surgery to the upper limb may also benefit function and daily care (for example, lengthening the elbow flexors in a GMFCS level 5 patient may improve hygiene in the elbow crease and a wrist fusion in a patient with hemiplegia may improve hand function). Improvement in hand and wrist posture may permit a patient to use a powered wheelchair or communication device.

Children and young people with spasticity caused by non-progressive brain disorders 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 preoperative 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 denote different operations at different anatomical levels performed in one 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 have a similar post-operative evaluation.

The impact of major orthopaedic surgery or SEMLS on the patient and their family should not be underestimated. It may take up to 1 year (or more than 1 year) for a patient to gain the maximum benefit from the procedure.

A key question is whether or not this 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 who have non-progressive brain disorders causing spasticity is being able to distinguish between the 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

In total four studies were included in this review and they addressed five comparisons as follows:

- 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 (one retrospective review of case notes; Yang 2008)
- hip adductor lengthening surgery versus injection of botulinum toxin type A (BoNT-A) in children under 6 years of age with bilateral spastic cerebral palsy followed for at least 18 months (one 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 (one prospective cohort study; Gorton 2009)
- lower extremity SEMLS and intensive therapy versus multilevel BoNT injections and casting in children and young people aged 4 to 21 years with hemiplegia or diplegia with generalised joint impairments (one retrospective comparative study; Molenaers 2001)
- SEMLS and physical therapy versus physical therapy alone in 19 children aged 6-12 years with cerebral palsy and who were in GMFCS level 2 or 3 (one RCT; Thomason 2011).

Evidence profiles

Orthopaedic surgery

Tendon lengthening versus no intervention

One retrospective study that examined case notes was identified for inclusion (Yang 2008). The study did not report optimisation of movement and function. The study evaluated prevention of deterioration.

Hip Migration Percentage

Number of studies	Number of patients		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	69	-	MD 8.00 lower (10.88 lower to 5.12 lower) 4*	LOW
Mean change hip migration percentage per year (Better indicated by lower values)					

1 study (Yang 2008)	60	69	-	MD 6 lower (8.89 to 3.11 lower) 4*	LOW

Hip Migration Percentage per year – all children and by functional ability

Number of studies	Number of patients		Effect		Quality
	Soft tissue surgery – gross motor function classification system (GMFCS) I and II	Soft tissue surgery – (GMFCS) III and IV	Relative (95% CI)	Absolute (95% CI)	
Mean change hip migration percentage per year (Better indicated by lower values) – sub group analysis by functional ability					
1 study (Yang 2008)	28 legs	72 legs	-	MD 2.4 lower	VERY LOW

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

Early bony and soft tissue versus no intervention

One prospective study was included (Gorton 2009). The study evaluated optimisation of movement and function.

Optimisation of movement and function

Number of studies	Number of patients		Effect		Quality
	Bony and/or soft tissue	Standard care	Relative (95% CI)	Absolute (95% CI)	
Velocity m/s at 1 year (indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 1. 6 higher*	VERY LOW
Gross motor function measure (GMFM) - D at 1 year (Better indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 2.4 lower*	VERY LOW
GMFM - E at 1 year (Better indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 2.8 lower*	VERY LOW
GMFM – 66 at 1 year (Better indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 1.8 lower*	VERY LOW

* Calculated by the NCC-WCH

The study did not report prevention of deterioration.

Quality of life

Number of studies	Number of patients		Effect		Quality
	Early bony and/or soft tissue	No intervention	Relative (95% CI)	Absolute (95% CI)	
Pediatric quality of life inventory (Peds QL) Physical Functioning at 1 year (indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 9 higher*	VERY LOW
Peds QL Emotional Functioning at 1 year (indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 3.4 higher*	VERY LOW
Peds QL Social Functioning at 1 year (indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 5.4 higher*	VERY LOW
Peds QL School Functioning at 1 year (indicated by higher values)					
1 study (Gorton 2009)	75	75	-	MD 0.6 lower*	VERY LOW

The study did not report acceptability and tolerability or adverse effects.

Orthopaedic surgery (any procedure) versus botulinum toxin

One retrospective study was included (Yang 2008). The study did not report optimisation of movement and function. The study evaluated prevention of deterioration.

Hip migration percentage

Number of studies	Number of patients		Effect		Quality
	Soft tissue surgery	Botulinum neurotoxin (BoNT)	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	65	-	MD 1.7 lower (4.26 lower to 0.86 higher)*	VERY LOW
Mean change hip migration percentage per year - all children (Better indicated by lower values)					
1 study (Yang 2008)	60	65	-	MD 0.9 lower (2.83 lower to 1.03 higher)*	VERY LOW
Mean change hip migration percentage per year - High functioning children gross motor function classification system (GMFCS) levels 1 and 2 (Better indicated by lower values)					
1 study (Yang 2008)	28 legs	40 legs	-	MD 1 lower (3.4 lower to 1.4 higher)*	VERY LOW
Mean change hip migration percentage per year - Low functioning children GMFCS levels 3 and 4 (Better indicated by lower values)					
1 study (Yang	72 legs	90 legs	-	MD 1 lower (2.71 lower to	VERY LOW

2008)				0.71 higher)*	

* Calculated by the NCC-WCH

Single-event multilevel surgery

Single-event multilevel surgery versus physical therapy

One RCT was included (Thomason 2011). The study evaluated range of motion, optimisation of function and quality of life outcomes. 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's needs (mean 8 interventions, SD 4 interventions).

Number of studies	Number of patients		Effect		Quality
	Single event multi-level surgery (SEMLS) and therapy	Therapy alone	Relative (95% CI)	Absolute (95% CI)	
Gross motor function measure (GMFM)-66 at 12 months(Better indicated by higher values)					
1 study (Thomason 2011)	1	8	-	MD 1.3 higher*	LOW
GMFM-66 at 24 months(Better indicated by higher values)					
1 study (Thomason 2011)	11	0	-	MD 4.9 (0.98 higher to 8.7 higher)*	VERY LOW
Gillette Gait Index at 12 months (Better indicated by lower values)					
1 study (Thomason 2011)	11	8	-	MD 211 lower*	LOW
Gillette Gait Index at 24 months (Better indicated by lower values)					
1 study (Thomason 2011)	11	0	-	MD 213 lower (327 lower to 100 lower)*	LOW

* Calculated by the NCC-WCH

Quality of life

Number of studies	Number of patients		Effect		Quality
	Single event multi-level surgery (SEMLS) and therapy	Therapy alone	Relative (95% CI)	Absolute (95% CI)	
Child health questionnaire (CHQ)-PF50 physical function at 12 months(Better indicated by higher values)					
1 study (Thomason 2011)	11	8	-	MD 3 lower	LOW
CHQ-PF50 physical function at 24 months(Better indicated by higher values)					

1 study (Thomason 2011)	11	0	-	MD 22 (from 4 higher to 39 higher)	VERY LOW
CHQ-PF50 social/emotional function at 12 months (Better indicated by higher values)					
1 study (Thomason 2011)	11	8	-	MD 12 lower	LOW
CHQ-PF50 family cohesion at 12 months (Better indicated by higher values)					
1 study (Thomason 2011)	11	8	-	MD 11 higher	LOW

* Calculated by the NCC-WCH

Single-event multilevel surgery versus botulinum toxin

One retrospective study was included (Molenaers 2001). The study evaluated optimisation of movement and function.

Optimisation of movement and function

Number of studies	Number of patients		Effect		Quality
	Single event multi-level surgery (SEMLS)	Botulinum neurotoxin (BoNT)	Relative (95% CI)	Absolute (95% CI)	
Walking velocity (m/s) (Better indicated by lower values)					
1 study (Molenaers 2001)	43 limbs	43 limbs	-	MD 0.07 lower*	VERY LOW

* Calculated by the NCC-WCH

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 relation to prevention of deterioration, one retrospective review of case notes reported that hip adductor lengthening surgery in children with diplegia and quadriplegia statistically significantly decreased hip migration percentage and hip migration percentage per year compared to no treatment. (LOW) Comparing the results of high- and low-functioning children with diplegia and quadriplegia (high = GMFCS level 1 or 2; low = GMFCS level 3 or 4) within the group receiving hip adductor lengthening surgery, there was a greater reduction in hip migration percentage per year in high functioning children although it is not clear if this was a statistically significant difference. (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 versus no intervention

With relation to optimisation of movement and function, one prospective cohort study of ambulatory children with hemiplegia, diplegia and quadriplegia found no statistically significant differences in velocity, GMFM-D, GMFM-E or GMFM-66 at 12 months after lower extremity orthopaedic surgery was performed compared to standard non-surgical care (VERY LOW).

No evidence was identified relating to prevention of deterioration.

With relation to quality of life, one prospective cohort study of ambulatory children with hemiplegia, diplegia and quadriplegia reported a statistically significant increase in PedsQL Physical Functioning score at 1 year after lower extremity orthopaedic surgery compared to standard non-surgical care (LOW). There were no statistically significant differences in the Peds QL Emotional, Social or School Functioning 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 relation to prevention of deterioration, one retrospective review of case notes of children with diplegia and quadriplegia reported no statistically significant difference in hip migration percentage per year when hip adductor lengthening surgery was compared to BoNT treatment. (VERY LOW)

No statistically significant differences in hip migration percentage per year were found in a subgroup analyses of these results by the child's functioning ability (high = GMFCS level1 and 2 and low = GMFCS level 3 and 4). (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 of children with cerebral palsy and who were in GMFCS level 2 or 3 reported a greater increase in GMFM-66 scores at 12 months in children who received SEMLS and physical therapy compared to children who received physical therapy alone, although whether or not this difference was statistically significant was not reported clearly. (LOW) At 24 months, there was a statistically significant increase in GMFM-66 scores compared to baseline in the group who received SEMLS and physical therapy. The same RCT reported a statistically significant improvement in Gillette gait index scores at 12 months in children who received SEMLS and physical therapy compared to children who received physical therapy alone. (LOW) At 24 months, there was a significant increase in Gillette gait index scores compared to baseline in the group who received SEMLS and physical therapy.

With regard to quality of life, one RCT of children with cerebral palsy who were in GMFCS level 2 or 3 reported no statistically significant differences in CHQ-PF50 physical function at 12 months in children who received SEMLS and physical therapy compared to children who received physical therapy alone. (LOW) At 24 months, there was a significant increase in CHQ-PF50 physical function compared to baseline in the group who received SEMLS and physical therapy.(VERY LOW) The same RCT reported that at 12 months, CHQ-PF50 social and emotional function scores were lower and CHQ-PF50 family cohesion scores higher in children who received SEMLS and physical therapy compared to those who received physical therapy alone, although whether or not the difference was statistically significant was not reported clearly. (LOW)

Single-event multilevel surgery versus botulinum toxin

One retrospective study of children with hemiplegia or diplegia with generalised joint impairments (this term was not defined in the article) reported no statistically significant differences in pre- and post-treatment walking velocity at 12 months after treatment with multilevel BoNT injections and casting or surgery and intensive rehabilitation therapy. (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 physiotherapy
- orthopaedic surgery (any procedure) versus orthoses.
- early orthopaedic surgery versus delayed orthopaedic surgery
- SEMLS versus interval surgery
- SEMLS versus orthoses.

Health economics

There was limited evidence available to answer the review questions and the evidence identified was of poor quality and involved short-term follow-up. The GDG's experience is that surgery can 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. 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 surgery considered here.

There was not enough 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 of quality of life. Long-term outcomes should be recorded to understand fully how surgery affects different groups of children and young people according to limb involvement and severity.

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 ease of care and cosmetic aims. The 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.

The hip migration percentage (MP) is the orthopaedic standard used to evaluate hip displacement in children and young people with non-progressive brain disorders causing spasticity. 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 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 caused by non-progressive brain disorders. Orthopaedic surgery is based on rational principles of altering 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 is aware that expert surgical intervention in appropriately selected patients will lead to worthwhile clinical improvements.

It is well recognised that the likelihood of hip displacement increases with the GMFCS level and children and young people in levels 4 and 5 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 for sitting and daily activities. The GDG agreed that surgery can benefit patients who have a symptomatic hip displacement by reducing pain and improving of ease of care. Monitoring of the hip using the hip migration percentage is therefore recommended to inform clinical management of the child at risk of hip displacement. The GDG drew up a consensus list of nine indications of hip displacement, based on their clinical experience and expertise.

Clearly, the risks of surgery include the general risks of any surgical procedure. Many patients in GMFCS levels 4 and 5 have significant co-morbidities, 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).

It may take 12-24 months 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. It is, therefore, important to select patients who are 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) carefully. To assist with the assessment, it may be important to have expert input from various members of the multidisciplinary team, including particularly the surgeon, the paediatrician or paediatric neurologist, and the physiotherapist or occupational therapist.

Fixed bony deformity is not amenable to non-surgical correction. There are also limits to non-operative improvement or correction of fixed shortening of a musculotendinous unit or a joint contracture. The choice for children and young people and their families and carers may be between accepting a fixed deformity and its disadvantages or the child or young person undergoing an orthopaedic procedure to improve or correct the deformity.

Orthopaedic surgery for the complications of spasticity may be a major procedure with attendant risks of pain, haemorrhage and infection. Immediate post-operative pain after surgery in the lower limbs can be managed effectively with epidural analgesia. The risks of haemorrhage requiring blood transfusion vary and will be higher 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 blood loss of 2.8 l during posterior spinal surgery for scoliosis surgery (Tsirikos 2008).

There is a risk of non-union of bone in operations that require division and stabilisation of bone with metallic internal fixation devices. 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).

The GDG considered that the potential benefits to the child or young person from judicious surgery would outweigh potential adverse effects. Children and young people and their parents or carers should, therefore, be given appropriate information about potential side effects.

Trade-off between net health benefits and resource use

Surgery is an expensive treatment option requiring time in hospital and rehabilitation afterwards. The GDG's experience is that surgery can be beneficial in improving function including mobility, reducing pain and increasing comfort, improving cosmesis, and also preventing deterioration. The GDG considered that 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 with a non-progressive neurological condition causing spasticity 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 was unclear.

Another low quality study reported a statistically significant increase in functioning one year after lower extremity orthopaedic surgery compared to standard non-surgical care. However, this was based on evidence of very low quality.

No studies were identified comparing SEMLS with staged surgery. One RCT was identified that compared SEMLS to physical therapy alone (Thomason 2011) and reported a statistically significant improvement in the Gillette gait index at 12 months in children undergoing additional surgery. One study comparing SEMLS and rehabilitation of children with hemiplegia or diplegia was identified, 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 patients with hemiplegia, diplegia and quadriplegia and reported results from all patients together. It would have been more informative to have reported results for each of these very different clinical subgroups separately. 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 of only 12 months and the RCT (Thomason 2011) only provided pre-post treatment data for the children who had received SEMLS to 24 months. The GDG's experience was that it may 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.

Other considerations

Spinal deformity 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. The 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. Clinical recognition of the deformity before it becomes very severe should prompt an orthopaedic referral because scoliosis surgery can improve the spinal deformity and provide the secondary benefits of stable and comfortable seating and potential improvement in upper limb function. The GDG agreed that scoliosis surgery should be considered as part of the management of spinal deformity in children and young people who have who have spasticity caused by non-progressive brain disorders. There should be clinical or radiological evidence of hip displacement or spinal deformity before referral is considered.

Problems with the posture of the shoulder girdle and upper limb can limit function and reduce a child or young person's independence and ability to participate in activities. Additionally, upper limb joint contractures can cause difficulties with skin hygiene, particularly in the axilla, wrist creases and hand. The GDG view was that surgery should be considered if adverse posture, loss of range of motion, fixed muscle shortening and skeletal deformities impair upper limb function.

Adverse posture, loss of range of motion, 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 non-operative management and orthopaedic surgery may be indicated to correct fixed deformities and improve walking efficiency. The GDG therefore agreed a list of the indications for referral for an orthopaedic opinion. Also the cosmetic appearance of the upper limb should be an indication where it causes significant concern for the child or young person.

The GDG considered the role of clinical monitoring and surveillance for hip problems. Based on current practice (Horstmann 2007) and the GDG's clinical experience the following criteria were agreed for identifying children and young people in whom a hip X-ray should be performed:

- by the age of 18 months in children and young people with bilateral cerebral palsy
- in children and young people with poor prognosis for walking (total body involved) or delayed walking or using an external support for spastic diplegia.

The GDG also considered that a repeat hip X-ray should be performed every 6 months in children and young people with hip migration percentage greater than 15% or in whom hip migration percentage is increasing by more than 10% per year.

Surgery should be considered as part of a wider management programme for the child or young person. The GDG view was that before undertaking orthopaedic surgery, the risks, harms and benefits should be discussed and agreed, and that the treatment plan should include a rehabilitation programme including, physical therapy (physiotherapy and occupational therapy), orthoses, other adjunctive treatments, such as oral drugs and BonT A, inpatient care and follow-up.

Management of the displaced hip is outside the scope of this guideline, but the GDG recognised that in every child with spasticity consideration should be given to the possibility of hip displacement. The GDG recognised that this was a complication of major importance, being common and having a major impact on the child or young person and forming a significant workload for orthopaedic surgeons.

The GDG considered that delaying surgery until function has deteriorated could reduce the effectiveness of surgery. The GDG considered, therefore, that access to an orthopaedic opinion (as part of the multidisciplinary team, rather than requiring a further referral) and possible treatment should be available to children and young people who have spasticity caused by non-progressive brain disorders. Surgery should not be considered a last resort but an adjunct to other management techniques. Early involvement in the multidisciplinary team of an orthopaedic surgeon with an expertise and interest in the management of spasticity is considered important, but does not necessarily commit a child or young person to a surgical procedure.

Orthopaedic surgery should be undertaken by a team with experience of cerebral palsy and non-progressive brain injury to allow the use of appropriate perioperative pain relief, paediatric anaesthesia, access to paediatric nursing skills and therapies. Many of the children and young people will have co-morbidities (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. Decisions should be made in conjunction with members of the multidisciplinary team to ensure that planning for post-operative rehabilitation is undertaken. This should include how and where rehabilitation will take place, and the likely requirement for additional equipment and orthoses. These decisions should be made before surgery is planned.

The GDG considered that SEMLS offers potential advantages over interval surgery for children and young people undergoing gait improvement surgery because, typically, the surgery would require one hospital admission and one period of rehabilitation. Patients require a thorough preoperative assessment. Gait analysis is considered to be the pre-operative 'gold standard' when evaluating patients 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 preoperatively informs the surgical team of procedures such as tendon and muscle surgery, osteotomies and foot stabilisation that are likely to benefit the patient. A thorough pre-operative assessment will also help to identify likely requirements for post-operative rehabilitation and orthoses. Optimal recovery from gait improvement surgery may take 12-24 months and so it is important to have in place an agreed programme of rehabilitation.

Recommendations

Number	Recommendation
	Orthopaedic surgery
	Referral
103 (KPI)	Offer children and young people referral to an orthopaedic surgeon if there is clinical or radiological evidence of hip displacement or spinal deformity.
104	Consider referring a child or young person for an orthopaedic opinion if any of the following indications is present: • the posture of an upper limb is causing difficulties with putting on or taking off clothing • hand or upper limb function is limited by functionally short muscles (where spasticity prevents muscles stretching to their full length during functional tasks), pain or an unfavourable limb posture • a contracture of the shoulder, elbow, wrist or hand causes difficulty with skin crease hygiene • lower limb function is limited by functionally short muscles or an unfavourable limb posture • walking is limited by functionally short lower limb muscles, joint contracture, abnormal torsion of the femur or tibia, foot deformity, or lower limb pain • the cosmetic appearance of the upper limb causes significant concern for the child or young person.
105	Consider orthopaedic surgery as an adjunct to other interventions because timely surgery can prevent deterioration and ameliorate function.
	Monitoring
106 (KPI)	Monitor children and young people to identify displacement of the hip and spinal deformity.
107	Clinically monitor all children and young people for signs of hip migration and recognise the following as evidence of hip displacement: • abnormal hip migration percentage (more than 30%) • increasing hip migration percentage • deterioration in hip abduction • pain arising from the hip • reduced range of hip movement • increased hip muscle tone • decreased ability or tolerance for sitting or standing because of worsening hip joint contracture or bony deformity • clinically important leg length difference • increasing difficulty of perineal care or hygiene.
108	Perform a hip X-ray to monitor hip migration: • by the age of 18 months in children with bilateral cerebral palsy • in children with poor prognosis for walking (total body involved), delayed

Number	Recommendation
	walking or who are using an external support for spastic diplegia • in children or young people with signs of hip displacement (see recommendation 107).
109	Repeat the hip X-ray every 6 months in children and young people with hip migration percentage greater than 15% or in whom hip migration percentage is increasing by more than 10% per year.
	Before undertaking orthopaedic surgery
110	Before undertaking orthopaedic surgery discuss and agree with the child or young person and their parents or carers a rehabilitation programme and how and where it will be delivered. The programme may include: • inpatient care and subsequent follow-up • physical therapy • orthoses • other adjunctive treatments, such as oral drugs and botulinum toxin type A.
	Performing orthopaedic surgery
111	Orthopaedic surgery should: • be undertaken by surgeons experienced in the concepts and techniques of performing such surgery in this group of patients and • take place in a paediatric setting.
112	Aim to perform single-event multilevel orthopaedic surgery to improve gait (rather than as staged surgical episodes) informed by a thorough preoperative functional assessment, preferably including a pre-operative gait analysis and interpretation of the results by a surgical team with experience in such analyses.
	Assessment
113	Assess outcomes of gait-improvement orthopaedic surgery 1–2 years after performing the surgery. Use the same criteria for pre- and post-operative assessments.

Number	Research recommendation
21	What is the effectiveness of soft tissue surgery in terms of preventing hip dislocation?
22	What is the effectiveness of SEMLS in terms of producing benefits that continue after skeletal maturity has been achieved?

10 Selective dorsal rhizotomy

Introduction

Selective dorsal rhizotomy (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 patients 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% (ref needed). Nerve roots to be cut are from lumbar 2 (L2) 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 with SDR.

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 Gross Motor Functional Classification System (GMFCS) level 2 or 3.

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 interventional procedure guidance 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 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 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 interventional procedure guidance (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 with spasticity, with or without other motor disorders (dystonia, muscle weakness or choreoathetosis) caused by non-progressive brain disorders.

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), and 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 physiotherapy), 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 Grading of Recommendations Assessment, Development and Evaluation (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 noncomparative 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 active range of motion. 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

Three parallel randomised controlled trials (RCTs; McLaughlin 1998; Steinbok 1997; Wright 1998), two non-randomised prospective comparative studies (Buckon 2004b; Engsberg 2006) and two case series were identified for inclusion (Abbott 1992; Kim 2001).

The three RCTs compared SDR plus physical therapy to therapy alone (McLaughlin 1998; Steinbok 1997; Wright 1998). A total of 90 children and young people, all of whom had diplegia, were included in the three trials. 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). One non-randomised prospective study also compared SDR plus physical therapy to therapy alone (Engsberg 2006). Outcomes were presented for 84% (65/77) of the children with spastic diplegic cerebral palsy (GMFCS levels 1 to 3) and 40 children with no disability included in the study, The mean ages (SDs) of the children were 9.0 (5.3) years in the SDR plus physical therapy group and 9.7(4.5) years in the 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 physiotherapy were received by both groups in one RCT (Steinbok 1997). The techniques used included passive movements, strengthening and neurodevelopmental treatment (NDT). Weight-bearing exercises were emphasised in both groups. Measures were taken to maintain blinding of physiotherapists. In another RCT (Wright 1998) all children received similar types of therapy, but those who underwent SDR plus physical therapy had higher treatment intensity during their 6-week postoperative stay to improve strength in the trunk and lower extremities. The physical therapy techniques used in both groups in this RCT included range of movement (ROM), 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's needs. The emphasis and techniques used were reported to be appropriate for children undergoing SDR, and 20 different categories of treatment were documented by the treating community therapists. In the non-randomised prospective study, the SDR plus physical therapy group received 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 therapy alone group received the same number of therapy sessions. Treatment in both 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 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 children. Children 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 the modified Ashworth scale to assess tone and reported the Gross Motor Function Measure (GMFM). One RCT reported ROM, and one reported walking. No evidence was identified for goal attainment scale (GAS), PEDI (pediatric evaluation of disability inventory; a physical but not global scale), acceptability and tolerability (as reported by the child or young person or their parent or carer) or the Child Health Questionnaire (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).

Another 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 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 (3 or 4 times per week); history of prematurity; no significant ataxia, athetosis or scoliosis; good lower-extremity antigravity strength; ambulatory with or without assistive devices; and cooperative. The inclusion criteria for soft tissue surgery were kinematic dysfunction and evidence of dynamic limitation of motion 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 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 1, n = 3; level 2, n = 8; level 3, 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 1, n = 2; level 2, n = 2; level 3, n = 4). The majority of orthopaedic procedures performed were releases and lengthenings, although two children also had osteotomies. Patients received post-surgical therapy that was standard for 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.

The 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

The three RCTs identified for inclusion used the modified Ashworth scale 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). ROM was measured at 9 months (Steinbok 1997), while active and passive ROM were measured at 6 months and 12 months (Wright 1998) and active ROM was measured at 8 months and 20 months in a non-randomised prospective study (Engsberg 2006).

Number of studies	Number of patients		Effect		Quality
	Selective dorsal rhizotomy (SDR) and Therapy	Therapy only	Relative (95% CI)	Absolute (95% CI)	
Mean change in active range of motion trunk rotation at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 4 lower*	VERY LOW

Mean change in active range of motion trunk rotation at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 lower*	VERY LOW
Mean change in active range of motion pelvis rotation at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 1 lower*	VERY LOW
Mean change in active range of motion pelvis rotation at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 2 lower*	VERY LOW
Mean change in active range of motion pelvic tilt at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 2 lower*	VERY LOW
Mean change in active range of motion pelvic tilt at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 2 lower*	VERY LOW
Mean change modified Ashworth hip adductors at 9m (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 active range of motion (ROM) hip extension at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 19.6 lower*	MODERATE
Mean change in active range of motion hip flexion/extension at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 higher*	VERY LOW
Mean change in range of motion hip extension at 9m (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 active ROM hip extension at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 3.7 lower*	MODERATE
Mean change in active range of motion hip flexion/extension at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 higher*	VERY LOW
Mean change in passive ROM hip extension at 6m (Better indicated by higher values)					
1 study (Wright	12	12	-	MD = 5.5	MODERATE

1998)				higher*	
Mean change in passive ROM hip extension at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 0*	MODERATE
Mean change modified Ashworth score at knee at 6m (Better indicated by lower values)					
1 study (Wright 1998)	12	12	-	MD = 1 lower*	MODERATE
Mean change modified Ashworth at knee at 9m (Better indicated by lower values)					
1 study (Steinbok 1997)	14	14	-	MD 1 lower (1.45 to 0.55 lower)*	MODERATE
Mean modified Ashworth score at knee at 12m (Better indicated by lower values)					
1 study (Wright 1998)	12	12	-	MD = 1 lower*	MODERATE
Mean change in active ROM knee extension at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 23.6 higher*	MODERATE
Mean change in active range of motion knee flexion/extension at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 4 higher*	VERY LOW
Mean change range of motion at knee at 9m (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 active ROM knee extension at 12m (Better indicated by higher values)					
1 study (Wright 1998)	Mean change =19.5 n=12	Mean change = -7.5 n=12	-	MD = 27 higher*	MODERATE
Mean change in active range of motion knee flexion/extension at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 4 higher*	VERY LOW
Mean change in active range of motion knee flexion at initial contact at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 lower*	VERY LOW
Mean change in active range of motion knee flexion at initial contact at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 5 lower*	VERY LOW

Mean change in passive ROM knee extension at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 7.5 lower*	MODERATE
Mean change in passive ROM knee extension at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 3 higher*	MODERATE
Mean change in passive ROM popliteal angle at 6 m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 8.4 lower*	MODERATE
Mean change in passive ROM popliteal angle at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 4.7 lower*	MODERATE
Mean modified Ashworth score at ankle at 6m (Better indicated by lower values)					
1 study (Wright 1998)	12	12	-	MD = 1 lower*	MODERATE
Mean change modified Ashworth at ankle at 9m (Better indicated by lower values)					
1 study (Steinbok 1997)	14	14	-	MD 1.5 lower (2.02 to 0.98 lower)*	HIGH
Mean change modified Ashworth score at ankle at 12m (Better indicated by lower values)					
1 study (Wright 1998)	12	12	-	MD = 0.5 lower*	MODERATE
Mean change in active ROM at ankle dorsiflexion 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 16.7 higher*	MODERATE
Mean change in active range of motion ankle dorsiflexion/plantarflexion at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 1 higher*	VERY LOW
Mean change range of motion at ankle at 9m (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 active ROM ankle dorsiflexion 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 27 higher*	MODERATE
Mean change in active range of motion ankle dorsiflexion/plantarflexion at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 1 lower*	VERY LOW
Mean change in active range of motion ankle dorsiflexion/plantarflexion at initial contact at 8m (Better indicated by higher values)					

1 study (Engsberg 2006)	29	36	-	MD = 1 higher*	VERY LOW
Mean change in active range of motion ankle dorsiflexion/plantarflexion at initial contact at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 0*	VERY LOW
Mean change in extension foot progression angle at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 lower*	VERY LOW
Mean change in extension foot progression angle at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 6 lower*	VERY LOW
Mean change in passive ROM ankle dorsiflexion (KE) at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 9.7 higher*	MODERATE
Mean change in passive ROM ankle dorsiflexion (KE) at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 11.2 higher*	MODERATE
Mean change total modified Ashworth score at 6m (read from graph) (Better indicated by lower values)					
1 study (McLaughlin 1998)	21	17	-	MD = 0.85 lower*	MODERATE
Mean change total modified Ashworth score at 12m (Better indicated by lower values)					
1 study (McLaughlin 1998)	21	17	-	MD = 0.55 lower*	LOW
Mean change total modified Ashworth score at 24m (Better indicated by lower values)					
1 study (McLaughlin 1998)	Mean change = -0.88 n=21[80]	Mean change = 0 n=17[81]	-	MD = 0.88 lower*	MODERATE

* Calculated by the NCC-WCH

Optimisation of function

The 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).

Number of studies	Number of patients		Effect		Quality
	Selective dorsal	Therapy only - function	Relative	Absolute	

	rhizotomy (SDR) and Therapy		**(95% CI)**	**(95% CI)**	
Mean change Gross motor function measure (GMFM) 88 score lying and rolling at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 3.1 lower*	MODERATE
Mean change GMFM score lying and rolling at 9m (Better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD = -0.2*	MODERATE
Mean change GMFM 88 score lying and rolling at 12m (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 GMFM 88 score lying and rolling at 24m (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 GMFM 88 score sitting at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 11.7 higher*	MODERATE
Mean change GMFM score sitting at 9m (Better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD = 15 higher*	MODERATE
Mean change GMFM 88 score sitting at 12m (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 GMFM 88 score sitting at 24m (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 GMFM 88 score crawl/kneel at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 0.3 higher*	MODERATE
Mean change GMFM score crawl/kneel at 9m (Better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD = 7.7 higher*	MODERATE
Mean change GMFM 88 score crawl/kneel at 12m (Better indicated by higher values)					
2 studies	21	17	-	MD 0.1 lower	LOW

(McLaughlin 1998; Wright 1998)				(6.61 lower to 6.41 higher)*	
Mean change GMFM 88 score crawl/kneel at 24m (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 GMFM 88 score standing at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 4.2 higher*	HIGH
Mean change GMFM score standing at 9m (Better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD = 2.3 higher*	MODERATE
Mean change GMFM 88 score standing at 12m (Better indicated by higher values)					
2 studies (McLaughlin 1998; Wright 1998)	21	17	-	MD 2.6 higher (8.02 lower to 13.22 higher)*	LOW
Mean change GMFM 88 score standing at 24m (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 GMFM 88 score walk/run/jump at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 2.9 higher*	MODERATE
Mean change GMFM score walk/run/jump at 9m (Better indicated by higher values)					
1 study (Steinbok 1997)	14	14	-	MD = 6.0 higher*	MODERATE
Mean change GMFM 88 score walk/run/jump at 12m (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 GMFM 88 score walk/run/jump at 24m (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 total GMFM 88 score at 6m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 4.8 higher*	MODERATE
Mean change total GMFM score at 9m (Better indicated by higher values)					
1 study (Steinbok	14	14	-	MD 6.2 higher (2.26 to 10.14	MODERATE

1997)				higher)*	
Mean change total GMFM 88 score at 12m (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 total GMFM 88 score at 24m (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 score (%) at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 0*	VERY LOW
Mean change in GMFM score (%) at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 3 higher*	VERY LOW
Mean change in timed walk at 6mths (m/60secs) (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 3.1 lower*	MODERATE
Mean change in timed walk at 12mths (m/60secs) (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 19.4 higher*	MODERATE
Mean change in Gait speed (cm/sec) at 8m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 11 higher*	VERY LOW
Mean change velocity (m/s) gait analysis at 12m (Better indicated by higher values)					
1 study (Wright 1998)	12	12	-	MD = 0.04 lower*	MODERATE
Mean change in Gait speed (cm/sec) at 20m (Better indicated by higher values)					
1 study (Engsberg 2006)	29	36	-	MD = 18 higher*	VERY LOW
Mean change in use of assistive device gait analysis at 12m (Better indicated by lower values)					
1 study (Wright 1998)	12	12	-	MD = 0.25 higher*	MODERATE

* Calculated by the NCC-WCH

Quality of life

No studies reported quality of life.

Adverse effects

Two 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).

No studies 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 postoperative back pain, which was controlled well using an intravenous fentanyl drip for 3 days postoperatively. 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 postoperative 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 postoperative 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 postoperative 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

No studies reported 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

No studies were identified for inclusion in relation to reduction of spasticity and optimisation of movement.

Optimisation of function

Pediatric evaluation of disability inventory

Number of studies	Number of patients		Effect		Quality
	Selective dorsal rhizotomy (SDR) and Therapy	Orthopaedic surgery	Relative (95% CI)	Absolute (95% CI)	
Mean change paediatric evaluation of disability inventory (PEDI) Functional skills: self care at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.17 higher (1.93 lower to 6.27 higher)*	VERY LOW
Mean change PEDI Functional skills: self care at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.68 higher (4.36 lower to 5.72 higher)*	VERY LOW
Mean change PEDI Functional skills: self care at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 3.72 higher (1.90 lower to 9.34 higher)*	VERY LOW
Mean change PEDI Functional skills: mobility at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.91 higher (2.05 lower to 7.87 higher)*	VERY LOW
Mean change PEDI Functional skills: mobility at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 1.89 higher (3.75 lower to 7.53 higher)*	VERY LOW
Mean change PEDI Functional skills: mobility at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.17 higher (6.30 lower to 6.64 higher)*	VERY LOW
Mean change PEDI Functional skills: social at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.10 higher (10.31 lower to 10.51 higher)*	VERY LOW
Mean change PEDI Functional skills: social at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.12 higher (8.16 lower to 8.40 higher)*	VERY LOW
Mean change PEDI Functional skills: social at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.82 higher (7.41 lower to 9.05 higher)*	VERY LOW

Mean change PEDI Caregiver assistance – self care at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 1.72 higher (4.04 lower to 7.48 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – self care at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.44 lower (8.75 lower to 3.87 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – self care at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.36 higher (3.68 lower to 8.40 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – mobility at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.28 higher (2.93 lower to 7.49 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – mobility at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 6.17 higher (0.83 lower to 13.17 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – mobility at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 7.75 higher (1.81 lower to 17.31 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – social at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.32 lower (12.86 lower to 12.22 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – social at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 6.21 higher (1.94 lower to 14.36 higher)*	VERY LOW
Mean change PEDI Caregiver assistance – social at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 4.47 higher (7.34 lower to 16.28 higher)*	VERY LOW

* Calculated by the NCC-WCH

Gross motor function measure

Number of studies	**Number of patients**		**Effect**		**Quality**
	Selective dorsal rhizotomy (SDR) and Therapy	**Orthopaedic surgery**	**Relative (95% CI)**	**Absolute (95% CI)**	
Mean change gross motor function measure (GMFM) 88 score lying and rolling at 6m (Better indicated					

by higher values)					
1 study (Buckon 2004b)	18	7	-	MD = 0	VERY LOW
Mean change GMFM 88 score lying and rolling at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD = 0	VERY LOW
Mean change GMFM 88 score lying and rolling at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD = 0	VERY LOW
Mean change GMFM 88 score sitting at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 0.57 higher (1.86 lower to 3.00 higher)*	VERY LOW
Mean change GMFM 88 score sitting at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7[7]	-	MD 1.10 higher (1.55 lower to 3.75 higher)*	VERY LOW
Mean change GMFM 88 score sitting at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18[8]	7	-	MD 0.72 higher (2.21 lower to 3.65 higher)*	VERY LOW
Mean change GMFM 88 score crawl/kneel at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 4.29 higher (0.15 lower to 8.73 higher)*	VERY LOW
Mean change GMFM 88 score crawl/kneel at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.68 higher (1.99 lower to 7.35 higher)*	VERY LOW
Mean change GMFM 88 score crawl/kneel at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.99 higher (0.52 lower to 6.50 higher)*	VERY LOW
Mean change GMFM 88 score standing at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 4.87 lower (15.15 lower to 5.41 higher)*	VERY LOW
Mean change GMFM 88 score standing at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 14.38 lower (29.07 lower to 0.31 higher)*	VERY LOW
Mean change GMFM 88 score standing at 24m (Better indicated by higher values)					

1 study (Buckon 2004b)	18	7	-	MD 12.40 lower (30.68 lower to 5.88 higher)*	VERY LOW
Mean change GMFM 88 score walk/run/jump at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 5.10 higher (4.33 lower to 14.53 higher)*	VERY LOW
Mean change GMFM 88 score walk/run/jump at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 1.69 lower (10.50 lower to 7.12 higher)*	VERY LOW
Mean change GMFM 88 score walk/run/jump at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.73 higher (13.30 lower to 18.76 higher)*	VERY LOW
Mean change total GMFM 88 score at 6m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 1.02 higher (3.06 lower to 5.10 higher)*	VERY LOW
Mean change total GMFM 88 score at 12m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 2.51 lower (7.63 lower to 2.61 higher)*	VERY LOW
Mean change total GMFM 88 score at 24m (Better indicated by higher values)					
1 study (Buckon 2004b)	18	7	-	MD 1.19 lower (8.29 lower to 5.91 higher)*	VERY LOW

* Calculated by the NCC-WCH

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.

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 reported that there were no significant differences in active range of motion at 8 months or 20 months when SDR plus physical therapy was compared to therapy alone. (VERY LOW)

With regard to pelvic tilt, one non-randomised prospective study reported that there was no significant difference in active range of motion at 8 months when SDR plus physical therapy was compared to therapy alone (VERY LOW), although there was a statistically significant reduction in the SDR plus physical therapy group compared to the therapy alone group at 20 months. (VERY LOW)

With regard to hip joints, one RCT reported a statistically significant reduction in tone at the hip joint (evaluated using the modified Ashworth scale) when SDR plus physical therapy was compared to therapy alone at 9 months. (MODERATE) One RCT provided evidence of no difference in active or passive ROM hip extension when SDR plus physical therapy was compared to therapy alone at 6 months and 12 months. (MODERATE) One RCT reported a significantly improved ROM at the hip joint when SDR plus physical therapy was compared to the therapy alone at 9 months. (HIGH) One non-randomised prospective study reported that there was no significant difference in active ROM hip flexion or extension at 8 months when SDR plus physical therapy was compared to therapy alone. (VERY LOW) However, there was a statistically significant increase in active ROM in the SDR plus physical therapy group compared to the therapy alone group at 20 months. (VERY LOW)

With regard to knee joints, two RCTs provided evidence of a statistically significant reduction in tone at the knee joint (evaluated using the modified Ashworth scale) when SDR plus physical therapy was compared to therapy alone. Assessments were made at 6 months and 12 months in one study and at 9 months in the other. (MODERATE) One RCT provided evidence of no difference in active or passive ROM for knee extension or in passive ROM of the popliteal angle when SDR plus physical therapy was compared to therapy alone at 6 months and 12 months. (MODERATE) No further details realting to the popliteal angle were reported. One RCT reported a significantly improved ROM at the knee joint when SDR plus physical therapy was compared to therapy alone at 9 months. (HIGH) One non-randomised prospective study reported that there was no significant difference in active ROM knee flexion or extension or for knee flexion at initial contact at 8 months or 20 months when SDR plus physical therapy was compared to therapy alone. (VERY LOW)

With regard to the ankle joint, two RCTs provided evidence of a statistically significant reduction in tone at the ankle joint (evaluated using the modified Ashworth scale) when SDR plus physical therapy was compared to therapy alone. Assessments were made at 6 months and 12 months in one study (MODERATE) and at 9 months in the other. (HIGH) One RCT provided evidence of a statistically significant improvement in active and passive ankle dorsiflexion when SDR plus physical therapy was compared to therapy alone at 6 months and 12 months. (MODERATE) One RCT reported no statistically significant difference in ROM at the ankle when SDR plus physical therapy was compared to therapy alone at 9 months. (MODERATE) One non-randomised prospective study reported that there was no significant difference in active ROM ankle dorsiflexion or plantarflexion or for ankle dorsiflexion or plantarflexion at initial contact at 8 months or 20 months when SDR plus physical therapy was compared to therapy alone. (VERY LOW) The same study reported no significant difference between groups in extension foot progression angle at 8 months, although a statistically significant reduction was reported in the SDR plus physical therapy group compared to the therapy alone group at 20 months. (VERY LOW)

With regard to total modified Ashworth scores, one RCT reported total modified Ashworth scores at 6 months, 12 months and 24 months. At 6 months there was no significant difference between the SDR plus physical therapy group compared to the therapy-only group. (MODERATE) However, statistically significant reductions in tone were identified at 12 months (LOW) and 24 months. (MODERATE)

Optimisation of function

With regard to the individual dimensions of the GMFM, three RCTs reported mean changes for lying and rolling, crawling or kneeling, sitting, and walking, running or jumping at different time points. No significant differences in scores for any of these dimensions were reported when SDR plus physical therapy was compared to physical therapy alone at 6 months (one RCT; MODERATE), 9 months (one RCT; MODERATE), 12 months (two RCTs; LOW) or 24 months (one RCT; MODERATE). Three RCTs reported mean changes for the GMFM standing dimension at different assessment points. There was evidence of a significant improvement in scores favouring the SDR plus physical therapy group over the therapy-only group at 6 months (one RCT; HIGH), although results at 9 months (one RCT; MODERATE), 12 months (two RCTs; LOW) and 24 months (one RCT; MODERATE) did not differ significantly between groups.

Three RCTs reported mean changes for total GMFM scores. There was evidence of a significant improvement in scores in the SDR plus physical therapy group compared to the therapy-only group at 9 months (one RCT; MODERATE), but the results at 6 months (one RCT; MODERATE), 12 months (two RCTS; VERY LOW) and 24 months (one RCT; MODERATE) did not differ significantly between treatment groups. One non-randomised prospective study reported no significant differences in GMFM percentage score at 8 months or 20 months when SDR plus physical therapy was compared to therapy alone. (VERY LOW)

With regard to walking, one RCT reported no statistically significant differences in the distance children were able to walk in 60 seconds when SDR plus physical therapy was compared to physical therapy alone at 6 months and 12 months. (MODERATE) One RCT reported no significant differences in the findings of gait analysis for velocity or use of assistive devices when SDR plus physical therapy was compared with therapy alone at 12 months. (MODERATE) One non-randomised prospective study reported no significant difference between groups in gait speed at 8 months although a statistically significant reduction was reported in the SDR plus physical therapy group compared to the therapy alone group at 20 months. (VERY LOW)

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 is 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 postoperative 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 postoperative 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 postoperative day; no cases were reported in the 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 therapy-only group. (MODERATE)

One case series reported an incidence rate of 1.2% (3/250) for postoperative 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 that compared the effects of SDR and orthopaedic (soft tissue) surgery at 6 months, 12 months and 24 months reported no statistically significant differences between treatment groups for any of the PEDI functional skill or caregiver assistance domains at any time point. (VERY LOW) The same study reported no statistically significant differences between treatment groups for any of the individual dimensions of the GMFM or the total GMFM score at any time point. (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 botulinum toxin plus physical therapy
- SDR plus physical therapy versus intrathecal baclofen plus physical therapy.

Health economics

The evidence identified in relation to clinical effectiveness 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. 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). Since no good-quality long-term outcome data (that is, outcomes measured at more than 24 months and, preferably, into adult life) are available it is not possible to determine whether the initial reduction in tone reported in the 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, outcome measures should, therefore, 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.

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, independance 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 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 total GMFM scores were statistically significant. However, even for those dimensions where such effects were demonstrated (for example, standing or 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 believes that in the first 6-12 months after the operation, quality of life for the child or young person and their family may decrease temporarily because of postoperative adverse effects of the surgery itself, the need for a period of inpatient therapy, and the prolonged rehabilitation period that follows.

The short- and medium-term reductions in spasticity and optimisation of movement demonstrated in improvements in muscle tone or ROM 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 could not be supported in the absence of high-quality evidence of a consistent and sustained (long-term) improvement in motor function or pain control. Anecdotal evidence from an unpublished report (Edwards 2010) suggests, however, that in appropriately selected children and young people SDR may achieve such 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 postoperative recovery. It may take a child or young person up to 18 months 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. 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 becomes 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 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 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. Dietary advice would be helpful, therefore, in controlling weight gain.

The GDG considered that it would be important to ensure that the commitment required to follow a rehabilitation programme after SDR did not affect other aspects of the child or young person's life (such as education) adversely.

The GDG concluded that the evidence for a long-term or permanent reduction in spasticity after SDR was not strong, and that the evidence for a long-term improvement in gross motor function was even weaker.

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 physiotherapy, orthotics 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

- 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 therapy programme than did the 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, 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 interventional procedure guidance 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 interventional procedure guidance 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 with spasticity and co-existing motor disorders caused by non-progressive brain disorders (and their early musculoskeletal complications) through multidisciplinary teams comprising similar groups of healthcare professionals, and they recommended involvement of such teams as a general principle in the provision of care for these children and young people (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 standing dimension of the GMFM at 6 months and the total GMFM score at 9 months (although these effects were not consistent 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 spastic diplegia cerebral palsy who are in GMFCS levels 1 to 3. The GDG considered that the possible functional gain in children and young people in GMFCS level 1 was not sufficient to outweigh the risks of complications, and so they did not recommend offering SDR to children and young people in this group. Children and young people in GMFCS levels 2 and 3 were, however, thought likely to be able to derive the clinical benefit of improved walking ability through undergoing SDR. Thus the GDG therefore prioritised further research into the effectiveness and safety of SDR in children and young people in GMFCS levels 2 and 3. 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 cause 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 will worsen immediately after SDR, and a child or young person who is already weak may lose other skills (such as standing or walking) permanently following SDR.

No evidence was identified to support the use of SDR in more severely affected children, in children with hemiplegia, 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 would reduce the effectiveness of SDR and make postoperative rehabilitation difficult (because the child or young person might be in pain, and sitting and standing might be difficult).

The postoperative 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. 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 the child 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 could include botulinum toxin type A injections or intrathecal baclofen, but no evidence was identified to allow comparison of the clinical benefits and harms between SDR and such treatments. 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 1000 children and young people having received SDR 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. Children who can walk with walking aids before the age of 10 years may lose the ability in 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 interventional procedure guidance 373).

Recommendations

Number	Recommendation
	Selective dorsal rhizotomy
114	Offer selective dorsal rhizotomy to improve walking ability only in the context of clinical research.

Number	Research recommendation
23 (KRR)	Does selective dorsal rhizotomy followed by intensive rehabilitation performed between the ages of 3 and 9 years in children who are in GMFCS level 2 or 3 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 in GMFCS level 2 or 3 (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; 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 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).
24	What is the effectiveness of SDR compared to CITB in children and young people who are in GMFCS level 4 or 5?

1

11 Health economics

11.1 Introduction

Health economic analysis allows decision makers to consider the opportunity costs alongside the benefits of a treatment in order to decide if it is good value compared to the next best alternative. 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 quality adjusted life year. For the treatment of spasticity it is the quality adjustment which is most important. Health related quality of life is measured in terms of effect on mobility, self-care, ability to perform usual activities, pain/discomfort, and anxiety/depression. The treatments in this guideline reduce spasticity which can reduce pain, improve function and mobility, provide cosmetic improvements, and prevent deterioration which may have resulted in loss of function. For many of the treatments considered in this guideline the GDG felt that the benefits to health related quality of life are enough to justify the costs of treatment. Patient selection is important, particularly for the intrathecal baclofen therapy (ITB) pump, selective dorsal rhizotomy (SDR) and orthopaedic surgery, 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 therapy programmes and wearing orthoses, is key to the success of the treatment.

Given the lack of published evidence, further comparative research is necessary which captures benefits in terms of function, pain, adverse events and quality of life ideally using the EQ-5D (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 treatments and invasive with risks associated. Also the studies should be designed to allow sub-group analysis by severity of spasticity in terms of 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 sub-group will provide better information for decision making.

Each question includes a health economic summary based on the evidence and GDG opinion.

11.2 Physical therapy (physiotherapy and occupational therapy)

As there was limited effectiveness evidence available for therapy it was not possible to develop an economic evaluation and so a simple costing analysis was carried out using staff costs from the PSSRU Unit 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.

Table 11.1 Cost analysis for therapy

	Cost per hour of client contact	**Intensity (hours per week)**		
		3x week	**2x week**	**1x week**
Community	£42	£6,048	£4,032	£2,016

physio				
Hospital physio	£40	£5,760	£3,840	£1,920
	Mean PT	£5,904	£3,936	£1,968
Community OT	£42	£6,048	£4,032	£2,016
Hospital OT	£43	£6,192	£4,128	£2,064
	Mean OT	£6,120	£4,080	£2,040

Cost data for therapy has limited use without associated benefits. The cost of increasing therapy for children with spasticity could be significant but without knowing the benefits of increasing 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

As with therapy there was limited good quality effectiveness evidence so a cost analysis was conducted. The following service description was developed with the assistance of Exeter University and the Royal Berkshire NHS Foundation Trust.

Appointments:

1. Assessment 20-30 minutes with a physiotherapist or occupational therapist, this includes taking measurements.
2. Fitting 20-30minutes about two weeks after the assessment
3. Follow-up to check everything is okay, usually only for someone 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[43] (band 5 median) to represent the cost of an orthotist then the appointments will cost about £27 (40mins) 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. The lower limb orthoses are usually custom made, whereas the upper limb orthoses can be stock products.

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 12months. If the orthosis does not fit well and is uncomfortable then the child will not wear it.

The minimum age a child can be fitted for an orthosis is 17/18 months. They can be worn throughout the growing period.

11.4 Botulinum toxin

Botulinum toxin (BoNT) works by relaxing spastic muscles. This could allow clinicians to address issues of weakness and functional difficulties brought about by the abnormal muscle tone. But it may also 'unmask' weak muscles and cause a temporary deterioration in function, and there are possible side effects of the toxin. The evidence from the literature review was unequivocal and so a cost-effectiveness analysis was developed to consider what level of effect would be needed to find BoNT injections cost-effective by the NICE threshold.

[43] £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.

To begin with a cost analysis was conducted based on service descriptions from Leeds and Great Ormond Street Hospital (GOSH).

The BoNT service team comprises:

- 2 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 done by a consultant.

The assessment includes:

- Clinical examination
- Video gait analysis
- Goniometry
- +/- Gross motor function measure
- Treatment goals are agreed and documented
- Integrated care pathway paperwork completed
- Patients are weighed, consent obtained, and the botulinum toxin 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 (GA)
- Parental consent for sedation / GA and for injection

The majority of injections will be 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 will perform 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 GOSH there are two appointments at 3 and 17 weeks post injection; at Leeds the follow-up appointment is at 6 weeks.

Costs

The cost of a pre-assessment before BoNT is chosen as treatment is approximately £125 (Table 11.2). This includes overheads, such as office space. There may be additional costs for the equipment needed for the assessment but as the equipment will be used for assessment for other treatments and also other conditions the individual cost per use of, for example, a video camera will be low compared to the staff costs for an assessment.

Table 11.2 Costs of pre-assessment (PSSRU unit costs of health and social care 2009)

Selection and pre-assessment	per hour patient contact	45min assessment

1 consultants	£167	£125

BoNT into muscles should be coded as (XD09Z) Torsion dystonia and other involuntary movements drugs band 1 as it is a high cost drug (NHS Classification Service Coding Clinic Vol. 3 June 2006 www.connectingforhealth.nhs.uk/.../data/.../vol3_issue4_final.pdf accessed 30/11/10). The reference cost for 2008-9 was £417 (lower quartile £214 – upper quartile £541). There is also a specialist uplift to tariffs for children of 78%, if this is applied then the cost increases to £742. This tariff 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 (Table 11.3) (physiotherapy and occupational therapy costs are assumed to be the same for both treatment arms).

Table 11.3 Cost of standard care 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

Effects

The clinical evidence from the trials was variable for reducing spasticity and optimising movement and function. The quality of life evidence only shows 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 (Reddishough 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.

Suggested costs for adverse events which are not transient are shown in Table 11.4**Error! Reference source not found.**. The GDG thought serious adverse events were very unlikely for patients receiving BoNT and so the baseline analysis has been done without adverse events.

Table 11.4 Costs for adverse effects (NHS reference costs 2008-9)

Non-elective inpatient	**average**	**Lower quartile**	**Upper quartile**
Epilepsy syndrome without CC	£474	£335	£546
Acute upper respiratory tract infection and common cold	£469	£347	£546

Results

It is assumed that patients are referred to BoNT treatment when oral drugs stop working and all patients continue with physiotherapy and occupational therapy. The comparator for BoNT will be

continuing on oral drugs and the conservative assumption for this simple analysis is that patients do not deteriorate if they continue on oral drugs.

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 a year is approximately £1,860 if the injections are given in a day case setting and only one follow-up appointment is needed. The cost of standard care is therefore 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 £1,985. If BoNT is given three times in a year then costs increases to £2,727 per person per year. If adverse events are included then the cost increases to £1,855 if two sets of injections are given in a year.

There may be additional costs for the equipment used for assessment, but these will be used for other assessments and was not thought likely to significantly change the overall costs of providing BoNT. Therapy costs are not included as it assumed these would continue for patients not receiving BoNT. The cost of standard care is therefore approximately £21 per year.

Table 5 Cost analysis for one set of injections of BoNT in one year

	N	unit cost	total cost
pre-assessment	159	£125	£19,915
injection as day case	159	£742	£118,019
follow-up	159	£125	£19,915

If the NICE threshold for cost-effectiveness of £20,000 is used, then BoNT would need to improve quality of life over one year by 0.09 for two sets of injections.

Incremental cost of BoNT – 2 sets of injections in one year:

£1,860 - £21 = £1,839

Cost ÷ QALYs = incremental cost effectiveness ratio

£1,839 ÷ QALYs = £20,000 per QALY

£1,839 ÷ £20,000 = 0.09

One set of injections in a year: £972 ÷ £20,000 = 0.05

Three sets of injections in one year: £2,707 ÷ £20,000 = 0.14

For patients who have moderate pain or discomfort approximately 75% 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, 75% 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; 75% 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 75% 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

Background literature

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. As the evaluation was carried out in 1999 the costs needed to be updated and the discount rate[44] used was 6%, the standard rate currently used by NICE is 3.5% for costs and 3.5% (and 1.5%) for benefits. The model was fairly simple comparing 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 effectiveness evidence was identified in a literature search. Trials were included if they had more than one patient and an average follow-up of at least 6 months. Studies had to allow calculation of the proportion of patients who achieved at least one of the following outcomes:

1. Bedbound patients becoming able to sit in a wheelchair
2. Patients who had severe difficulty sitting in a wheelchair being able to sit comfortably
3. Wheelchair users improving their wheelchair mobility
4. Wheelchair users improving their ability to transfer
5. Wheelchair-bound patients becoming ambulatory
6. Ambulatory patients improving their ability to walk
7. Improved ability to perform activities of daily living
8. Improved ease of nursing care
9. Patients with skin integrity problems who showed improvements in these symptoms
10. Reduction in spasm-related pain

The studies identified used a wide variety of different outcomes and the authors found that functional and quality of life outcomes were generally not measured using standard scores. In all the studies included patients had severe disabling spasticity that could no longer be treated by oral medications and where the patients had responded to a bolus dose of ITB. The studies included both children and adults with different causes of spasticity, but the results were reported for all patients together. The results of the included studies are shown in Table 11.6.

Table 11.6 Results of included studies (Sampson 2002)

		No. Of patients	
Outcome measure	**No. Of studies**	**Affected**	**Responding (%)**

[44] A discount rate is applied to benefits and costs that will occur in the future to reflect our preference for benefits now and to defer costs.

Bedbound patients becoming able to sit in a wheelchair	4	76	50 (**66**)
Patients who had severe difficulty sitting in a wheelchair being able to sit comfortably	3	36	31 (86)
Wheelchair users improving their wheelchair mobility	2	18	13 (72)
Wheelchair users improving their ability to transfer	3	26	25 (96)
Wheelchair-bound patients becoming ambulatory	3	36	4 (11)
Ambulatory patients improving their ability to walk	5	45	18 (40)
Improved ability to perform activities of daily living	3	62	45 (**73**)
Improved ease of nursing care	6	90	83 (92)
Patients with skin integrity problems who showed improvements in these symptoms	3	23	19 (83)
Reduction in spasm-related pain	6	62	55 (**89**)

As none of the studies used quality of life measures the EQ-5D scores were calculated based on the evidence review supported by clinical opinion (Table 11.7). The outcome measures used to estimate the EQ-5D scores are shown in bold in Table 11.6.

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

Table 11.7 Estimated EQ-5D scores (Sampson 2002)

Category	Baseline quality of life value (EQ-5D score)	Changes in quality of life measured by EQ-5D	Adjusted quality of life improvement
1	-0.594 (33333)	11% no change (33333) 23% reduction in pain (33323) 66% reduction in pain, able to sit in wheelchair, reduction in anxiety and depression scores (23322)	0.50
2	-0.208 (33313)	34% no change (33313) 66% able to sit in wheelchair, reduction in anxiety and depression scores (23312)	0.27
3	0.079 (23322)	11% no change (23322) 73% reduction in pain, improved ability to care for self and perform ADL (22212) 16% reduction in pain only (23312)	0.43

Cost estimates were derived from 1999 data from 3 centres within the UK. Benefits of the ITB pump were assumed to last 5 years as this is the lifetime of the pump's battery. Table 11.8 shows the costs reported from 1999 and converted to 2008/9 costs (using the hospital and community health services pay and prices index uplift (1.42) from the personal social services research unit (PSSRU) unit costs of health and social care 2009 (Curtis 2009)).

Table 11.8 Costs of ITB test and pump (Sampson 2002)

	1999 Cost	2008/9 Cost		
		Min	max	mean
Pre-screening assessment costs (30mins neurosurgeon time and outpatient clinic visit)	£330 - £556	£470	£792	£631
test dose (Lumbar puncture, lumbar catheter, procedure HRG A452: injection of a therapeutic substance, 2 days hospitalisation, drug costs, physiotherapist, and nursing time for patient observation)	£940 - £1570	£1,339	£2,236	£1,787
cost of implantation procedure (incl. cost of pump, catheter, procedure, drugs, 5-day inpatient stay)	£8730 - £10,260	£12,433	£14,612	£13,522
other costs (tests, pathology, radiology, microbiology), excluding potential transport costs	£550			£783
cost of follow-up (refill kit, drug costs, physiotherapist assessment, and outpatient visit) average of 4 to 8 refills per year	£140 - £150	£199	£214	£206
Procedure	£11,743			£16,724
follow-up 1 year	£870			£1,239
follow-up 5 years	£4,066			£5,790
TOTAL	£15,809			£22,514

Methods

This published economic evaluation was used as the basis for a new model which looked at the cost-effectiveness of both testing and implanting the ITB pump. The costs of testing, implanting the pump and follow-up visits over 5 years have been taken from Sampson 2002 (Table 11.8).

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)[44]. 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 have been identified that were not included in Sampson 2002. The main change to the published model structure was the inclusion of comparator treatments. 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:

1. 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.
2. Children and young people considered suitable candidates by their clinicians have a pre-screening assessment, and get the pump implanted without a test dose.
3. ITB testing and pump is not available for any patients. Children and young people considered suitable candidates by their clinicians will continue to receive oral drugs.

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 can

generally 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), although these are for adults and children whereas we are only interested in the effect on children and young people.

Standard therapy will be the continuation of physiotherapy and oral drugs (baclofen) for 5 years (Table 11.9). It is assumed that patients with the ITB pump will also continue with physiotherapy and so this cost was not included in either arm of the model. Where the ITB treatment is unsuccessful and the patient has the pump removed they will go back to taking oral baclofen, assuming this will be six months less cost than patients who go straight to standard therapy.

Table 11.9 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 11.10, the costs are assumed to be the same whether the infection is due to the test procedure or the pump implant procedure.

Table 11.10 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	Children's BNF 2010-11
Major infection	Non-elective inpatient stay for major infection without complications*	£2,375	4.67 days	NHS reference costs 2009/10

*non-elective inpatient reference costs for infections range from £466 to £4,276 and have a length of stay of 1 to 7 days

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 11.11.

Table 11.11 Cost of removing the pump due to major infection

		Cost	Inpatient stay	reference
Pump removal	**Cost of having pump implanted less the cost of**	£13,522 - £9,446 =	5 days	Cost of implant procedure taken from Sampson 2002. Cost of pump and catheters taken from

	the pump	£4,077		the East Midlands Specialised Commissioning Group - Commissioning Policy for Intrathecal Baclofen. 25/09/2009.
Catheter revision or other correction	**2nd operation required to fix a problem with the pump**	£3,383	1.63 days	Reference cost for catheter 18 years or under NHS reference costs 2009/10

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:

1. Technical failure of the pump which would require the pump to be removed.
2. Where no effect is seen or the effect is too small then the dose is increased resulting in an additional follow-up visit.
3. Orthopaedic surgery. One possible outcome of using the ITB pump was thought to be delayed surgery and possibly prevention of surgery.

Results

The results of three small studies (reported in seven papers) from the review of clinical evidence were combined to populate the baseline model parameters. The studies were:

- Awaad et al. study (Awaad 2003)
- Gilmartin-Krach et al. study (Gilmartin 2000; Krach 2004)
- Hoving et al. study (Hoving 2007; Hoving 2009a; Hoving 2009b)

(see Table 11.21). Seven patients have been excluded from the clinical evidence from those who had a positive test but did not have the pump implanted. Six patients were excluded as they were ineligible to have a pump implanted, and the one death unrelated to treatment. Three of the children with a positive test chose not to have the pump implanted. Although it is not clear from the studies the exact reasons for these decisions they have been included in the analysis reflect the fact that some patients may choose not to have the pump implanted after the test (see Table 11.12).

Table 11.12 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	117		
Negative test	7	6%	-
Positive test	110	94%	-
Pump implanted	100	97% (of positive tests)	100%
Positive test but pump not implanted	Included; 3 chose to stay on oral medications Excluded; 1 death which was unrelated to the treatment 6 ineligible for a pump	3%	-

The GDG was asked to identify which adverse events should be included. Adverse events related to baclofen are considered to be transient with low cost implications and minimal impact on quality of life. Meningitis is a major adverse event which can cause death or serious disability, with high associated costs and is therefore included in the model. The risk of gastroenteritis was also included. It is assumed that if a patient has a major infection the pump will not be implanted.

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 11.13) In the model arm with no test it was assumed that the 7 children with negative test results would also have their pumps removed due to lack of effect.

Table 11.13 Clinical values and corresponding inputs for the test and no test arms of the model for adverse events and pump removal (% values rounded)

Model parameter	Values from clinical evidence	Inputs into model (%) test arm	Inputs into model (%) no test arm
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	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 cost of care for a population of 100 children and young people was calculated. Table 11.14 reports the mean and total cost associated with specific events (test results, adverse events) throughout the clinical pathway and the total cost for children who were tested prior to planned treatment. Table 11.15 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 11.14 Population numbers, mean and total cost of ITB treatment with testing (N=100) (figures are rounded from the model)

	Number	Cost per patient	Total cost
Patients having a pre-screening assessment	100	£631	£63,091
Patients having a test	100	£1,787	£178,734
Major infection due to test	1	£2,375	£2,030
Minor infection due to test	1	£4	£3
Patients with positive test result	94		
Patients with negative test result	6		
Patients who stay on standard therapy	9	£97	£896
Negative test result	6		

Positive test result but choose not to have pump	2		
Major infection due to test	1		
Patients who have pump implanted after positive test result	91	£14,306	£1,298,282
Number of patients who have pump removed	6	£4,077	£25,675
Due to infection during surgery	5	£2,375	£12,931
Lack of effect of baclofen	1		
Patients who go back to standard therapy after pump removed	6	£86	£545
Number of patients who have 2nd surgery to fix a problem with the pump	3	£3,383	£9,211
Number of patients with pump at 5 year follow-up	84	£5,790	£488,998
Total cost of care of children and young people tested before pump implanted	**100**	**£20,804**	**£2,080,396**

Table 11.15 Population numbers, mean and total cost of ITB treatment without testing (N=100) (figures are rounded from the model)

	Number	Cost per patient	Total cost
Patients having a pre-screening assessment	100	£631	£63,091
Number of patients with pump implanted	100	£14,306	£1,430,587
Number of patients who have pump removed	15	£4,077	£60,487
Due to infection from surgery	6	£2,375	£14,249
Due to lack of or poor effect of baclofen	9		
Patients who go back to standard therapy after pump removed	15	£86	£1,283
Number of patients who have 2nd surgery to fix a problem with the pump	3	£3,383	£10,150
Number of patients with pump at 5 year follow-up	85	£5,790	£493,102
Total cost of care of children and young people not tested before pump implanted	**100**	**£20,729**	**£2,072,949**

Table 11.16 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. In this case standard therapy should be chosen because implanting the pump is not worth the additional cost (approximately £20,000 per patient 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 therapy in wheelchair users with

moderate spasm-related pain (Table 11.18). 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 (£20,804 vs. £20,729 per person, and 1.76 vs. 1.78 QALYs over 5 years).

Table 11.17 Quality of life improvement scores from Sampson 2002 used in sensitivity analysis

Treatment arm	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
ITB pump with no test	0.43	2.01
ITB pump with testing	0.43	2.01

Table 11.18 Sensitivity analysis - Incremental cost-effectiveness results using quality of life outcomes from Sampson 2002 (benefits discounted by 3.5%)

Treatment arm	Effects	Incremental effects	Costs	Incremental costs	Incremental cost effectiveness ratio
Standard treatment	0		£9,686		
ITB pump with no test	171.1	171.1	£2,072,949	£2,063,263	**£12,057**
ITB pump with testing	169.7	-1.4	£2,080,396	£7,447	dominated

Table 11.19 Sensitivity analysis - Incremental cost-effectiveness results using quality of life outcomes from Sampson 2002 (benefits discounted by 1.5%)

Treatment arm	Effects	Incremental effects	Costs	Incremental costs	Incremental cost effectiveness ratio
Standard treatment	0		£9,686		
ITB pump with no test	177.6	177.6	£2,072,949	£2,063,263	**£11,607**
ITB pump with testing	176.2	-1.5	£2,080,396	£7,447	dominated

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. 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 becomes a cost-effective treatment compared to standard treatment. Sampson 2002 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 with spasticity caused by non-progressive brain disorders. Also the scores were estimated based on their evidence review and supporting clinical opinions.

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 0.25 each year for the 5 year lifetime of the pump, then implanting a pump would be cost-effective by the NICE threshold. For this quality of life improvement 50% of wheelchair users with moderate spasm-related pain who had the pump implanted would have to experience a reduction in pain, improved ability to care for self and improved ability to perform activities of daily living. Or these patients would be prevented from experiencing increased pain, and they would not deteriorate so they were unable to care for themselves or perform activities of daily living.

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, £1,787 per patient, which is not offset by the additional number of surgeries required to remove the pump in this analysis. 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))

Table 11.20 Cost of ITB pump for year for paediatrics (East Midlands Specialised Commissioning Group)

Test dose	**£1,048**	**Admission usually 2 days**
implant procedure	£ 901	AB05Z (for intermediate pain procedures)
device and catheters	£ 9,446	
refills (4 per year)	£3,599	
Total	**£14,994**	

The costs from Sampson 2002 were more detailed and so used in the model, but these 2009 costs show that uplifting the 1999 is not significantly different. 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.

Table 11.21 Results of the review of clinical evidence for questions 5 and 6

Number of patients who underwent the test	
Hoving et al study (3 papers)	17 children (all younger than 18 years)
Gilmartin-Krach et al study (3 papers)	51 patients (aged between 4 years and 31.3 years; mean 10y 3mo, median 11y 2mo)
Awaad et al study (1 paper)	49 (aged between 4 years and 32 years; mean age 13.09 y SD 7.49) We know that 28 of these were younger than 18 years but it's unclear how many of those 28 are represented in the outcomes
TOTAL	**117**
Number of adverse effects	
Hoving et al study (3 papers)	-Total number of adverse effects: 9 -Total number of children affected: 8 7 children slightly lethargic, including one who also experienced transient excessive hypotonia One child: excessive perspiration of hands and feet -Total number of complications: 19 -Total number of children affected: 16 14 children: symptoms of lowered CSF pressure 3 children, CSF leaked from the catheter connection One child: radicular pain in his right leg postoperatively. One child: gastroenteritis
Gilmartin-Krach et al study (3 papers)	-Total number of adverse effects: 29 -Total number of patients affected: 18 (There were 7 adverse effects during placebo but unclear how many patients were involved. They are included in the figure given here) 1 patient developed meningitis (withdraw from study) 1 patient intercurrent gastroenteritis (withdraw from study) Nausea, vomiting and drowsiness were common effects reported during baclofen, but unclear how many children involved in each of them
Awaad et al study (1 paper)	None reported
Number of patients with a positive test who went on to have the pump	
Hoving et al study (3 papers)	17
Gilmartin-Krach et al study (3 papers)	44
Awaad et al study (1 paper)	39
TOTAL	**100**

Number of patients with a positive test who did not go to have the pump	
Hoving et al study (3 papers)	0
Gilmartin-Krach et al study (3 papers)	0
Awaad et al study (1 paper)	10 Reasons for this: 3 patients elected to use oral medications 2 had “family issues” 1 child’s body size was “too small” 1 child died “unrelated to baclofen trial” 1 child had “medical issues” 1 child underwent spinal fusion 1 family decided not to undergo implant at the time of the study, unclear why
TOTAL	**10**
Number of patients in whom the pump was effective at 12 months	
Hoving et al study (3 papers)	17 (at 12 months)
Gilmartin-Krach et al study (3 papers)	40
Awaad et al study (1 paper)	18
TOTAL	75
Number of patients in which the pump was not effective due to baclofen not having an effect	
Hoving et al study (3 papers)	0
Gilmartin-Krach et al study (3 papers)	0
Awaad et al study (1 paper)	1
TOTAL	**1**
Number of patients with adverse effects (or complications?) which required explantation of pump	
Hoving et al study (3 papers)	None required explanation of the pump, but 3 procedure or device related events required children to undergo a second operation resulting in a prolonged hospital stay: 1 incomplete operation 1 abrupt lack of ITB effect 4 hours postoperatively 1 postoperative pain at pump site
Gilmartin-Krach et al study (3 papers)	Total number of patients: 3 (unclear whether any of these patients were children)

	Reasons: The 3 because of infections of the pump pocket: 1 had a second pump re-implanted to complete study and the other 2 withdrew from study)
Awaad et al study (1 paper)	Total number of patients: 4 (unclear whether any of these patients were children) Reasons: Meningitis=1 Infection: 2 (1 was a "pocket infection", unclear about the other one) Lack of effect-no clinical improvement: 1 (unclear if the latte the same patient in which the pump had to be stopped after 5 months because of a change of behaviour owing to an increased in seizure activity)
TOTAL	7 pumps explanted (unclear how many of these were in children) 3 procedure or device related events required children to undergo a second operation resulting in a prolonged hospital stay

11.6 Orthopaedic surgery

Given the lack of clinical evidence for the outcomes considered important for this question it was not possible to develop an economic evaluation. 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.

A cost analysis was requested by the GDG and is presented here.

The cost of surgery varies in the reference costs depending on the limb, whether it is minor or major surgery, and there is a 78% uplift to tariffs for children.

Reference costs 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 £1,638 (minor hand procedures) to £6,118 (major hip procedures). With the children's tariff uplift these become £2,915 to £10,889. The average length of stay ranged from 1 day for hand procedures, to 21 days for major hip procedures. Scoliosis or surgery for other spinal deformities cost on average £2,091 (£3,722 with uplift) and required on average 4 days in hospital.

These costs are for a finished consultant episode and so do not include rehabilitation therapy in the community after surgery.

11.7 Selective dorsal rhizotomy

Selective dorsal rhizotomy (SDR) is an operation where nerve roots are identified coming back into the spinal cord from the muscles in the legs and a percentage of them are cut. SDR has been offered in the UK since 1994 at Robert Jones and Agnes Hunt Orthopaedic and District Hospital NHS Trust (RJAH). In the 10 years up to 2006 they treated 27 patients.

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 intraoperative spinal monitoring. Postoperative 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. (Selective Dorsal Rhizotomy. Assessment for Nationally Funded Centre Status. A report by the Medical Services Advisory Committee to the Australian Health Ministers' Advisory Council. November 2006)

The NICE IPG group were given 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 RJAH 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. 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.

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 here. 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.

Costs

A thorough cost analysis was conducted for each patient. 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 was recorded and then costs applied, rather than taking tariffs or reference costs for episodes (Table 11.22).

Table 11.22 Unit costs for treatment

RESOURCE	COST	Comment
Initial clinical screening		
Initial outpatient appointment	£94	Standard tariff
Gait assessment	£1245	Locally derived tariff
X-ray (spine and hips)	£25	Standard tariff
MRI of brain and spinal cord	£2467	Standard tariff
Paediatric consultant review of imaging	£21	15 minutes at consultant salary
Pre-operative assessment clinic		
Pre-op clinic attendance	£94	Standard tariff, includes consultant

		time
Dietician	£13	Based on 0.5 hours of salary Band 6
Psychologist	£57	1.0 hour of salary Band 8a
Orthotist	£30	1.0 hour of salary Band 7
SDR – theatre procedure		
Theatre apportionment based on minutes – standard	£3600	Theatre time 240 mins x standard £15 per minute – includes all variable pay and non-pay resources
Theatre – surgeon (2)	£634	Two surgeons for 4 hours at standard salary
Special tooling – gold anspach drill	£130	A new drill at £130 per case
Intraoperative spinal monitoring		
Spinal monitoring	£2680	SLA Daily cost for team attending from Birmingham
Bioengineering support	£54	4 hours of in-house bioengineer Band 7
Recovery		
Recovery – paediatric nurses (2)	£40	Average of 1 hour in recovery
WARD: 7 weeks		
consultant ward round	£148	Weekly ward round by consultant, 20 mins per visit
Ward costs	£8459	Standard ward costs 49 days@ £172.64 per day
Dietician	£13	Follow up visit 0.5 hours
Psychologist	£28	Follow up visit 0.5 hours
Physiotherapy – group session	£277	Based on staff input x time divided by number of children in group
Physiotherapy – individual	£2217	
Hydrotherapy	£623	Based on staff input x time divided by number of children in group
Orthotics – contracture correction devices	£201	Approx. 15% of children supplied with CCD orthoses following surgery @£1340 per pair
Orthotist to fit and supply CCDs	£45	Total 1.5 hours orthotist time
Therapeutic electrical stimulation		1 in 5 children benefit from TES after surgery
	£160	Locally derived tariff, includes staff, admin and clerical, and non-pay costs.
Net total	**£21,135**	
Overheads	£4227	Calculated at 20% of total costs to incorporate capital, corporate and estates overheads

Grand Total	**£25,362**

They 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).

They reported all the patient contacts for each group including musculoskeletal surgery (Table 11.23 and Table 11.24). They found the number of outpatient visits showed no significant variation between groups. Non-SDR patients underwent an average of 3 periods of surgery in total and SDR an average of 1.9, 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.

Table 11.23 Patient contacts in SDR group

Patient	Periods of surgery post SDR	Periods of surgery including SDR	Total inpatient days including top-up physio admission	Total outpatient visits
SDR1	0	1	62	33
SDR2	0	1	45	33
SDR3	2	3	107	38
SDR4	1	2	96	39
SDR5	0	1	51	40
SDR6	2	3	120	20
SDR7	1	2	103	34
SDR8	0	1	60	23
SDR9	2	3	103	36
Mean		1.9	83	32.9

Table 11.24 Patient contacts in non-SDR group

Patient	Periods of surgery	Total inpatient days including top-up physio admissions	Total outpatient visits
NON1	4	67	42
NON2	4	55	26
NON3	2	39	31
NON4	2	69	22
Mean	3	57.5	30.3

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.

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13 Abbreviations and glossary

The final published guideline will include a list of abbreviations and a glossary.

Appendices A–M are in a separate file.