National Institute for Health and Care Excellence

Draft for consultation

Cerebral palsy in adults

[A2] Management of abnormal muscle tone: neurosurgical procedures to reduce spasticity

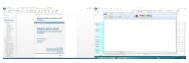
NICE guideline tbc

Evidence reviews

July 2018

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists



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Management of abnormal muscle tone in adults aged 19 and over with cerebral palsy, including spasticity and associated movement disorders such as dystonia

Review question

A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Introduction

When aggravating factors are removed and enteral or intramuscular pharmacological agents have been tried to their maximum tolerated dosage, neurosurgical interventions, such as intrathecal baclofen therapy and selective dorsal rhizotomy, are available for spasticity management. Both procedures require anaesthetic, and have surgical and recovery risks. However, they also have the potential to reduce spasticity and pain and improve quality of life. The aim of this review question is to examine the effectiveness of these interventions, taking into account the burden of having surgery, follow up and potential adverse events, as well as patient and carer experience.

PICO table

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Adults aged 19 and over with cerebral palsy and spasticity with or without dystonia
Intervention	• Intrathecal baclofen pump • Selective dorsal rhizotomy
Comparison	• Usual care (including, for example: oral drugs, botulinum toxin and physiotherapy) • Placebo
Outcome	**Critical** • Walking (for ambulant people only) • Gross motor function (both upper / lower limb) • Tone (for example Ashworth scale) • Health related quality of life **Important** • Pain • Adverse events (CSF leakage, infection, respiratory depression, baclofen withdrawal and baclofen overdose)

	• Satisfaction (patient or carer reported) • Use of concurrent medications

CSF: cerebrospinal fluid.

For full details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual 2014. Methods specific to this review question are described in the review protocol in appendix A and for a full description of the methods see supplementary document C.

Declaration of interests were recorded according to NICE's 2014 conflicts of interest policy from May 2016 until April 2018. From April 2018 onwards they were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Interests Register).

Clinical evidence

Included studies

Two randomised cross-over trials (number of participants, N=18; Albright 1991 and van Shaeybroeck 2000) and 6 before and after observational studies (N=99; Bertelli 2003, Gerszten 1997, Meythaler 2001, Motta 2011, Reynolds 2011 and Tassell-Ponche 2010) were included in the review. The clinical studies included in this evidence review are summarised in Table 2 and evidence from these is summarised in the clinical evidence profiles (Table 3 and Table 4).

Five studies were of long term continuous intrathecal baclofen infusion (Gerszten 1997, Meythaler 2001, Motta 2011, Tassell-Ponche 2010 and van Shaeybroeck 2000), 2 studies were randomised blinded comparisons of different doses of short term bolus injections of intrathecal baclofen (Albright 1991 and van Shaeybroeck 2000) and 2 studies concerned dorsal rhizotomy (Bertelli 2003 and Reynolds 2011).

The clinical studies included on this evidence review are summarised in Table 2 and evidence from these are summarised in the clinical evidence profile below (Table 3 and Table 4).

See also the literature search strategy in appendix B, study selection flow chart in appendix C, forest plots and dose comparison graph in appendix E and study evidence tables in appendix D.

Excluded studies

Studies excluded from this systematic review, with reasons for their exclusion, are provided in appendix K.

Summary of clinical studies included in the evidence review

Table 2 provides a brief summary of the included studies.

Table 2: Summary of included studies

Study	Design	Participants	Comparisons	Outcomes
Albright 1991	Randomised cross-over trial	N=7, age 15 to 31 years (median 18 years), with CP and moderate or severe spastic quadriplegia. USA	Bolus ITB injection versus baseline and other ITB doses	• Tone (follow up 8 hours)
Bertelli 2003	Before & after study	N=7, age 16 to 20 years (median 19 years), with hemiplegic CP and moderate or severe spasticity. Brazil	Brachial plexus dorsal rhizotomy: pre versus post-operative	• Gross motor function • Tone (follow up 15 months)
Gerszten 1997	Before & after study	N=24 (21 with CP, 3 with TBI), age 9 to 30 years (mean 18 years), with moderate or severe spasticity. USA	Continuous ITB infusion: pre versus post-operative	• Walking • Adverse events (mean follow-up 4.3 years)
Meythaler 2001	Before & after study	N=13, age 13 to 43 years (mean 25 years), with CP, intractable spastic hypertonia and quadriparesis. USA	Continuous ITB infusion: pre versus post-operative	• Tone • Adverse events (follow up one year)
Motta 2011	Before & after study	N=9, age 18 or older (mean 23 years) and CP. Italy	Continuous ITB infusion: pre versus post-operative	• Gross motor function (follow up one year)
Reynolds 2011	Before & after study	N=21, age 18 to 36 years (mean 26 years), with CP spastic diplegia, with independent ambulation USA.	Selective dorsal rhizotomy: pre versus post-operative	• Walking • Gross motor function • Tone • Health related quality of life • Pain (follow up 4 months – for objective physical assessment; mean 5 years for function self-assessment)

Study	Design	Participants	Comparisons	Outcomes
Tasseel Ponche 2010	Before & after study	N=25, mean age 30 years, with CP and moderate or severe spasticity. France	Continuous ITB infusion: pre versus post-operative	• Tone • Adverse events (follow up – up to 5 years)
Van Schaeybroeck 2000	Randomised cross-over trial and before & after study	N=11, age 8 to 55 years (median 22 years), with CP and spasticity. Belgium	• Bolus ITB injection versus placebo, baseline and other ITB doses • Continuous ITB infusion: standard dose versus baseline and reduced dose	• Tone • Adverse events (follow up 1 year)

CP: cerebral palsy; ITB: intrathecal baclofen; N: number of participants in study; TBI: traumatic brain injury.

See appendix D for full evidence tables.

Quality assessment of clinical outcomes included in the evidence review

The clinical evidence profiles for this review question are presented in Table 3 and Table 4.

Table 3: Summary clinical evidence profile: Comparison 1: intrathecal baclofen pre-operative versus post-operative

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Risk pre-operative	Risk with Intrathecal baclofen (post-operative)			
Walking - household or community ambulation Follow-up: 4 years	625 per 1,000	750 per 1,000 (513 to 1,000)	RR 1.20 (0.82 to 1.77)	24 (1 observational study)	Very low[1]
Gross motor function GMFM total score Scale from: 0 to 100 Follow-up: 1 year	The mean gross motor function was 55.22 %	The mean gross motor function in the intervention group was 2.34 % higher (2.34 lower to 7.02 higher)	-	9 (1 observational study)	Very low[2]
Tone upper extremity (ITB bolus 100µg) Ashworth scale Scale from: 1 to 5 Follow-up: 4 hours	The mean tone upper extremity (ITB bolus 100µg) was 1.64	The mean tone upper extremity (ITB bolus 100µg) in the intervention group was 0.23 lower (0.71 lower to 0.25 higher)	-	8 (1 RCT)	Low [3,4]
Tone lower extremity (ITB bolus 100µg) Ashworth scale Scale from: 1 to 5 Follow-up: 4 hours	The mean tone lower extremity (ITB bolus 100µg) was 2.75	The mean tone lower extremity (ITB bolus 100µg) in the intervention group was 1.4	-	8 (1 RCT)	Low [2,3]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Risk pre-operative	Risk with Intrathecal baclofen (post-operative)			
		lower (2.44 lower to 0.36 lower)			
Tone lower extremity (ITB continuous infusion) Ashworth scale Scale from: 1 to 5 Follow-up: range 1 years to 5 years	The mean tone lower extremity (ITB continuous infusion) ranged from 3.16 to 3.4	The mean tone lower extremity (ITB continuous infusion) in the intervention group ranged from 1.90 lower (2.66 to 1.14 lower) to 1.16 lower (1.45 to 0.87 lower)	-	38 (2 observational studies)	Very low [2,5]
Tone upper extremity (ITB continuous infusion) Ashworth scale Scale from: 1 to 5 Follow-up: 1 years	The mean tone upper extremity (ITB continuous infusion) was 3	The mean tone upper extremity (ITB continuous infusion) in the intervention group was 1.3 lower (2.15 lower to 0.45 lower)	-	13 (1 observational study)	Very low [2]
HRQOL - not reported	-	-	-	-	-
Pain - not reported	-	-	-	-	-
Adverse events (ITB continuous infusion) - catheter or pump infections Follow-up: range 4 to 5 years	Rate ranged from 4.2 to 8%		-	49 (2 observational studies)	Very low[1,4]
Adverse events (ITB continuous infusion) - catheter disconnection / breakage Follow-up: range 4 years to 5 years	Rate ranged from 4.2% to 17%		-	55 (3 observational studies)	Very low[1,4]
Adverse events (ITB continuous infusion) - Constipation Follow-up: range 1 years to 5 years	Rate ranged from 4% to 15%		-	38 (2 observational studies)	Very low[1,4]
Adverse events (ITB continuous infusion) - Anxiety and depression Follow-up: 5 years	Rate was 8%		-	13 (1 observational study)	Very low[1,4]
Adverse events (ITB continuous infusion) - Seizures Follow-up: 1 years	Rate was 15%		-	13 (1 observational study)	Very low[1,4]
Satisfaction - not reported	-	-	-	-	-
Concurrent medications - not reported	-	-	-	-	-

CI: confidence interval; GMFM: gross motor function measure; HRQOL: health related quality of life; ITB: intrathecal baclofen; RR: risk ratio.

1 No comparator

2 Confidence interval includes one default MID threshold

3 Intrathecal bolus injection rather than implanted pump

4 Number of participants <400
5 Extremity not reported in one of the studies

Table 4: Summary clinical evidence profile: Comparison 2: selective dorsal rhizotomy – pre-operative versus post-operative

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Risk with pre-operative	Risk with Selective dorsal rhizotomy (post-operative)			
Walking Self rated ambulatory ability on visual analogue scale Scale from: 0 to 10 Follow-up: 5 years	The mean walking score was 6	The mean walking - in the intervention group was 2.3 higher (2 lower to 6.6 higher)	-	21 (1 observational study)	Very low[1]
Walking Walking, running & jumping dimension of GMFM Scale from: 0 to 100 f Follow-up: 5 years	The mean GMFM walking scale was 65.57	The mean walking in the intervention group was 15.09 higher (6.1 higher to 24.08 higher)	-	7 (1 observational study)	Very low[2]
Gross Motor Function Measure (GMFM) Scale from: 0 to 100 follow up: 4 months	The mean gross motor function was 87.14	The mean gross motor function in the intervention group was 6.25 higher (1.73 lower to 14.23 higher)	-	7 (1 observational study)	Very low[1]
Gross motor function Jebsen-Taylor hand function test Scale from: 0 to 720 Follow-up: 15 months	The mean gross motor function was 72	The mean gross motor function in the intervention group was 35.29 lower (55.71 lower to 14.87 lower)	-	7 (1 observational study)	Very low[2]
Tone - hip adductors Modified Ashworth score Scale from: 1 to 4 Follow-up: 4 months	The mean tone - hip adductors was 2.16	The mean tone - hip adductors in the intervention group was 2.11 lower (2.8 lower to 1.42 lower)	-	19 (1 observational study)	Very low[2]
Tone - hamstrings Modified Ashworth score Scale from: 1 to 4 follow up: 4 months	The mean tone - hamstrings was 3.58	The mean tone - hamstrings in the intervention group was 3.47 lower (3.83 lower to 3.11 lower)	-	19 (1 observational study)	Very low[2]
Tone - gastroc / soleus Modified Ashworth score Scale from: 1 to 4 Follow-up: 4 months	The mean tone - gastroc / soleus was 3.25	The mean tone - gastroc / soleus in the intervention group was 2.96 lower (3.52 lower to 2.4 lower)	-	19 (1 observational study)	Very low[2]
Tone - wrist flexors Ashworth score	The mean tone - wrist flexors was 3.5	The mean tone - wrist flexors in the intervention group	-	6 (1 observational study)	Very low[2]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
	Risk with pre-operative	Risk with Selective dorsal rhizotomy (post-operative)			
Scale from: 1 to 5 Follow-up: 15 months		was 2.5 lower (3.6 lower to 1.4 lower)			
Tone - digital flexors Ashworth score Scale from: 1 to 5 Follow-up: 15 months	The mean tone - digital flexors was 3.42	The mean tone - digital flexors in the intervention group was 2.28 lower (3.25 lower to 1.3 lower)	-	7 (1 observational study)	Very low[2]
Health related quality of life Self rated visual analogue scale Scale from: 0 to 10 Follow-up: 5 years	The mean quality of life was 6.9	The mean quality of life in the intervention group was 2 higher (2.3 lower to 6.3 higher)	-	21 (1 observational study)	Very low[1]
Pain Self rated visual analogue scale Scale from: 0 to 10 Follow-up: 5 years	The mean pain was 4	The mean pain in the intervention group was 1.9 lower (9.61 lower to 5.81 higher)	-	21 (1 observational study)	Very low[1]
Adverse events - not reported	-	-	-	-	-
Satisfaction - not reported	-	-	-	-	-
Concurrent medications - not reported	-	-	-	-	-

CI: confidence interval; GMFM, gross motor function measure; MID: minimally important difference.
1 Confidence interval includes one default MID threshold
2 Number of participants <400

See appendix F for full GRADE tables.

Economic evidence

Included studies

See supplementary material D for the economic evidence tables.

Excluded studies

See supplementary material D for the excluded studies.

Summary of studies included in the economic evidence review

Bensmail 2009 is a cost effectiveness study comparing intrathecal baclofen as a first-line strategy to current specific treatment options offered to patients with disabling spasticity. The study took a French public healthcare payer perspective and reported outcomes in terms of cost per success defined as increased patient and caregiver satisfaction and a decrease of at least one point on the Ashworth score. Effectiveness data was taken from historical databases which were not defined in the paper. The study population was for people with disabling spasticity and was not exclusive to people with cerebral palsy. Whilst the databases

would include people with cerebral palsy the paper did not report the total number or proportion this group made up. Costs were taken from one retrospective resource utilisation study of 170 patients with disabling spasticity at 1 French hospital.

Sampson 2002 was a study looking at the change in QALYs and costs incurred with the use of intrathecal baclofen from pre-treatment on people with severe spasticity. The study took a UK NHS perspective and reported outcomes in terms of change in QALYs from baseline and total costs. Given this was a before and after type study no incremental costs were calculated between competing interventions. Effectiveness data for the study was taken from 1 meta-analysis of 17 comparative and non-comparative trials. The meta-analysis did not report the total number or proportion of patients with cerebral palsy (as some of the included studies did not report this) and it included trials in populations without cerebral palsy. This data was used by clinicians to estimate the baseline and change in the 5 dimensions of the EQ-5D and the impact on quality of life for the use of intrathecal baclofen. 3 categories of patients with different levels of disability were considered by the study: Category 1, bedbound patients experiencing severe spasm-related pain; Category 2, bedbound patients who were not in pain; Category 3, wheelchair users with moderate spasm related pain. Cost drivers were identified from discussion with clinicians and costs estimated using costing data from three UK centres.

Saulino 2015 compared the cost of care before and after intrathecal baclofen pump based on a retrospective analysis of commercial administrative claims data for people with severe spasticity [people with cerebral palsy (n=131), multiple sclerosis (n=124), and spinal cord injury (n=40)]. The costs considered were those to a private US healthcare payer and included all healthcare related costs. A 30 year time horizon was considered using decision analytical modelling to estimate costs over the remainder of the patient's lifetime.

See appendix I for the full health economic evidence profiles.

Economic model

This question was not prioritised for economic modelling given that previous economic evidence was identified. Instead, a cost-description was undertaken to aid considerations of resource impact and cost effectiveness.

Resource impact

Selective dorsal rhizotomy (SDR)

Edwards 2010 was a detailed cost-analysis that gave a thorough understanding of the costs involved in SDR in adolescents. Those costs are reproduced in Table 5. 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.

Table 5: Unit costs of selective dorsal rhizotomy treatment

Resource	Cost	Source
Initial clinical screening		

Resource	Cost	Source
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-operative 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 (7 weeks on ward)		
Recovery – paediatric nurses (2)	£40	Average of 1 hour in recovery
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	Based on staff input x time divided by number of children in group
Hydrotherapy	£623	Based on staff input x time divided by number of children in group
Orthotics – contracture correction devices	£201	Approximately 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

Resource	Cost	Source
Grand Total (2009/10 prices)	**£25,362**	
Grand Total (2015/16 prices)	**£28,044**	**Calculated [a]**

CCD: Contracture correction devices; MRI: Magnetic resonance imaging; mins: minutes; SDR: Selective Dorsal Rhizotomy; SLA: Service Level Agreement; TES: Therapeutic electrical stimulation
(a) HSHC inflation factor 1.1057 (2015/16 PPI 297/ 2009/10 PPI 268.6)

The cost of additional follow-up clinic visits was not included since all patients are followed up routinely post-surgery. The neurophysiological spinal monitoring equipment was also not included in the costing as it was treated as a sunk cost for other spinal surgeries.

They reported all the patient contacts for each group including musculoskeletal surgery. They found the number of outpatient visits showed no significant variation between groups. Non-SDR patients (n=4) underwent an average of 3 periods of surgery in total and SDR an average of 1.9, although the SDR patients (n=9) spent longer in hospital (83 days compared to 57.5 in the non-SDR group).

The cost data presented by Edwards 2010 was thorough and provides useful information. However, these are small patient numbers so it may be unreliable to compare the groups. Moreover, the costs were taken from procedures undertaken in adolescents which may not be reflective of adults. For example, the committee advised that a recovery on the ward would be reduced to 2 weeks for adults in clinical practice today. In order to provide a useful analysis for decision making, evidence on the long-term benefits and risks of treatment compared to the next best alternative are needed.

Intrathecal baclofen (ITB)

Sampson 2002 published a study on ITB in which detailed cost estimates were derived from 3 centres in the UK where the procedure was being performed. The costs included in the study were obtained in 1999 and have been converted to 2015/16 costs using the hospital and community health services pay and prices index uplift (Curtis PSSRU 2015) in Table 6.

Table 6: Cost of intrathecal baclofen reproduced from Sampson 2002

Resource use	1999 prices (mean)	Mean 2015/16 prices [a]
Pre-screening assessment costs (30 minutes neurosurgeon time and outpatient clinic visit)	£330 to £556 (£443)	£698
Test dose (Lumbar puncture, lumbar catheter, injection of a therapeutic substance, 2 days hospitalisation, drug costs, physiotherapist, and nursing time for patient observation)	£940 to £1,570 (£1,255)	£1,976
Cost of implantation procedure (cost of pump, catheter, procedure, drugs, 5-day inpatient stay)	£8,730 to £10,260 (£9,495)	£14,952
Other costs (tests, pathology, radiology, microbiology), excluding potential transport	£550	£866
Total cost of procedure	**£11,743**	**£18,492**
Cost of follow-up (refill kit, drug costs, physiotherapist assessment, and outpatient visit) with an average of 4 to 8 refills per year	£140 to £150 per refill £145 x 6 refills per year = £870 annual cost	£1,370

Resource use	1999 prices (mean)	Mean 2015/16 prices [a]
Discounted follow-up over 5 years	£3,677	£5,790
Total discounted cost over 5 years	**£15,420**	**£24,283**

(a) HSHC inflation factor 1.5748 (2015/16 PPI 297/ 1999/2000 PPI 188.6)

The East Midlands Specialised Commissioning Group also produced detailed paediatric and adult costs for ITB treatment in 2009. They assumed the admission for the test dose usually takes 2 days whilst the admission for the implant usually takes an additional 5 days. The test dose, implant and refills were worked out using the contract code AB05Z (for intermediate pain procedures), at 2009/2010 prices. Those prices are presented alongside 2015/16 costs in Table 7.

Table 7: Cost of ITB treatment based on East Midlands commissioning policy 2009

Resource use	Adult cost, 2009/10 prices	2015/16 prices [a]
Test dose	£680	£752
Implant procedure	£515	£569
Device and catheters	£9,446	£10,445
Total cost of procedure	**£10,641**	**£11,766**
Annual cost of refills (assuming 4 per year)	£2,130	£2,355
Total cost of procedure and follow-up in first year	£12,771	£14,121
Discounted follow-up appointments over 4 further years	£7,685	£8,497
Total discounted cost over 5 years	**£20,456**	**£22,618**

(a) HSHC inflation factor 1.1057 (2015/16 PPI 297/ 2009/10 PPI 268.6)

The total costs over 5 years are similar in the Sampson 2002 study and in the East Midlands Commissioning Policy; however, it is likely that the costs from the latter source are more accurate as costs were based on an HRG code, reflecting more recent UK practice. It is also important to note that the committee advised that the number of refills reported by those sources is overestimated as 2 to 3 refills a year are seen in UK clinical practice today.

Evidence statements

Clinical evidence statements

Comparison 1: intrathecal baclofen pre-operative versus post-operative

Critical outcomes

Walking

- Very low quality evidence from one before and after study including 24 people with cerebral palsy indicated no clinically significant improvement in the rates of household or community ambulation after four years of continuous baclofen infusion

Gross motor function

- Very low quality evidence from one before and after study including nine people with cerebral palsy indicated no clinically significant improvement in gross motor function after one year of continuous baclofen infusion.

Muscle tone

- Low quality evidence from 1 randomised study including 8 people with cerebral palsy and moderate or severe spasticity indicated bolus intrathecal injections of baclofen did not produce a clinically significant reduction in upper extremity muscle tone (at 4 hour follow-up.
- Low quality evidence from 1 randomised study including 8 people with cerebral palsy and moderate or severe spasticity indicated bolus intrathecal injections of baclofen led to a clinically significant reduction in lower extremity muscle tone (at 4 hour follow-up).
- Low quality evidence from 2 randomised studies including 18 people indicated higher dose bolus intrathecal injections of baclofen were more effective in lowering the muscle tone of people with cerebral palsy and moderate or severe spasticity
- Very low quality evidence from 2 before and after studies including 38 people with cerebral palsy who responded to trial bolus injections of intrathecal baclofen suggested continuous baclofen infusion via an implanted pump can maintain a clinically significant reduction in lower extremity muscle tone over one to five years of follow-up.
- Very low quality evidence from 1 before and after study including 13 people with cerebral palsy who responded to trial bolus injections of intrathecal baclofen suggested continuous baclofen infusion via an implanted pump can maintain a clinically significant reduction in upper extremity muscle tone over one year of follow-up.

Health related quality of life

- No evidence was found for this outcome

Important outcomes

Pain

- No evidence was found for this outcome

Adverse events

- Very low quality evidence about the rate of catheter or pump infections following implantation of baclofen infusion pumps was provided by 2 observational studies including 49 people followed for up to five years. Infections were reported by both studies at rates ranging from 4 to 8% over the period of follow-up.
- Very low quality evidence about the rate of catheter disconnection or breakage following implantation of baclofen infusion pumps was provided by 3 observational studies including 55 people followed for up to 5 years. Catheter disconnection or breakage was observed in all the studies, at rates ranging from 4 to 17% over the period of follow-up.
- Very low quality evidence about the rate of constipation following implantation of baclofen infusion pumps was provided by 2 observational studies including 38 people followed for

up to 5 years. There was no comparison group in these studies so it was unclear whether constipation was more or less likely following pump implantation.

- Very low quality evidence about the rate of anxiety and depression following implantation of baclofen infusion pumps was provided by 1 observational study including 13 people followed for five years. There was no comparison group in this study so it was unclear whether anxiety and depression were more or less likely following pump implantation.
- Very low quality evidence about the rate of seizures following implantation of baclofen infusion pumps was provided by 1 observational study including 13 people followed for five years. There was no comparison group in this study so it was unclear whether seizures were more or less likely following pump implantation.

Satisfaction (patient or carer reported)

- No evidence was found for this outcome

Use of concurrent medications

- No evidence was found for this outcome

Comparison 2: Selective dorsal rhizotomy pre-operative versus post-operative

Critical outcomes

Walking

- Very low quality evidence from 1 before and after study including 21 people indicated no clinically significant improvement in self rated ambulatory ability five years after selective dorsal rhizotomy.
- Very low quality evidence from 1 before and after study including 7 people indicated a clinically significant improvement in the walking, running and jumping component of the GMFM scale five years after selective dorsal rhizotomy.

Gross motor function

- Very low quality evidence from 1 before and after study including 7 people indicated no improvement in the total GMFM score four months after selective dorsal rhizotomy.
- Very low quality evidence from 1 before and after study of 7 people with cerebral palsy and spastic hemiplegia indicated a clinically significant improvement in hand function 15 months after brachial plexus selective dorsal rhizotomy.

Muscle tone

- Low quality evidence from two before and after studies including 26 people with cerebral palsy and spasticity indicated that selective dorsal rhizotomy can produce a clinically significant reduction in muscle tone, at four to 15 months follow-up.

Health related quality of life

- Very low quality evidence from 1 observational study including 21 people with cerebral palsy indicated no clinically significant change in self-rated health related quality of life 5 years after selective dorsal rhizotomy.

Important outcomes

Pain

- Very low quality evidence from 1 observational study including 21 people with cerebral palsy indicated no clinically significant change in self-rated pain 5 years after selective dorsal rhizotomy.

Adverse events

- No evidence was found for this outcome

Satisfaction (patient or carer reported)

- No evidence was found for this outcome

Use of concurrent medications

- No evidence was found for this outcome

Health economic evidence statements

- One cost effectiveness analysis (Bensmail 2009) found that over 2 years, intrathecal baclofen dominated other established treatment patterns by providing greater effectiveness at a lower cost. The study showed a significantly lower average cost per success with ITB as a first-line strategy (€75,204/ success versus €148,822/success; p<0.001). This analysis is partially applicable with potentially serious limitations, namely as the population was not exclusive to people with cerebral palsy and did not report outcomes in terms of QALYs. It is also unclear from the paper what clinical effectiveness data was used to inform the model as no values are reported in the paper. The study reported the mean results from 5000 PSA iterations. Deterministic results or deterministic sensitivity analyses of alternate assumptions were not reported.
- One cost utility analysis (Sampson 2002) estimated that the mean cost per QALY ranged from £6,900 to £12,790 over 5 years. Threshold analyses were reported which looked at the QALY gain needed to give mean costs of between £5000 and £25,000 per QALY. These were not comparative results with competing interventions and should be interpreted against cost per QALY thresholds with caution. This analysis is partially applicable as the population was not exclusive to people with cerebral palsy and NICE's preferred discount rate was not applied. The evidence was associated with potentially serious limitations due to the limited sensitivity analysis reported.
- One cost analysis (Saulino 2015) found that at 30 years, intrathecal baclofen had a cumulative cost saving of $240,272 per patient equating to an annual saving of $8,009 compared with conventional treatment. This analysis is partially applicable as US costs will not be easily generalisable to the UK and no health related outcomes were estimated. The evidence was associated with potentially serious limitations as clinical effectiveness data was informed by a retrospective analysis of commercial administrative claims data rather than a systematic review of the literature. The study was funded by Medtronic Inc a manufacturer of intrathecal baclofen pumps.

Recommendations

A2.1 Consider referring adults with cerebral palsy to a tone or spasticity management service offering continuous pump-administered intrathecal baclofen therapy if they still have difficulties with spasticity, despite enteral muscle relaxant drug treatment or botulinum toxin type A treatment.

A2.2 When considering continuous pump-administered intrathecal baclofen, give the person (and their family and carers, if agreed) information and discuss the procedure with them. This should include:

- the need for a test dose to ensure treatment is suitable
- the surgical procedure for implanting the pump
- the need for regular hospital follow-up visits to ensure optimal dosage and pump refill
- the risks of implanting a pump and pump-related complications (for example battery failure or catheter leakage), which can result in baclofen withdrawal or overdose
- a review of 24-hour postural needs.

A2.3 If continuous pump-administered intrathecal baclofen is being considered for an adult with cerebral palsy, perform an intrathecal baclofen test to assess if it is suitable before implanting a pump. This should involve:

- a test dose or doses of intrathecal baclofen given to the person by lumbar puncture **or**
- a test dose or doses of intrathecal baclofen given to the person through a spinal catheter.

A2.4 Assess the effect of the test dose or doses of intrathecal baclofen on:

- reducing increased muscle tone
- reducing pain
- reducing the frequency of muscle spasms
- motor function, such as sitting, standing, walking.

A2.5 Discuss with the adult with cerebral palsy (and their family and carers, if agreed) their views on the response to the intrathecal baclofen test.

A2.6 Only consider selective dorsal rhizotomy for adults with cerebral palsy and spasticity after they have been assessed by a multidisciplinary team with:

- specialist training and expertise in the care of spasticity **and**
- access to the full range of treatment options.

See also NICE interventional procedure guidance on selective dorsal rhizotomy for spasticity in cerebral palsy.

A2.7 When considering selective dorsal rhizotomy, give the person (and their family and carers, if agreed) information and discuss the impact of the procedure with them. This should include:

- that the procedure cannot be reversed
- the possible complications
- the need for prolonged physiotherapy and aftercare
- the possible impact on function
- that the long-term benefits are uncertain.

Research recommendations

What is the effectiveness and cost effectiveness of selective dorsal rhizotomy compared to continuous intrathecal baclofen pump to reduce spasticity in adults with cerebral palsy?

Rationale and impact

Why the committee made the recommendations

There was some evidence with high uncertainty suggesting that both intrathecal baclofen and selective dorsal rhizotomy are effective in reducing muscle tone in adults with spasticity. However, there are risks involved, both in having surgery and of long-term complications. The committee highlighted the importance of discussing the procedure with the person and their family or carers, so that they fully understand what the treatment involves and the potential risks and benefits.

Intrathecal baclofen

Using the evidence and their experience of current practice, the committee agreed that intrathecal baclofen pumps can be beneficial for treating spasticity in some adults with cerebral palsy. However, they should only be considered by a specialist service that can safely carry out the procedure and has the expertise to assess whether it is a suitable treatment for the person. There are potential risks of intrathecal baclofen pump treatment. These include infections, catheter breakage, seizures, constipation and anxiety or depression. After selective dorsal rhizotomy there may be a deterioration in walking ability or bladder function, and later spinal deformity. Taking into account these factors, the committee agreed that referral should only be considered if a person still has difficulties with spasticity after trying enteral muscle relaxant drug treatment or botulinum toxin type A injections.

Due to the complex nature of this procedure the committee noted that the adult with cerebral palsy will need sufficient information to make an informed choice and that this is not always consistently provided. A number of issues should be considered when providing information specifically related to this surgical procedure, such as the need for a test dose preimplantation, requirement of pump refill and regular follow-ups, the details of what the surgical procedure involves, and a review of their 24 hour postural needs.

The committee recognised that the response to intrathecal baclofen needs to be tested before the pump would be implanted. They therefore highlighted a couple of particular points about how the test dose (or doses if the person does not respond to the initial test dose) would be administered. The committee did not want to be too detailed about dosage and how the testing would be carried out because this is described in the British National Formulary (BNF). The response should then be assessed and discussed with the adult with cerebral palsy to ensure that a pump is only implanted when a benefit is established in advance.

Selective dorsal rhizotomy

The committee was aware that there is a risk of complications with selective dorsal rhizotomy, including deterioration in walking ability and bladder function, and later spinal deformity. Because of this and the limited evidence, the committee also took into account NICE's interventional procedures guidance on selective dorsal rhizotomy for spasticity in cerebral palsy, published in 2010. Although they noted that the evidence for the interventional procedure guidance was mostly in children. The committee agreed that selective dorsal rhizotomy should only be considered after multidisciplinary assessment in a specialist spasticity service, in line with the NICE interventional procedures guidance.

The committee also recommended further research, comparing the safety and effectiveness of selective dorsal rhizotomy with continuous intrathecal baclofen pump treatment. Both procedures are currently used to treat spasticity in people with cerebral palsy and there is some evidence that both are effective. However, the committee noted that the procedures, and their risks and benefits, are very different. They agreed that a comparative study would be helpful to inform decision-making.

Impact of the recommendations on practice

The recommendations reinforce current best practice and should not lead to additional resource use. Specialist services already exist and neurosurgical procedures are currently available for the treatment of spasticity. Including specific criteria for referral should reduce the number of inappropriate referrals to these services.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The critical outcomes were gross motor function, walking, muscle tone and health related quality of life because neurosurgical procedures are primarily aimed at improving these outcomes. Important outcomes were reduction in pain and adverse events. Patient satisfaction and use of concurrent medications were also outcomes that the committee considered to be important. However, these outcomes were not reported.

The quality of the evidence

The quality of the evidence for this review was assessed using GRADE. The evidence for outcomes related to the effectiveness of intrathecal baclofen pumps and selective dorsal rhizotomy was very low to low quality. Overall this was due to the following general pattern common to the evidence related to intrathecal baclofen and selective dorsal rhizotomy:

- Although two blinded studies showed a dose response relationship between the dose of bolus intrathecal baclofen injections and muscle tone, the evidence for all outcomes from these studies was downgraded for indirectness as it came from the test dose using intrathecal injections rather than the dose following implantation of the pump. Intrathecal baclofen pumps would only be implanted after a response to a test dose and the results from these studies may therefore underestimate the effectiveness of this procedure.

- The level of evidence was also downgraded due to study design. This was because the majority of the evidence came from before and after observational studies: only two randomised dose comparison trials were included.
- The number of participants in each study was also very small due to the invasive nature of the treatments which led to wide confidence intervals and further downgrading of the evidence quality due to imprecision.
- One of the selective dorsal rhizotomy studies was agreed to be only partially applicable to the review question as it looked at brachial plexus dorsal rhizotomy to improve upper limb function rather than selective dorsal rhizotomy to improve lower limb function. Because only limited evidence was available the committee agreed to include this study but had little confidence in the findings.

The low quality of the evidence meant that strong recommendations for neurosurgical procedures could not be made and that the committee was not confident in the findings. They therefore based the recommendations on intrathecal baclofen and selective dorsal rhizotomy predominantly on their experience and expertise.

Although outcomes related to adverse events associated with intrathecal baclofen pumps, evidence were all rated as very low, they featured in the discussion of the committee and contributed to decision making. The committee agreed, based on their knowledge and experience, that neurosurgical treatments are associated with the reported adverse events (catheter or pump infections, constipation, anxiety or depression and seizures) because the surgical procedures are complex and invasive.

Due to the limited low quality evidence on selective dorsal rhizotomy the committee decided to both cross reference to the NICE interventional procedures guidance Selective dorsal rhizotomy for spasticity in cerebral palsy IPG373 (2010) as well as recommending further research on the use of selective dorsal rhizotomy.

Benefits and harms

The evidence showed that there are potentially serious adverse events associated with intrathecal baclofen pumps. The adverse events reported in the included studies were infections, catheter breakage, seizures, constipation and anxiety or depression. Even though serious adverse events were not reported in the studies for selective dorsal rhizotomy, the committee agreed that adverse events were well recognised, such as deterioration in walking ability or bladder function, and later complications including spinal deformity. Based on their knowledge and experience, the committee agreed that there were more risks associated with surgery compared to enteral medication and therefore recommended that such procedures should only be considered when people on enteral or intramuscular pharmacological agents develop side effects, or when they are found to be ineffective, i.e. when other treatment options had been exhausted.

Based on their knowledge and experience, the committee noted that shared decision making between healthcare professionals and the person with spasticity and cerebral palsy (and their family or carer as appropriate) was an integral part of good service provision. Information about the benefits and risks associated with neurosurgical options should be provided to the adult with cerebral palsy as part of a multidisciplinary treatment strategy. The committee agreed that clear treatment goals need to be established prior to the procedure in order to assess its effectiveness according to individual needs and circumstances.

Due to the complex nature of this procedure the committee noted that the adult with cerebral palsy will need sufficient information to make an informed choice and that this is not always consistently provided. A number of issues should be considered when providing information specifically related to this surgical procedure, such as the need for a test dose preimplantation, requirement of pump refill and regular follow-ups, the details of what the surgical procedure involves, and a review of their 24 hour postural needs.

The uncertainty about the benefits and harms of selective dorsal rhizotomy meant that the committee could not recommend its use outside the context of a specialist multidisciplinary team (with the relevant expertise in the management of spasticity) approach to assessment. The committee noted that selective dorsal rhizotomy should not be considered in isolation but as part of the full range of treatment options. They were aware that there was related NICE guidance (NICE interventional procedure guidance on selective dorsal rhizotomy for spasticity in cerebral palsy) and cross-referenced to this.

The committee also agreed that there were specific issues and uncertainties that would need to be highlighted to the adult with cerebral palsy in relation to selective dorsal rhizotomy (for example irreversibility of the procedure or uncertainties about the long-term benefits) to allow them to make an informed choice.

The committee recognised that the response to intrathecal baclofen needs to be tested before the pump would be implanted. They therefore highlighted a couple of particular points about how the test dose (or doses if the person does not respond to the initial test dose) would be administered. The committee did not want to be too detailed about dosage and how the testing would be carried out because this is described in the British National Formulary (BNF).

The committee considered, based on the evidence, that intrathecal baclofen therapy reduces muscle tone and this could therefore lead to improved motor function and health related quality of life. The committee agreed there were likely to be risks associated with intrathecal baclofen therapy (as described above). The committee recognised that some people with cerebral palsy make functional use of increased muscle tone that can be associated with spasticity, for example to help them to walk or to transfer from a sitting to standing position. For these people reduction in muscle tone could have a negative impact on certain motor functions and therefore this was highlighted in one of the recommendations

The response to the test dose should then be assessed and discussed with the adult with cerebral palsy to ensure that a pump is only implanted when a benefit is established in advance.

Due to the limited evidence and the uncertainty around selective dorsal rhizotomy the committee decided to draft a research recommendation comparing it with continuous intrathecal baclofen pump treatment. The committee agreed that this is important because of the differences between the two procedures: selective dorsal rhizotomy is a one off surgical procedure that reduces sensory input to the sensory–motor reflex arcs in the spinal cord responsible for increased muscle tone by dividing some of the lumbar sensory nerve roots. Intensive physiotherapy is necessary for several months after the procedure particularly in patients who were previously able to walk and may have to learn different walking skills. It is a recommended NICE procedure usually offered to people with cerebral palsy and GMFCS level I-III, however the committee noted that most of the evidence comes from children under the age of 10. Intrathecal baclofen is a surgical procedure to implant an infusing pump

allowing continuous delivery of baclofen into the cerebrospinal fluid of the spine. The pump requires ongoing refilling at least twice a year and further surgery to replace the pump at end of battery life (6.5 years). It was discussed that this procedure is a recognised NICE approved treatment usually offered to people with cerebral palsy and GMFCS level III-V. The committee recommended this research because they know that both selective dorsal rhizotomy and intrathecal baclofen are effective in reducing spasticity; however there is very little comparative safety or effectiveness data and a lack of studies of selective dorsal rhizotomy in the adult population.

Cost effectiveness and resource use

Three partially applicable economic evaluations were included in this review that assessed the cost effectiveness of intrathecal baclofen. Those analyses were associated with minor to potentially serious limitations, but all three evaluations concluded intrathecal baclofen was a cost effective treatment for spasticity as intrathecal baclofen provided additional benefits to outweigh its high cost. The committee acknowledged the high cost to administer and maintain intrathecal baclofen and stated that a stepwise approach to management would be taken by using the least expensive and least invasive options first. Combined with the clinical evidence that found intrathecal baclofen to reduce muscle tone, the committee concluded there was good quality evidence that recommending intrathecal baclofen would be cost effective.

The committee also agreed that referral to a tone or spasticity management service offering continuous pump-administered intrathecal baclofen therapy should be considered only for adults who still have difficulties with spasticity despite other treatment. Targeted referral and assessment by specialists would minimise the downstream costs to manage decreases in function.

Before intrathecal baclofen pumps are implanted, the committee reiterated that a test dose (of intrathecal baclofen via lumbar puncture bolus or continuous infusion) should be provided to assess the potential effects on symptoms and function. The committee felt the cost of the test dose was justifiable as it can pre-empt treatment failure and reduce the number of people who would need additional procedures to remove the implant.

No economic evaluations were identified that assessed selective dorsal rhizotomy, but the high cost of the procedure was reported by Edwards 2010. The committee weighed up the clinical evidence from 2 before and after studies that found selective dorsal rhizotomy to reduce muscle tone, but concluded that there was not enough high quality evidence to recommend selective dorsal rhizotomy as a cost effective use of resources. Instead a research recommendation was prioritised to compare selective dorsal rhizotomy and intrathecal baclofen in adults with cerebral palsy.

Other factors the committee took into account

The committee recognised that there was an interventional procedure guideline on Selective dorsal rhizotomy for spasticity in cerebral palsy IPG373 (2010) and cross-referenced to this guideline in the recommendation.

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Appendices

Appendix A – Review protocols

Review protocol for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Table 8: Review protocol for neurosurgical procedures for spasticity

Field (based on PRISMA-P)	Content
Review question	Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?
Type of review question	Intervention review
Objective of the review	The aim of this review is to determine the relative effectiveness of intrathecal baclofen pump and selective dorsal rhizotomy compared with standard care or placebo in reducing spasticity and or dystonia in adults with cerebral palsy
Eligibility criteria – **population**/disease/condition/issue/domain	Adults aged 19 and over with cerebral palsy and spasticity with or without dystonia (median age in studies should be at least 18 years)
Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	• Intrathecal baclofen pump • Selective dorsal rhizotomy
Eligibility criteria – **comparator(s)/**control or reference (gold) standard	• Usual care (including, for example: oral drugs, botulinum toxin and physiotherapy) • Placebo
Outcomes and prioritisation	**Critical outcomes** • Walking (for ambulant people only) • Gross motor function (both upper / lower limb) ○ posture • Tone (for example Ashworth scale) • Health related quality of life

Field (based on PRISMA-P)	Content

	Important outcomes
	• Pain
	• Adverse events:
	  ○ CSF leakage
	  ○ infection
	  ○ respiratory depression
	  ○ baclofen withdrawal
	  ○ baclofen overdose.
	• Satisfaction (patient or carer reported)
	• Use of concurrent medications
	
	Minimally important differences
	• Goal Attainment Scale: 7 units
	• Modified Ashworth Scale: 1 unit
	• Quality of Upper Extremities Test: 5 units
	• ICF - Measure of Participation and Activities Screener: 2 units
	• Community Balance and Mobility Scale: 10 units
	• Five Times Sit to Stand Test: 2.5 seconds
	• Seated Shot-Put: 40cm
	• Timed Up and Go: 5 seconds
	• Pain: 30% reduction – corresponding to “much improved” or “very much improved” on a global impression of change, or 2 points on a 0 to 11 pain intensity numerical rating scale
	• Other dichotomous outcomes will use default MIDs [RR thresholds of 0.80 and 1.2]
	• Other continuous outcomes will use default MIDs [0.5 times the SD of the control group]

Eligibility criteria – **study design**	• Systematic reviews of RCTs • RCTs • Comparative cohort studies (only if RCTs unavailable or limited data to inform decision making) Consider conference abstracts only related to RCTs.

Field (based on PRISMA-P)	Content
Other inclusion / **exclusion criteria**	• Only published full text papers • Date limit 1980 onwards
Proposed sensitivity/**sub-group analysis**, or meta-regression	Groups that will be reviewed and analysed separately: • Ambulant vs. non-ambulant: GMFCS level I to III vs. GMFCS IV to V) No subgroups were identified for sensitivity analysis in the presence of heterogeneity. Important confounders (when comparative observational studies are included for interventional reviews): • degree of dystonia / spasticity • prior treatment with baclofen pumps (previous pump removed because of the infection) • adjunct medications • presence of scoliosis.
Selection process – duplicate screening/selection/analysis	A random sample of the references identified in the search will be sifted by a second reviewer. This sample size will be 10% of the total, or 100 studies if the search identifies fewer than 1000 studies. All disagreements in study inclusion will be discussed and resolved between the two reviewers. The senior systematic reviewer or guideline lead will be involved if discrepancies cannot be resolved between the two reviewers.
Data management (software)	STAR was used to sift through the references identified by the search, and for data extraction Pairwise meta-analyses and production of forest plots was done using Cochrane Review Manager (RevMan5). 'GRADEpro' was used to assess the quality of evidence for each outcome.
Information sources – databases and dates	Database(s): Embase 1974 to Present, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present; Cochrane Library; WEB OF SCIENCE
Identify if an update	Not an update
Author contacts	For details please see the guideline in development web site.
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014

Field (based on PRISMA-P)	Content
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014 The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see supplementary document C for a description of methods.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
Rationale/context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Alliance (NGA) and chaired by Dr Paul Eunson in line with section 3 of Developing NICE guidelines: the manual 2014. Staff from the NGA undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods see supplementary document C.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Roles of sponsor	NICE funds NGA to develop guidelines for those working in the NHS, public health and social care in England

Field (based on PRISMA-P)	Content
PROSPERO registration number	Not applicable

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; CSF, cerebrospinal fluid; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; GMFCS, gross motor function classification system; HTA: Health Technology Assessment; ICF: International Classification of Functioning, Disability and Health; MID: minimally important difference; NICE: National Institute for Health and Care Excellence; NGA: National Guideline Alliance; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Literature search strategies for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

This appendix is a combined search strategy and will be the same for all the evidence reviews for the A review questions as listed below:

A1: Which pharmacological treatments for spasticity (for example, enteral baclofen, tizanidine, diazepam, cannabinoids, and botulinum toxin injections) are most effective for improving motor function, participation and quality of life in adults with cerebral palsy?

A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

A3: Which treatments (pharmacological treatment (levodopa, anticholinergic drugs, and botulinum toxin injections), neurosurgical procedure (deep brain stimulation, ITB)) are most effective for managing dystonia in adults with cerebral palsy where dystonia is the predominant abnormality of tone?

Database: Medline & Embase (Multifile)

Database(s): Embase 1974 to 2018 March 22, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Table 9: Last searched on 22 March 2018

#	Searches
1	exp Cerebral Palsy/ use prmz
2	exp cerebral palsy/ use oemezd
3	((cerebral or brain or central) adj2 (pal* or paralys#s or pares#s)).tw.
4	cerebral palsy.ti,ab.
5	little? disease.tw.
6	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj5 spastic*).tw.
7	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) adj3 ataxi*).tw.
8	or/1-6
9	limit 8 to english language
10	limit 9 to (adult <18 to 64 years> or aged <65+ years>) use oemezd [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process; records were retained]
11	limit 9 to "all adult (19 plus years)" [Limit not valid in Embase; records were retained]
12	11 use prmz
13	or/10,12
14	exp Muscle Spasticity/ use prmz
15	exp spasticity/ use oemezd
16	spastic*.tw.
17	exp Dystonia/
18	dystoni*.ti,ab.

#	Searches
19	abnormal muscle tone.ti,ab.
20	14 or 15 or 16 or 17 or 18 or 19
21	exp Muscle Spasticity/ or exp Dystonia/ or exp Infusion Pumps, Implantable/ or exp Physical Therapy Modalities/ or exp Rhizotomy/ or exp Splints/ or exp Orthotic Devices/ or exp Deep Brain Stimulation/ or exp Baclofen/ad, ae, tu or exp Botulinum Toxins/ad, ae, tu or exp Diazepam/ad, ae, tu or exp Cannabinoids/ad, ae, tu or exp Acetylcholine Release Inhibitors/ad, ae, tu or exp Muscle Relaxants, Central/ad, ae, tu or exp Levodopa/ad, ae, tu or exp Dantrolene/ad, ae, tu or exp Clonazepam/ad, ae, tu or exp Pregabalin/ad, ae, tu or exp Clonidine/ad, ae, tu or exp Trihexyphenidyl/ad, ae, tu or exp Tetrabenazine/ad, ae, tu or exp Anti-Dyskinesia Agents/ad, ae, tu
22	21 use prmz
23	exp implantable infusion pump/ or exp physiotherapy/ or exp dorsal rhizotomy/ or exp splint/ or exp orthosis/ or exp brain depth stimulation/ or exp baclofen/ae, ad, cb, dt or exp botulinum toxin/ae, ad, cb, dt or exp diazepam/ae, ad, cb, dt or exp cannabinoid/ae, ad, cb, dt or exp acetylcholine release inhibitor/ae, ad, cb, dt or exp central muscle relaxant/ae, ad, cb, dt or exp levodopa/ae, ad, cb, dt or exp tizanidine/ae, ad, cb, dt or exp gabapentin/ae, ad, cb, dt or exp dantrolene/ae, ad, cb, dt or exp clonazepam/ae, ad, cb, dt or exp pregabalin/ae, ad, cb, dt or exp clonidine/ae, ad, cb, dt or exp trihexyphenidyl/ae, ad, cb, dt or exp tetrabenazine/ae, ad, cb, dt
24	23 use oemezd
25	(physiotherap* or botulinum or baclofen or tizanidine or intrathecal baclofen pump or gabapentin or levodopa or dantrolene or clonazepam or pregabalin or clonidine or dorsal rhizotomy or tetrabenazine or trihexyphenidyl or lycra or DBS or deep brain stimulat* or splint* or serial cast*).ti,ab.
26	22 or 24 or 25
27	13 and 20
28	13 and 26
29	27 or 28
30	conference abstract.pt. use oemezd
31	letter.pt. or LETTER/ use oemezd
32	Letter/ use prmz
33	EDITORIAL/ use prmz
34	editorial.pt. use oemezd
35	NEWS/ use prmz
36	exp HISTORICAL ARTICLE/ use prmz
37	note.pt. use oemezd
38	ANECDOTES AS TOPIC/ use prmz
39	COMMENT/ use prmz
40	CASE REPORT/ use prmz
41	CASE REPORT/ use oemezd
42	CASE STUDY/ use oemezd
43	(letter or comment* or abstracts).ti.
44	or/30-43
45	RANDOMIZED CONTROLLED TRIAL/ use prmz

#	Searches
46	RANDOMIZED CONTROLLED TRIAL/ use oemezd
47	random*.ti,ab.
48	or/45-47
49	44 not 48
50	ANIMALS/ not HUMANS/ use prmz
51	ANIMAL/ not HUMAN/ use oemezd
52	exp ANIMALS, LABORATORY/ use prmz
53	exp ANIMAL EXPERIMENTATION/ use prmz
54	exp MODELS, ANIMAL/ use prmz
55	exp RODENTIA/ use prmz
56	NONHUMAN/ use oemezd
57	exp ANIMAL EXPERIMENT/ use oemezd
58	exp EXPERIMENTAL ANIMAL/ use oemezd
59	ANIMAL MODEL/ use oemezd
60	exp RODENT/ use oemezd
61	(rat or rats or mouse or mice).ti.
62	or/49-61
63	29 not 62
64	remove duplicates from 63

Database: Cochrane Library

Table 10: Last searched on 22 March 2018

#1	MeSH descriptor: [Cerebral Palsy] explode all trees
#2	((cerebral or brain or central) N2 (pal* or paralys?s or pare?s))
#3	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N5 spastic*)
#4	((hemipleg* or dipleg* or tripleg* or quadripleg* or unilateral*) N3 ataxi*)
#5	#1 or #2 or #3 or #4
#6	MeSH descriptor: [Muscle Spasticity] explode all trees
#7	MeSH descriptor: [Dystonia] explode all trees
#8	Dystoni* or spastic*
#9	#6 or #7 or #8
#10	MeSH descriptor: [Baclofen] explode all trees
#11	MeSH descriptor: [Botulinum Toxins] explode all trees
#12	MeSH descriptor: [Diazepam] explode all trees
#13	MeSH descriptor: [Cannabinoids] explode all trees
#14	MeSH descriptor: [Acetylcholine Release Inhibitors] explode all trees
#15	MeSH descriptor: [Muscle Relaxants, Central] explode all trees
#16	MeSH descriptor: [Infusion Pumps, Implantable] explode all trees
#17	MeSH descriptor: [Levodopa] explode all trees
#18	MeSH descriptor: [Physical Therapy Modalities] explode all trees

#1	MeSH descriptor: [Cerebral Palsy] explode all trees
#19	physiotherap* or Botulinum or baclofen or tizanidine or intrathecal pump or gabapentin or levodopa
#20	MeSH descriptor: [Dantrolene] explode all trees
#21	MeSH descriptor: [Clonazepam] explode all trees
#22	MeSH descriptor: [Pregabalin] explode all trees
#23	MeSH descriptor: [Clonidine] explode all trees
#24	MeSH descriptor: [Trihexyphenidyl] explode all trees
#25	MeSH descriptor: [Rhizotomy] explode all trees
#26	MeSH descriptor: [Splints] explode all trees
#27	MeSH descriptor: [Orthotic Devices] explode all trees
#28	MeSH descriptor: [Deep Brain Stimulation] explode all trees
#29	MeSH descriptor: [Tetrabenazine] explode all trees
#30	Tetrabenazine or Deep Brain Stimulation or DBS or Splint* or orthotic* or dorsal Rhizotomy or Trihexyphenidyl or Clonidine or Pregabalin or Clonazepam or Dantrolene or serial cast* or lycra or splint cast*
#31	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32	#5 and #31
#33	#5 and #9
#34	#32 or #33

Database: Web of Science

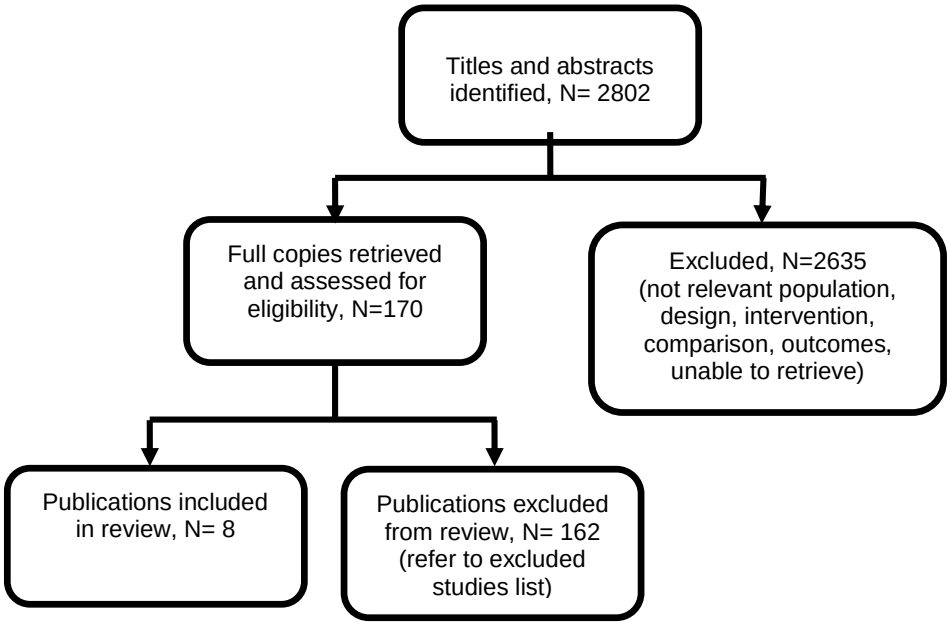
Table 11: Last searched on 27 March 2018

#6	#5 OR #3
#5	#4 AND #1
#4	ts=spasticity or ts=spastic* or ts=dystonia or ts=dystoni*
#3	#2 AND #1
#2	ts=physiotherap* or ts=Botulinum or ts=baclofen or ts=tizanidine or ts=intrathecal pump or ts=gabapentin or ts=levodopa or ts=Muscle Relaxant* or ts=Acetylcholine Release Inhibitor* or ts=Cannabinoid* or ts=Diazepam or ts=Tetrabenazine or ts=Deep Brain Stimulation or ts=DBS or ts=Splint* or ts=orthotic* or ts=dorsal Rhizotomy or ts=Trihexyphenidyl or ts=Clonidine or ts=Pregabalin or ts=Clonazepam or ts=Dantrolene or ts=serial cast* or ts=lycra or ts=splint cast*
#1	ts=Cerebral Palsy

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Figure 1: Flow diagram of clinical article selection for neurosurgery for spasticity review



Appendix D – Clinical evidence tables

Clinical evidence tables for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Table 12: Studies included in the evidence review for neurosurgical procedures for spasticity

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Albright,A.L., Cervi,A., Singletary,J., Intrathecal baclofen for spasticity in cerebral palsy, JAMA, 265, 1418-1422, 1991 **Ref Id** 58579 **Country/ies where the study was carried out** USA **Study type** Randomised cross-over trial **Aim of the study** To assess the effect of ITB on spasticity in people with CP **Study dates**	**Sample size** N = 7 (aged 15 or older) **Characteristics** Age: 15 to 31 (median 18 years) Ambulant (GMFCS I to III): NR Non-ambulant (GMFCS IV or V): NR Degree of dystonia / spasticity: moderately severe spastic quadriparetic Prior treatment with baclofen pump: NR Adjunct medications: no oral spasmolytics Presence of scoliosis: NR **Inclusion criteria** Moderately severe spastic quadriplegic CP, who used	**Interventions** Patients treated for 6 days with one lumbar puncture and intrathecal or placebo injection each day. These were done in a paired randomised double blind manner days 1 & 2 : placebo or 25µg baclofen (in a randomised order) days 3 & 4 : placebo or 50µg baclofen (in a randomised order) days 5 & 6 : placebo or 100µg baclofen (in a randomised order)	**Details** Physical therapists assessed upper and lower limb muscle tone before each injection (the baseline value) and at 2, 4, 6 and 8 hours post injection. Upper limb function was assessed before and at 4 hours after injection.	**Outcomes** Tone (follow up 8 hours) **Results** See forest plots in appendix E	**Limitations** Cochrane risk of bias Random sequence generation - low risk (coin toss) Allocation concealment - low risk Blinding of participants and personnel - low risk Blinding of outcome assessment - low risk Incomplete outcome data - low risk Selective reporting - low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Not reported **Source of funding** Grant 5M01RR00084 from the NIH general clinical research center, Bethesda, MD.	spasticity to maintain erect posture but whose gait or other movements might improve if spasticity were alleviated. Not candidates for selective posterior rhizotomy. **Exclusion criteria** Not reported				Other sources of bias - not applicable Overall low risk **Other information**
Full citation Bertelli, J. A., Ghizoni, M. F., Rodrigues Frasson, T., Fernandes Borges, K. S., Brachial plexus dorsal rhizotomy in hemiplegic cerebral palsy, Hand Clinics, 19, 687-699, 2003 **Ref Id** 586436 **Country/ies where the study was carried out** Brazil **Study type** Before and after study **Aim of the study**	**Sample size** N=7 (aged 16 or more) **Characteristics** Age: 16 - 20 (Median 19 years) Ambulant (GMFCS I to III): NR Non-ambulant (GMFCS IV or V): NR Degree of dystonia / spasticity: Ashworth 3 or more Prior treatment with baclofen pump: NR Adjunct medications: NR Presence of scoliosis: NR **Inclusion criteria**	**Interventions** Brachial plexus dorsal rhizotomy	**Details** After general anaesthesia induction, the patient was placed prone with the head in a Mayfield pin head-holder. The spinous processes of C2 and C7 were marked and confirmed by fluoroscopy. A midline incision was made across the cervical region. A two- or three-level hemilaminectomy was performed. The yellow ligament was divided and the duramere was opened. The dorsal roots were identified and sectioned; major vessels always were preserved. The duramere was closed with a watertight seal and the yellow ligament sutured. The removed bone chips then were replaced. The muscle and fascial layers were reapproximated and the skin	**Outcomes** Gross motor function Tone (follow up 15 months) **Results** See forest plots in appendix E	**Limitations** EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - done Data were analysed appropriately - done Sample size calculation performed - not done Shape of the intervention effect was

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To evaluate the effect of brachial plexus dorsal rhizotomy on spasticity and functional use of the hand. **Study dates** 2000 - 2001 **Source of funding** Not reported	Age < 20, hemiplegic CP, with spasticity, capable of understanding instructions, one muscle scoring 3 or more on the Ashworth scale **Exclusion criteria** Not reported		was closed. No postoperative neck immobilization was used. Outcomes were assessed before surgery and at 3 and 15 months after surgery.		specified - not done Protection against detection bias: Intervention unlikely to affect data collection - done Protection against detection bias: Blinded assessment of primary outcome(s) - done **Other information**
Full citation Gerszten,P.C., Albright,A.L., Barry,M.J., Effect on ambulation of continuous intrathecal baclofen infusion, Pediatric Neurosurgery, 27, 40-44, 1997 **Ref Id** 58679	**Sample size** N=24 (21 with CP, 3 with TBI) **Characteristics** Diagnosis: 21/24 CP, 3/24 traumatic brain injusry Age: mean 18 years (range 9 to 30 years)	**Interventions** Intrathecal baclofen pump, mean dose 200µg per day (range 22 to 550µg).	**Details** Pre and postoperative ambulatory status was assessed by a physiotherapist, orthopaedic surgeon or neurosurgeon. Mean postoperative follow-up was 52 months (range 12 to 93 months). Ambulatory status was classified in four levels as follows: community ambulators, household	**Outcomes** Walking Adverse events (mean follow-up 4.3 years) **Results** See forest plots in appendix E	**Limitations** EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - not clear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out USA **Study type** Before-after study **Aim of the study** To asses the effect of intrathecal baclofen on ambulatory status in people with CP **Study dates** 1989 to 1995 **Source of funding** Not reported	Ambulant (GMFCS I to III): all were ambulatory to some extent Non-ambulant (GMFCS IV or V): NR Degree of dystonia / spasticity: moderate or severe Prior treatment with baclofen pump: Adjunct medications: Presence of scoliosis: **Inclusion criteria** Ambulatory to some extent Patients had shown response to a screening trial of intrathecal baclofen (lower extremity improvement of at least 1 on the Ashworth scale - a requirement for pump implantation) **Exclusion criteria** Not reported		ambulators, non-functional ambulators or non-ambulators.		Data were analysed appropriately - done Sample size calculation performed - not done Shape of the intervention effect was specified - not done Protection against detection bias: Intervention unlikely to affect data collection - done Protection against detection bias: Blinded assessment of primary outcome(s) - not clear **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Meythaler,J.M., Guin-Renfroe,S., Law,C., Grabb,P., Hadley,M.N., Continuously infused intrathecal baclofen over 12 months for spastic hypertonia in adolescents and adults with cerebral palsy, Archives of Physical Medicine & Rehabilitation, 82, 155-161, 2001 **Ref Id** 58767 **Country/ies where the study was carried out** USA **Study type** Before and after study **Aim of the study** To determine if the continuous intrathecal delivery of baclofen will control spastic hypertonia caused by long-standing cerebral palsy (CP).	**Sample size** N=13 **Characteristics** Age: mean 25 years (13 to 43 years) Ambulant (GMFCS I to III): NR Non-ambulant (GMFCS IV or V): NR Degree of dystonia / spasticity: intractable spastic hypertonia and quadriparesis Prior treatment with baclofen pump: NR Adjunct medications: NR Presence of scoliosis: 2 patients required surgery to correct scoliosis **Inclusion criteria** People with CP with intractable spastic hypertonia, aged over 13 years old. The spastic hypertonia functionally interfered with their ADLs, sleep, mobility,	**Interventions** Intrathecal baclofen pump, starting at a dose of 100µg per day. By 12 months the mean dose was 263µg per day (±91µg; range 160 to 470µg)	**Details** The following outcomes were measured at 1, 3, 6, 9 months, and 1-year post-pump placement; The Ashworth (rigidity) scale for tone in both the LEs and the UEs a 4-point scale reflecting the number of spontaneous sustained flexor and extensor muscle spasms per hour a 5-point scale documenting deep tendon reflexes was used at the biceps, patella, and Achilles the current 24-hour infused dosage complications including cognitive dysfunction, urologic problems, infections, problems regarding physical and occupational therapy, as well as equipment malfunction	**Outcomes** Tone Adverse events (follow up one year) **Results** See forest plots in appendix E	**Limitations** EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - done Data were analysed appropriately - done Sample size calculation performed - not done Shape of the intervention effect was specified - not clear Protection against detection bias: Intervention unlikely to affect data collection - done

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Not reported **Source of funding** Funded in part by Medtronics, Inc (supplier of intrathecal baclofen pumps).	and positioning, or caused significant contractures or pain. All patients had failed to respond to oral antispasmodic treatment or had untoward side-effects. Patients were only implanted if they responded to a screening intrathecal baclofen injection (decrease of 2 points on the Ashworth scale or reduction in the number of spasms in the affected limbs, without untoward side effects) **Exclusion criteria**				Protection against detection bias: Blinded assessment of primary outcome(s) - not clear **Other information**
Full citation Motta,F., Antonello,C.E., Stignani,C., Intrathecal baclofen and motor function in cerebral palsy, Developmental Medicine and Child Neurology, 53, 443-448, 2011 **Ref Id** 133141 **Country/ies where the study was carried out** Italy	**Sample size** N=9 (aged 18 or older) **Characteristics** Age: mean age at implant 23.3 years Ambulant (GMFCS I to III): NR by age subgroup Non-ambulant (GMFCS IV or V): NR by age subgroup Degree of dystonia / spasticity: NR by age subgroup	**Interventions** Intrathecal baclofen pump	**Details** Patients were evaluated before pump implantation and 12 months after by the same team of rehabilitation therapists and orthopaedic physician	**Outcomes** Gross motor function (follow up one year) **Results** See forest plots in appendix E	**Limitations** EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - done Data were analysed appropriately - done

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Before and after study **Aim of the study** To measure the effect of intrathecal baclofen on motor function in people with CP **Study dates** 2003 to 2008 **Source of funding** Not reported	Prior treatment with baclofen pump: NR Adjunct medications: protocol implies no additional therapies Presence of scoliosis: NR **Inclusion criteria** Patients with CP who received ITB pump at a single institution **Exclusion criteria** People with learning disabilities that prevented evaluation with the Gross Motor Function Measure (GMFM). Those who underwent additional treatment (for example orthopaedic surgery or botox therapy) in the period 6 months before to 12 months after implantation. Those who did not attend follow-up visits.				Sample size calculation performed - not done Shape of the intervention effect was specified - not clear Protection against detection bias: Intervention unlikely to affect data collection - done Protection against detection bias: Blinded assessment of primary outcome(s) - not clear **Other information**
Full citation	**Sample size** N=21	**Interventions**	**Details**	**Outcomes** Walking	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Reynolds,M.R., Ray,W.Z., Strom,R.G., Blackburn,S.L., Lee,A., Park,T.S., Clinical outcomes after selective dorsal rhizotomy in an adult population, World Neurosurgery, 75, 138-144, 2011 **Ref Id** 132414 **Country/ies where the study was carried out** USA **Study type** Before and after study **Aim of the study** To evaluate the effectiveness of SDR for adults with CP related spastic diplegia. **Study dates** 1989 - 2007 **Source of funding** No commercial or financial relationships influenced the content of the article.	**Characteristics** Age: mean 26 years (range 18 to 39 years) Ambulant (GMFCS I to III): 21/21 - all had independent ambulation with or without an assistive device Non-ambulant (GMFCS IV or V): 0/21 Degree of dystonia / spasticity: Prior treatment with baclofen pump: Adjunct medications: Presence of scoliosis: **Inclusion criteria** Patients treated by a single surgeon (1989 - 2007) who had cerebral palsy-related spastic diplegia, with independent ambulation with or without an assistive device, and relatively mild orthopedic deformities. All had disabilities which were an obstacle toward achieving an acceptable quality of life. A subjective assessment was performed for those patients exhibiting the highest potential	Selective dorsal rhizotomy	The T12-L1 level was verified by plain radiographs of the thoracolumbar junction. After a single-level laminectomy, the conus medullaris was localized under ultrasonographic guidance before dural opening. The operating microscope was then used to separate the dorsal nerve roots from the ventral roots. After identification of the L2-S2 dorsal roots, electromyographic testing was performed to ensure that no ventral roots were included. Electromyographic studies were used to examine the innervation pattern of individual roots. Subsequently, each root was subdivided into three to five rootlets, which were tested in a stepwise fashion and graded for reflex threshold. Rootlets that produced excessive responses were cut. At least 25% to 33% of the rootlets were preserved at each level to avoid a postoperative sensory deficit. Patients were evaluated preoperatively several days before surgery and postoperatively at 4 months. Most patients (11/21) participated in longer periods of postoperative follow-up (mean, 17.6 ± 30.2 months; range, 4-138	Gross motor function Tone Health related quality of life Pain (follow up 4 months – for objective physical assessment; mean 5 years for function self-assessment) **Results** See forest plots in appendix E	EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - done Data were analysed appropriately - done Sample size calculation performed - not done Shape of the intervention effect was specified - not clear Protection against detection bias: Intervention unlikely to affect data collection - done Protection against detection bias:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	for functional gain after SDR and motivation to perform a home exercise program **Exclusion criteria** Not reported.		months). Assessments included baseline ambulatory status, joint ROM, GMFM, degree of spasticity, and adequate conservative therapy. Studies of joint ROM were performed with the use of a 360-degree goniometer . Muscle tone was quantified by use of the modified Ashworth scale. Each patient completed a telephone survey of subjective pre- and postoperative function. All surveys were conducted during the month of July 2007 (62.3 ± 37.4 months after SDR surgery; range, 9-132 months after SDR surgery). The survey consisted of 48 questions, including “pre-operative chief complaint” and “functional status following surgery” (improved, no change, or worse). Assist devices required for ambulation were also assessed pre- and postoperatively. Patients were instructed to estimate the time required to walk 10 feet before and after SDR surgery. Patients were asked to rate the following on a scale of 0 to 10 preoperatively versus postoperatively: ambulatory ability, spasticity, coordination, joint ROM, pain, overall quality of life, and independence.		Blinded assessment of primary outcome(s) - not clear **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			Each patient was evaluated with the Katz and Lawton ADL scales		
Full citation Tasseel Ponche, S., Ferrapie, A. L., Chenet, A., Menei, P., Gambart, G., Menegalli Bogeli, D., Perrouin Verbe, B., Gay, S., Richard, I., Intrathecal baclofen in cerebral palsy. A retrospective study of 25 wheelchair-assisted adults, Annals of Physical & Rehabilitation Medicine, 53, 483-98, 2010 **Ref Id** 343952 **Country/ies where the study was carried out** France **Study type** Before and after study **Aim of the study**	**Sample size** N=25 **Characteristics** Age: Mean 29.6 years (±12.66) Ambulant (GMFCS I to III): 6 independent with wheelchair Non-ambulant (GMFCS IV or V): 19 third party dependent with wheelchair Degree of dystonia / spasticity: bilateral spastic CP (N=21), choreo-athetotic CP (N=4). Prior treatment with baclofen pump: Adjunct medications: Presence of scoliosis: **Inclusion criteria** Functional impairment caused by treatment-refractory, generalized spasticity and a	**Interventions** Intrathecal baclofen pumps. Mean daily dose was 128µg (±97µg) in the first year rising to 401µg in the 5th year.	**Details** All implanted pumps were programmable models, except for one with continuous flow. Most were Medtronic SynchroMed II devices (16) After pump implantation, dose was adjusted and outcomes were recorded at 1, 3, 6 and 9 months post-surgery and then every year after that. Efficacy was measured subjectively using questionnaires	**Outcomes** Tone Adverse events (follow up – up to 5 years) **Results** See forest plots in appendix E	**Limitations** EPOC Quality criteria for interrupted time series (ITS) Protection against secular changes - not clear Data were analysed appropriately - done Sample size calculation performed - not done Shape of the intervention effect was specified - not clear Protection against

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To measure the effectiveness and safety of intrathecal baclofen therapy in wheelchair-dependent adults with cerebral palsy. **Study dates** 1999 - 2009 **Source of funding** Not reported. Authors insist there were no conflicts of interest.	modified Ashworth score greater or equal to 3. Patients were selected for implanted pumps using a trial bolus intrathecal injection of baclofen with the aim of decreasing Ashworth score by 1 unit. **Exclusion criteria** Not reported				detection bias: Intervention unlikely to affect data collection - done Protection against detection bias: Blinded assessment of primary outcome(s) - not clear **Other information**
Full citation Van Schaeybroeck, P., Nuttin, B., Lagae, L., Schrijvers, E., Borghgraef, C., Feys, P., Intrathecal baclofen for intractable cerebral spasticity: a prospective placebo-controlled, double-blind study, Neurosurgery, 46, 603-9; discussion 609-12, 2000 **Ref Id** 339237	**Sample size** N=11, for screening study. N=8 were implanted with baclofen pumps **Characteristics** Diagnosis: 9/11 CP, 1 stroke, 1 craniocerebral trauma Age: 8 to 55 years (median 22 years) Ambulant (GMFCS I to III): Non-ambulant (GMFCS IV or V):	**Interventions** Bolus intrathecal baclofen injection via lumbar puncture. Continuous baclofen infusion via implanted pump.	**Details** Screening trial (N=11) was done to select candidates for implanted baclofen pump. A lumbar puncture was done once daily and injections of 25, 50, 75 or 100µg baclofen or saline were given in random order & double blinded starting with 25, 50 of baclofen or saline. Spasticity of a range of muscle groups was measured before the injection and at 2, 4 and 6 hours. 8 patients then had an implanted SynchroMed infusion system programmable pump (Medtronic	**Outcomes** Tone Adverse events (follow up 1 year) **Results** See forest plots in appendix E	**Limitations** Cochrane risk of bias Random sequence generation - unclear risk Allocation concealment - unclear risk Blinding of participants and personnel - low risk

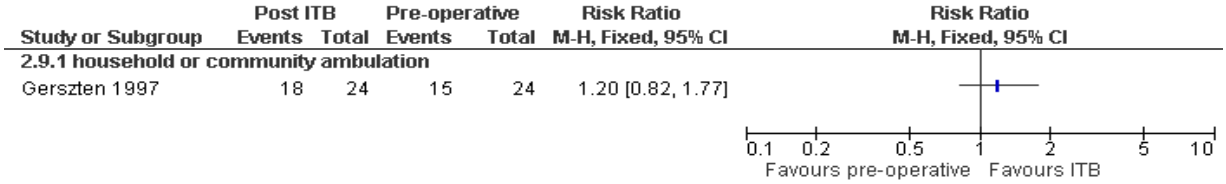
Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out Belgium **Study type** Randomised cross-over study **Aim of the study** To measure the effectiveness of intrathecal bolus injections and continuous administration of baclofen. To compare spasticity scores with functional evaluations in different muscle groups. **Study dates** Not reported **Source of funding** Not reported	Degree of dystonia / spasticity: Prior treatment with baclofen pump: Adjunct medications: Presence of scoliosis: **Inclusion criteria** Spasticity of cerebral origin. Those with severe quadriparesis as well as those with relatively good motor function were included All had received multiple oral antispasmodics in high doses - which proved ineffective or had intolerable side effects. **Exclusion criteria** Child bearing potential, pregnancy and renal or hepatic dysfunction. Those who did not respond to the baclofen screening trial (N=3) did not have pumps implanted.		Inc., MN). The tip of the catheter was placed at the 10th thoracic vertebra, using fluroscopy, with the pumps in a hypochodriac subcutaneous pocket. The minimal effective bolus injection dose was doubled to calculate the starting chronic infusion dose and adpated in the days after implantation (range 50µg to 200µg per day). During the first year of follow-up each patient was subjected to a blinded dose reduction test (where the continuous baclofen infusion was reduced to the lowest possible rate - 25 or 50 µg per day)		Blinding of outcome assessment - low risk Incomplete outcome data - low risk Selective reporting - low risk Other sources of bias - not applicable Overall unclear risk **Other information**

Appendix E – Forest plots

Forest plots for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

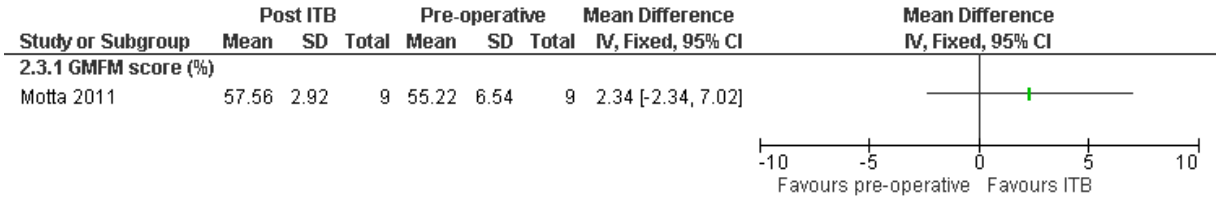
Comparison 1. Intrathecal baclofen, post versus pre-operative outcomes

Figure 2: Walking after 4 years of continuous infusion ITB versus pre-operative



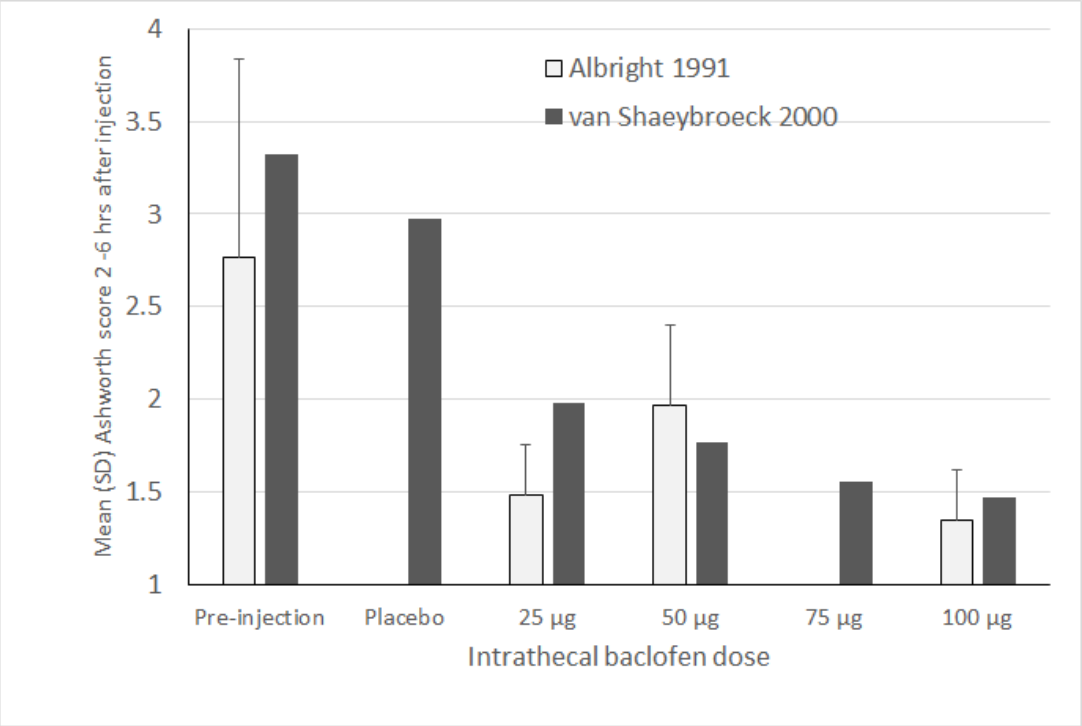
CI: confidence interval; ITB: intrathecal baclofen; M-H, Mantel-Haenszel

Figure 3: Gross motor function after 1 year of continuous infusion ITB versus pre-operative



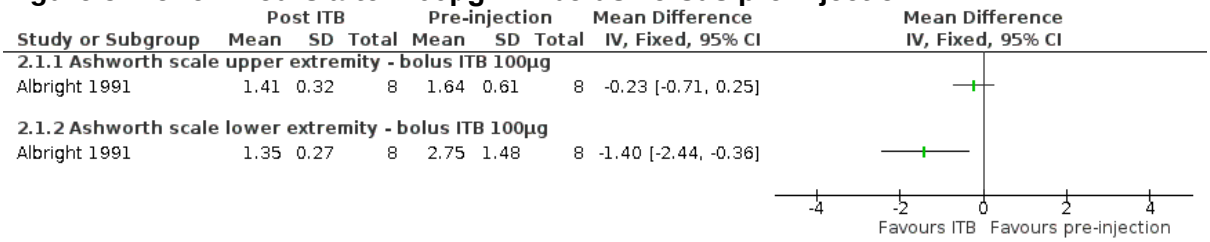
CI: confidence interval; ITB: intrathecal baclofen; IV: inverse variance; SD: standard deviation

Figure 4: Tone (Ashworth score) versus bolus intrathecal baclofen dose in adults with cerebral palsy, before and 2 to 6 hours after injection



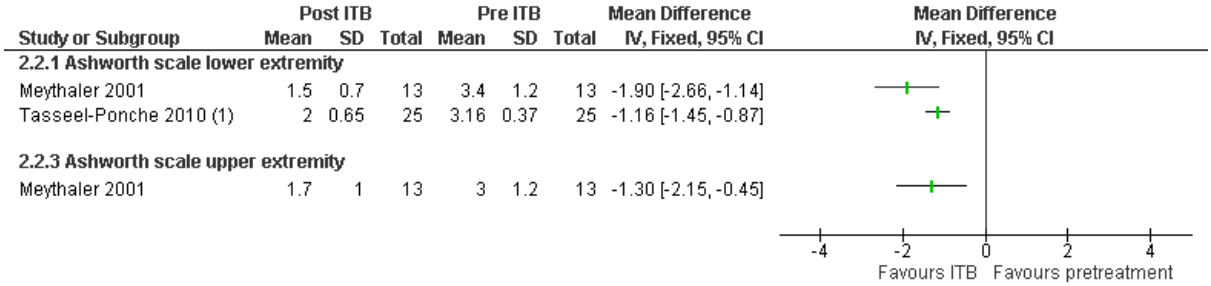
µg: microgram; SD: standard deviation

Figure 5: Tone 4 hours after 100µg ITB bolus versus pre-injection



CI: confidence interval; ITB: intrathecal baclofen; IV, inverse variance; SD: standard deviation

Figure 6: Tone after 1 to 4 years of continuous infusion ITB versus pre-operative



Footnotes
(1) Extremity not reported in Tasseel-Ponche 2010

CI: confidence interval; ITB: intrathecal baclofen; IV, inverse variance; SD: standard deviation

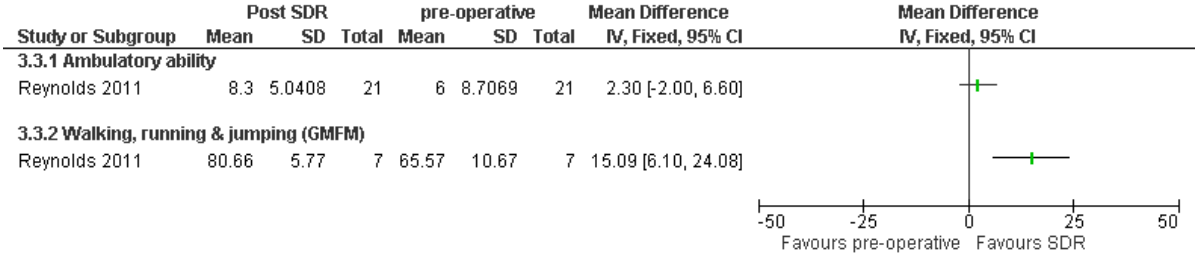
Figure 7: Adverse events after implantation of intrathecal baclofen pump (follow-up range 1 to 5 years)

Study or Subgroup	Post ITB Events	Post ITB Total
2.6.1 infection		
Gerszten 1997	1	24
Tasseel-Ponche 2010	2	25
2.6.2 catheter disconnection / breakage		
Gerszten 1997	1	24
Tasseel-Ponche 2010	2	25
van Shaeybrock 2000	1	6
2.6.3 Constipation		
Meythaler 2001	2	13
Tasseel-Ponche 2010	1	25
2.6.4 Anxiety and depression		
Tasseel-Ponche 2010	2	25
2.6.5 Seizures		
Meythaler 2001	2	13

ITB: intrathecal baclofen

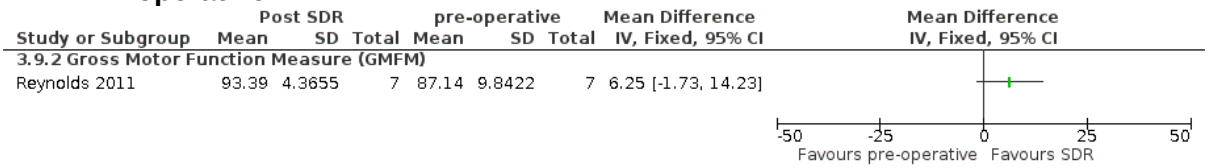
Comparison 2. Selective dorsal rhizotomy, post versus pre-operative outcomes

Figure 8: Walking up to 5 years after selective dorsal rhizotomy versus pre-operative



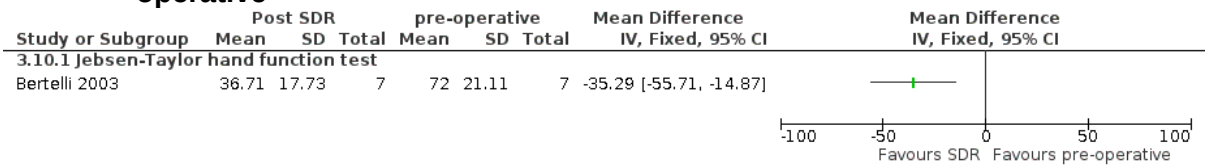
CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Figure 9: Gross motor function 4 months after selective dorsal rhizotomy versus pre-operative



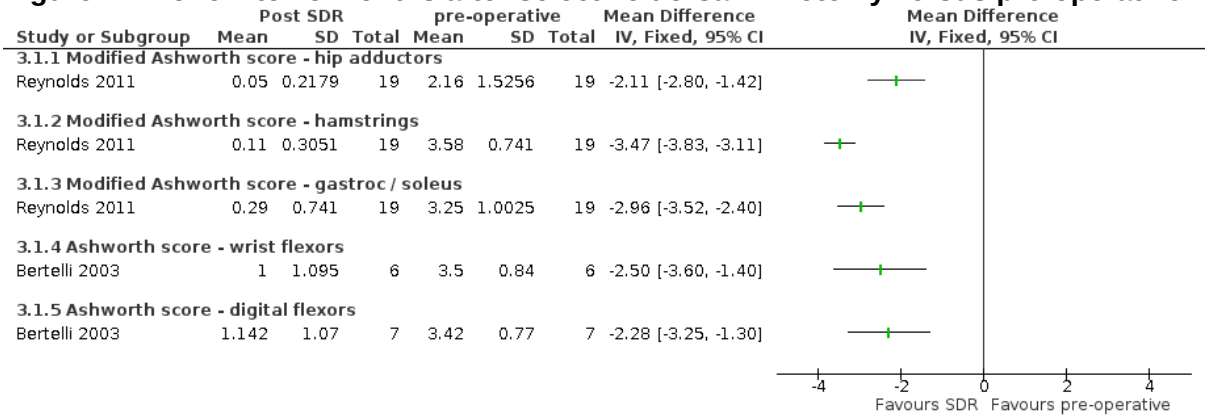
CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Figure 10: Hand function 15 months after selective dorsal rhizotomy versus pre-operative



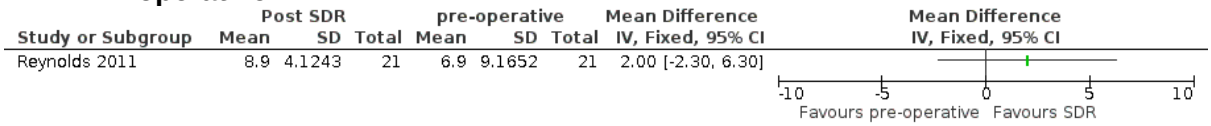
CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Figure 11: Tone 4 to 15 months after selective dorsal rhizotomy versus pre-operative



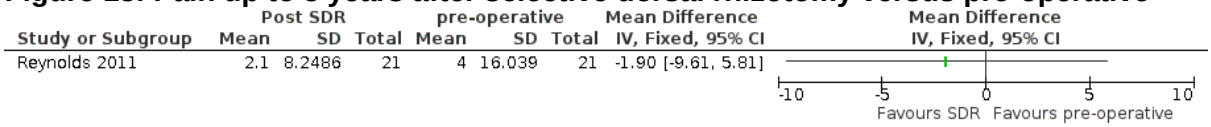
CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Figure 12: Quality of life up to 5 years after selective dorsal rhizotomy versus pre-operative



CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Figure 13: Pain up to 5 years after selective dorsal rhizotomy versus pre-operative



CI: confidence interval; IV: inverse variance; SD: standard deviation SDR: selective dorsal rhizotomy

Appendix F– GRADE tables

GRADE tables for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Table 13: Clinical evidence profile: Comparison 1: intrathecal baclofen, post-operative versus pre-operative outcomes

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intrathecal baclofen**	**Pre-operative**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Walking (follow-up 4 years; assessed with: household or community ambulation)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	18/24 (75%)	15/24 (62.5 %)	RR 1.2 (0.82 to 1.77)	125 more per 1000 (from 113 fewer to 481 more)	VERY LOW	CRITICAL
Gross motor function (follow-up 1 years; measured with: GMFM score; range of scores: 0-100; Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	9	9	-	MD 2.34 higher (2.34 lower to 7.02 higher)	VERY LOW	CRITICAL
Tone (ITB 100µg bolus) upper extremity (follow-up 4 hours; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[4]	none	8	8	-	MD 0.23 lower (0.71 lower to	LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intrathecal baclofen**	**Pre-operative**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
										0.25 higher)		
Tone (ITB 100µg bolus) lower extremity (follow-up 4 hours; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[3]	serious[2]	none	8	8	-	MD 1.4 lower (2.44 to 0.36 lower)	LOW	CRITICAL
Tone (ITB pump) lower extremity (follow-up 1 to 5 years; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
2	observational studies	no serious risk of bias	no serious inconsistency	serious[5]	serious[2]	none	38	38	-	MD ranged from 1.9 to 1.16 lower	VERY LOW	CRITICAL
Tone (ITB pump) upper extremity (follow-up 1 years; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	13	13	-	MD 1.3 lower (2.15 to 0.45 lower)	VERY LOW	CRITICAL
Health related quality of life - not reported												
-	-	-	-	-	-	-	-	-	-	-		CRITICAL
Pain - not reported												
-	-	-	-	-	-	-	-	-	-	-		IMPORTANT
Adverse events (ITB continuous infusion) (follow-up 4 to 5 years; assessed with: catheter or pump infections)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intrathecal baclofen**	**Pre-operative**	**Relative (95% CI)**	**Absolute**		
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Rate ranged from 4.2 to 8%				VERY LOW	IMPORTANT
Adverse events (ITB continuous infusion) (follow-up 4 to 5 years; assessed with: catheter disconnection / breakage)												
3	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Rate ranged from 4.2% to 17%				VERY LOW	IMPORTANT
Adverse events (ITB continuous infusion) (assessed with: Constipation)												
2	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Rate ranged from 4% to 15%				VERY LOW	IMPORTANT
Adverse events (ITB continuous infusion) (follow-up 1 to 5 years; assessed with: Anxiety and depression)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Rate was 8%				VERY LOW	IMPORTANT
Adverse events (ITB continuous infusion) (follow-up 1 years; assessed with: Seizures)												
1	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Rate was 15%				VERY LOW	IMPORTANT
Satisfaction - not reported												
-	-	-	-	-	-	-	-	-	-	-		IMPORTANT
Concurrent medications - not reported												
-	-	-	-	-	-	-	-	-	-	-		IMPORTANT

CI: confidence interval; GMFM: Gross Motor Function Measure; HRQoL: Health related quality of life; ITB: intrathecal baclofen; MD: mean difference; MID: minimally important difference; RR: risk ratio
1 No comparator
2 Confidence interval includes one default MID threshold

3 Intrathecal bolus injection rather than implanted pump
4 Number of participants <400
5 Extremity not reported in one of the studies

Table 14: Clinical evidence profile: Comparison 2: selective dorsal rhizotomy, post-operative versus pre-operative outcomes

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SDR**	**Pre-operative**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Walking (follow-up 5 years; measured with: Self rated ambulatory ability; range of scores: 0-10; Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	21	21	-	MD 2.3 higher (2 lower to 6.6 higher)	VERY LOW	CRITICAL
Walking (follow-up 5 years; measured with: walking, running & jumping sub-scale of GMFM; range of scores: 0-100; Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	7	7	-	MD 15.09 higher (6.1 to 24.08 higher)	VERY LOW	CRITICAL
Gross motor function (follow-up 15 months; measured with: Jebsen-Taylor hand function test; range of scores: 0-720; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	7	7	-	MD 35.29 lower (55.71 to 14.87 lower)	VERY LOW	CRITICAL
Gross motor function (follow-up 4 months; measured with: Gross Motor Function Measure (GMFM); range of scores: 0-100; Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	7	7	-	MD 6.25 higher (1.73 lower to	LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SDR	Pre-operative	Relative (95% CI)	Absolute	Quality	Importance
										14.23 higher)		
Tone - hip adductors (follow-up 4 months; measured with: Modified Ashworth scale; range of scores: 0-4; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19	19	-	MD 2.11 lower (2.8 to 1.42 lower)	VERY LOW	CRITICAL
Tone - hamstrings (follow-up 4 months; measured with: Modified Ashworth scale; range of scores: 0-4; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19	19	-	MD 3.47 lower (3.83 to 3.11 lower)	VERY LOW	CRITICAL
Tone - gastroc / soleus (follow-up 4 months; measured with: Modified Ashworth scale; range of scores: 0-4; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19	19	-	MD 2.96 lower (3.52 to 2.4 lower)	VERY LOW	CRITICAL
Tone - wrist flexors (follow-up 15 months; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	6	6	-	MD 2.5 lower (3.6 to 1.4 lower)	VERY LOW	CRITICAL
Tone - digital flexors (follow-up 15 months; measured with: Ashworth scale; range of scores: 1-5; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	7	7	-	MD 2.28 lower (3.25 to 1.3 lower)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SDR**	**Pre-operative**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Health related quality of life (follow-up 5 years; measured with: Self rated visual analogue scale; range of scores: 0-10; Better indicated by higher values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	21	21	-	MD 2 higher (2.3 lower to 6.3 higher)	VERY LOW	CRITICAL
Pain (follow-up 5 years; measured with: Self rated visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	21	21	-	MD 1.9 lower (9.61 lower to 5.81 higher)	VERY LOW	IMPORTANT
Adverse events - not reported												
-	-	-	-	-	-	-	-	-	-	-		IMPORTANT
Satisfaction - not reported												
-	**-**	**-**	**-**	**-**	**-**	**-**	-	-	-	-		IMPORTANT
Concurrent medications - not reported												
-	-	-	-	-	-	-	-	-	-	-		IMPORTANT

CI: confidence interval; GMFM: Gross Motor Function Measure; MD: mean difference; MID: minimally important difference; SDR: selective dorsal rhizotomy
1 Confidence interval includes one default MID threshold
2 Number of participants <400

Appendix G – Economic evidence study selection

Economic evidence study selection for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

See supplementary material D for the economic evidence study selection.

Appendix H – Economic evidence tables

Economic evidence tables for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

See supplementary material D for the economic evidence tables.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

See supplementary material D for the economic evidence profiles.

Appendix J – Health economic analysis

Health economic analysis for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

No economic analysis was included in this review.

Appendix K – Excluded studies

Clinical and economic lists of excluded studies for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Clinical studies

Table 15: Excluded clinical studies for neurosurgical procedures for spasticiy

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Agarwal, S., Patel, T., Shah, N., Patel, B. M., Comparative study of therapeutic response to baclofen vs tolperisone in spasticity, Biomedicine and Pharmacotherapy, 87, 628-635, 2017	Not intrathecal.
Aiona, M. D., Sussman, M. D., Treatment of spastic diplegia in patients with cerebral palsy: Part II, Journal of Pediatric Orthopaedics-Part B, 13, S13-S38, 2004	Expert review
Albright, A. L., Intrathecal baclofen in cerebral palsy movement disorders, Journal of Child Neurology, 11 Suppl 1, S29-35, 1996	Expert review
Albright, A. L., Spastic Cerebral-Palsy - Approaches to Drug-Treatment, Cns Drugs, 4, 17-27, 1995	Expert review
Albright, Al, Cervi, A, Singletary, J, Intrathecal baclofen for spasticity in cerebral palsy, Jama, 265, 1418-22, 1991	Duplicate record
Albright,A.L., Barron,W.B., Fasick,M.P., Polinko,P., Janosky,J., Continuous intrathecal baclofen infusion for spasticity of cerebral origin, JAMA: Journal of the American Medical Association, 270, 2475-2477, 1993	Mean age 14 years
Albright,A.L., Barry,M.J., Fasick,P., Barron,W., Shultz,B., Continuous intrathecal baclofen infusion for symptomatic generalized dystonia, Neurosurgery, 38, 934-938, 1996	3/5 had CP - 2 were aged 7
Albright,A.L., Barry,M.J., Hoffmann,P., Intrathecal L-baclofen for cerebral spasticity: case report, Neurology, 45, 2110-2111, 1995	Case report
Albright,A.L., Barry,M.J., Painter,M.J., Shultz,B., Infusion of intrathecal baclofen for generalized dystonia in cerebral palsy, Journal of Neurosurgery, 88, 73-76, 1998	Median age 12 years
Albright,A.L., Barry,M.J., Shafton,D.H., Ferson,S.S., Intrathecal baclofen for generalized dystonia, Developmental Medicine and Child Neurology, 43, 652-657, 2001	Median age 13 years
Albright,A.L., Thompson,K., Carlos,S., Minnigh,M.B., Cerebrospinal fluid baclofen concentrations in patients undergoing continuous intrathecal baclofen therapy, Developmental Medicine and Child Neurology, 49, 423-425, 2007	Outcome not in protocol
Aldahondo, N., Munger, M., Krach, L., Novacheck, T., Schwartz, M., Comprehensive long-term outcomes after Selective Dorsal Rhizotomy, Developmental Medicine and Child Neurology, 58, 28, 2016	Abstract only - insufficient detail reported to extract outcomes.

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Alden, T. D., Lytle, R. A., Park, T. S., Noetzel, M. J., Ojemann, J. G., Intrathecal baclofen withdrawal: a case report and review of the literature, Childs Nervous System, 18, 522-525, 2002	Case report -expert review
Al-Shaar, H. A., Alkhani, A., Intrathecal baclofen therapy for spasticity: A compliance-based study to indicate effectiveness, Surgical Neurology International, 7, S539-S541, 2016	8/27 had CP - not reported separately
Arishima, H., Kikuta, K. I., Intrathecal baclofen pump implantation in prone position for a cerebral palsy patient with severe scoliosis: A case report, Neuromodulation, 18, 214-216, 2015	Case report
Avellino, A. M., Loeser, J. D., Intrathecal baclofen for the treatment of intractable spasticity of spine or brain etiology, Neuromodulation, 3, 75-81, 2000	Case series (N=4 with CP)
Bakay, R. A. E., Intrathecal baclofen for intractable cerebral spasticity: A prospective placebo-controlled, double-blind study - Comment, Neurosurgery, 46, 610-611, 2000	comment on Albright trial
Bassani, L., Harter, D. H., Paraspinal subfascial placement of lumbar intrathecal baclofen catheters: Short-term outcomes of a novel technique - Clinical article, Journal of Neurosurgery: Pediatrics, 9, 93-98, 2012	Median age < 12. Outcomes not relevant
Beaufils, J., Ferrapie, A. L., Dinomais, M., Saout, V., Menei, P., Richard, I., Progression of scoliosis after intrathecal baclofen in an adult patient with multiple sclerosis, Evolutivite d'une scoliose apres baclofene intrathecal chez une patiente adulte sclerosee en plaque. [French, English], Annals of Physical and Rehabilitation Medicine, 55, e206-e207+e208, 2012	Case report
Becker,R., Alberti,O., Bauer,B.L., Continuous intrathecal baclofen infusion in severe spasticity after traumatic or hypoxic brain injury, Journal of Neurology, 244, 160-166, 1997	Not CP
Becker,W.J., Harris,C.J., Long,M.L., Ablett,D.P., Klein,G.M., DeForge,D.A., Long-term intrathecal baclofen therapy in patients with intractable spasticity, Canadian Journal of Neurological Sciences, 22, 208-217, 1995	Not CP
Beecham, E., Candy, B., Howard, R., McCulloch, R., Laddie, J., Rees, H., Vickerstaff, V., Bluebond-Langner, M., Jones, L., Pharmacological interventions for pain in children and adolescents with life-limiting conditions, Cochrane Database of Systematic Reviews, 3, CD010750, 2015	Systematic review - includes Bonouvire
Belverud, S., Mogilner, A., Schulder, M., Intrathecal pumps, Neurotherapeutics, 5, 114-122, 2008	Expert review
Bensmail,D., Quera Salva,M.A., Roche,N., Benyahia,S., Bohic,M., Denys,P., Bussel,B., Lofaso,F., Effect of intrathecal baclofen on sleep and respiratory function in patients with spasticity, Neurology, 67, 1432-1436, 2006	Outcomes not in protocol
Berman, B., Vaughan, C. L., Peacock, W. J., The Effect of Rhizotomy on Movement in Patients with Cerebral-Palsy, American Journal of Occupational TherapyAm J Occup Ther, 44, 511-516, 1990	Mean age 9.3 years

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Bonouvrie, L. A., Becher, J. G., Vles, J. S. H., Boeschoten, K., Soudant, D., de Groot, V., van Ouwerkerk, W. J. R., Strijers, R. L. M., Foncke, E., Geytenbeek, J., van de Ven, P. M., Teernstra, O., Vermeulen, R. J., Intrathecal baclofen treatment in dystonic cerebral palsy: A randomized clinical trial: The IDYS trial, BMC Pediatrics, 13, 2013	Trial protocol - see Bonouvrie 2016 for results
Bonouvrie, L., Becher, J., Soudant, D., Buizer, A., Van Ouwerkerk, W., Vles, G., Vermeulen, R. J., The effect of intrathecal baclofen treatment on activities of daily life in children and young adults with cerebral palsy and progressive neurological disorders, European Journal of Paediatric Neurology, 20, 538-544, 2016	Mean age at implantation was 12.4 years for those with spastic CP and 16.0 for those with dystonic CP
Borrini,L., Bensmail,D., Thiebaut,J.B., Hugeron,C., Rech,C., Jourdan,C., Occurrence of adverse events in long-term intrathecal baclofen infusion: a 1-year follow-up study of 158 adults, Archives of Physical Medicine and Rehabilitation, 95, 1032-1038, 2014	Minority had CP - results not reported separately
Brennan, P. M., Whittle, I. R., Intrathecal baclofen therapy for neurological disorders: a sound knowledge base but many challenges remain, British Journal of Neurosurgery, 22, 508-19, 2008	expert review
Brochard,S., Lempereur,M., Filipetti,P., Remy-Neris,O., Changes in gait following continuous intrathecal baclofen infusion in ambulant children and young adults with cerebral palsy, Developmental Neurorehabilitation, 12, 397-405, 2009	Only one person aged > 16 years
Broseta,J., Garcia-March,G., Sanchez-Ledesma,M.J., Anaya,J., Silva,I., Chronic intrathecal baclofen administration in severe spasticity, Stereotactic and Functional Neurosurgery, 54-55, 147-153, 1990	Not CP
Burke, D., Dorsal Rhizotomy for Cerebral-Palsy, Muscle & NerveMuscle Nerve, 18, 126-127, 1995	Comment on Logigian 1994 study
Butler,C., Campbell,S., Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy, Developmental Medicine & Child Neurology, 42, 634-645, 2000	Systematic review, outdated
Cahan,L.D., Adams,J.M., Perry,J., Beeler,L.M., Instrumented gait analysis after selective dorsal rhizotomy, Developmental Medicine and Child Neurology, 32, 1037-1043, 1990	Median age 6.5 years.
Caird,M.S., Palanca,A.A., Garton,H., Hensinger,R.N., Ayyangar,R.N., Drongowski,A., Farley,F.A., Outcomes of posterior spinal fusion and instrumentation in patients with continuous intrathecal baclofen infusion pumps, Spine, 33, E94-E99, 2008	Intervention not in protocol
Campbell,W.M., Ferrel,A., McLaughlin,J.F., Grant,G.A., Loeser,J.D., Graubert,C., Bjornson,K., Long-term safety and efficacy of continuous intrathecal baclofen, Developmental Medicine & Child Neurology, 44, 660-665, 2002	Median age 12 years
Cevikol, A., Ecerkale, O., Sancioglu, H., Sorar, M., Cakci, A., Intrathecal Baclofen Therapy Applications: Assessment of Our Cases Between 2004-2012, Turkiye Fiziksel Tip Ve Rehabilitasyon Dergisi-Turkish Journal of Physical Medicine and Rehabilitation, 60, 295-301, 2014	Not CP

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Clearfield, J. S., Nelson, M. E. S., McGuire, J., Rein, L. E., Tarima, S., Intrathecal Baclofen Dosing Regimens: A Retrospective Chart Review, Neuromodulation, 19, 642-649, 2016	N=5, outcome not in protocol (dosage)
Collin,C., Young,C., Cerebral palsy: The adult perspective, Current Paediatrics, 10, 172-176, 2000	Expert review
Concalves,J., Garcia-March,G., Sanchez-Ledesma,M.J., Onzain,I., Broseta,J., Management of intractable spasticity of supraspinal origin by chronic cervical intrathecal infusion of baclofen, Stereotactic and Functional Neurosurgery, 62, 108-112, 1994	3/11 had CP
Cruikshank,M., Eunson,P., Intravenous diazepam infusion in the management of planned intrathecal baclofen withdrawal, Developmental Medicine & Child Neurology, 49, 626-628, 2007	Intervention not in protocol
de Lissovoy, G., Matza, L. S., Green, H., Werner, M., Edgar, T., Cost-effectiveness of intrathecal baclofen therapy for the treatment of severe spasticity associated with cerebral palsy, Journal of Child Neurology, 22, 49-59, 2007	Cost effectiveness study - children with CP
Delhaas,E.M., Beersen,N., Redekop,W.K., Klazinga,N.S., Long-term outcomes of continuous intrathecal baclofen infusion for treatment of spasticity: A prospective multicenter follow-up study, Neuromodulation, 11, 227-236, 2008	12/115 had CP, no subgroup analysis
Devilliers, J. C., Selective Posterior Rhizotomy in the Treatment of Spasticity, South African Medical Journal, 83, 709-710, 1993	6/23 had CP
Dickerman, R. D., Stevens, Q. E., Schneider, S. J., The role of surgical placement and pump orientation in intrathecal pump system failure: a technical report, Pediatric Neurosurgery, 38, 107-9, 2003	No details about the study population
Duan, Y., Luo, X., Gao, X., Sun, C., Cervical selective dorsal rhizotomy for treating spasticity in upper limb neurosurgical way to neurosurgical technique, Interdisciplinary Neurosurgery: Advanced Techniques and Case Management, 2, 57-60, 2015	Case report
Dudgeon,B.J., Libby,A.K., McLaughlin,J.F., Hays,R.M., Bjornson,K.P., Roberts,T.S., Prospective measurement of functional changes after selective dorsal rhizotomy, Archives of Physical Medicine and Rehabilitation, 75, 46-53, 1994	SDR in childhood
Dudley, R. W. R., Parolin, M., Gagnon, B., Saluja, R. S., Yap, R., Monpetit, K., Ruck, J., Poulin, C., Cantin, M. A., Benaroch, T., Farmer, J. P., Beneficial Functional Outcomes of Selective Dorsal Rhizotomy (SDR) Are Long Lasting and Alter the Natural History of Motor Development in Spastic Cerebral Palsy, Neurosurgery, 71, E564-E565, 2012	Abstract only- SDR in childhood
Eldabe, S., Intrathecal Baclofen Pump Implantation in Prone Position for a Cerebral Palsy Patient With Severe Scoliosis: A Case Report COMMENT, Neuromodulation, 18, 216-216, 2015	Case report
Engsberg,J.R., Ross,S.A., Park,T.S., Changes in ankle spasticity and strength following selective dorsal rhizotomy and physical therapy for spastic cerebral palsy, Journal of Neurosurgery, 91, 727-732, 1999	mean age 12
Ethans,K.D., Schryvers,O.I., Nance,P.W., Casey,A.R., Intrathecal drug therapy using the Codman Model 3000 Constant Flow	1/17 had CP

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Implantable Infusion Pumps: experience with 17 cases, Spinal Cord, 43, 214-218, 2005	
Fares,Y., Khazim,R.M., del Barrio,E.R., Burzaco,J.A., Dosage of intrathecal baclofen maintenance therapy in the spastic syndromes, Journal Medical Libanais - Lebanese Medical Journal, 52, 13-18, 2004	6/23 had CP
Fink, J. K., Fillingkatz, M. R., Barton, N. W., Macrae, P. R., Hallett, M., Cohen, W. E., Treatable Dystonia Presenting as Spastic Cerebral-Palsy, Pediatrics, 82, 137-138, 1988	Case report
Francisco,G.E., The role of intrathecal baclofen therapy in the upper motor neuron syndrome, Europa Medicophysica, 40, 131-143, 2004	Not CP
Gage, J. R., Novacheck, T. F., An update on the treatment of gait problems in cerebral palsy, Journal of Pediatric Orthopaedics-Part B, 10, 265-274, 2001	Expert review
Gelber, D. A., Jozefczyk, P. B., Therapeutics in the management of spasticity, Neurorehabilitation and Neural Repair, 13, 5-14, 1999	Expert review
Gerszten,P.C., Albright,A.L., Johnstone,G.F., Intrathecal baclofen infusion and subsequent orthopedic surgery in patients with spastic cerebral palsy, Journal of Neurosurgery, 88, 1009-1013, 1998	Relevant outcomes not reported
Gilmartin, R. C., Rawlins, P., Seizures in Epileptic Cerebral-Palsy Patients Receiving Intrathecal Baclofen Infusion, Epilepsia, 36, G12-G12, 1995	Abstract only - insufficient detail
Gilmartin,R., Bruce,D., Storrs,B.B., Abbott,R., Krach,L., Ward,J., Bloom,K., Brooks,W.H., Johnson,D.L., Madsen,J.R., McLaughlin,J.F., Nadell,J., Intrathecal baclofen for management of spastic cerebral palsy: multicenter trial, Journal of Child Neurology, 15, 71-77, 2000	Median age 11.2 years
Ginsburg,G.M., Lauder,A.J., Progression of scoliosis in patients with spastic quadriplegia after the insertion of an intrathecal baclofen pump, Spine, 32, 2745-2750, 2007	Most patients were not skeletally mature
Gormley, M. E., Jr., O'Brien, C. F., Yablon, S. A., A clinical overview of treatment decisions in the management of spasticity, Muscle & Nerve SupplementMuscle Nerve Suppl, 6, S14-20, 1997	expert review
Goyal, V., Laisram, N., Wadhwa, R. K., Kothari, S. Y., Prospective randomized study of oral Diazepam and Baclofen on spasticity in cerebral palsy, Journal of Clinical and Diagnostic Research, 10, RC01-RC05, 2016	Oral baclofen in children
Green,C., Proch,C., Gara,S.E., The changing face of cerebral palsy: A review of the disorder and its treatment, Journal of Neurologic Rehabilitation, 11, 245-253, 1997	Expert review
Gump, W. C., Mutchnick, I. S., Moriarty, T. M., Selective dorsal rhizotomy for spasticity not associated with cerebral palsy: reconsideration of surgical inclusion criteria, Neurosurgical Focus, 35, E6, 2013	Not CP
Gunnarsson, S., Samuelsson, K., Patient experiences with intrathecal baclofen as a treatment for spasticity - a pilot study, Disability & Rehabilitation, 37, 834-41, 2015	2/14 had CP, qualitative study

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Hattori, N., Hirayama, T., Katayama, Y., Cost-Effectiveness Analysis of Intrathecal Baclofen Therapy in Japan, Neurologia Medico-Chirurgica, 52, 482-487, 2012	Not CP
Heimburger,R.F., Slominski,A., Griswold,P., Cervical posterior rhizotomy for reducing spasticity in cerebral palsy, Journal of Neurosurgery, 39, 30-34, 1973	Median age not reported
Humphreys, R. P., Cost-Analysis of Continuous Intrathecal Baclofen Versus Selective Functional Posterior Rhizotomy in the Treatment of Spastic Quadriplegia Associated with Cerebral-Palsy - Editorial Comment, Pediatric Neurosurgery, 22, 265-265, 1995	Cost effectiveness of ITB in children with CP
Hurvitz, E. A., Marciniak, C. M., Daunter, A. K., Haapala, H. J., Stibb, S. M., McCormick, S. F., Muraszko, K. M., Gaebler-Spira, D., Functional outcomes of childhood dorsal rhizotomy in adults and adolescents with cerebral palsy: Clinical article, Journal of Neurosurgery: Pediatrics, 11, 380-388, 2013	Mean age at SDR 6 years
Hurvitz, E. A., Marciniak, C. M., Muraszko, K. M., Gaebler-Spira, D., Dorsal rhizotomy Response, Journal of Neurosurgery-Pediatrics, 11, 378-379, 2013	Response to editorial on Horvitz 2013
Jones,R.F., Lance,J.W., Bacloffen (Lioresal) in the long-term management of spasticity, Medical Journal of Australia, 1, 654-657, 1976	2/113 had CP
Kai, M., Yongjie, L., Ping, Z., Long-term results of selective dorsal rhizotomy for hereditary spastic paraparesis, Journal of Clinical Neuroscience, 21, 116-20, 2014	Not CP
Kamensek, J., Continuous intrathecal baclofen infusions. An introduction and overview, AXON, 20, 67-72, 1999	Expert review
Keating, R. F., Butler, S., DeFreitas, T., Oluigbo, C., Rabin, J., Lavenstein, B., Magge, S., Myseros, J., Indwelling intrathecal baclofen trial: Assessment of efficacy and safety in 124 pediatric patients with cerebral palsy and dystonic overlay, Journal of Neurosurgery, 122 (6), A1573, 2015	Abstract, mean age 13 years
Khan, A. A., Birks-Agnew, I., Bullock, P., Rushton, D., Clinical outcome and complications of intrathecal baclofen pump in multiple sclerosis patients: A retrospective study, NeuroRehabilitation, 27, 117-120, 2010	Not CP
Kim,H.S., Steinbok,P., Wickenheiser,D., Predictors of poor outcome after selective dorsal rhizotomy in treatment of spastic cerebral palsy, Childs Nervous System, 22, 60-66, 2006	Mean age at SDR: 5.5 years
Kishima, H., Yanagisawa, T., Goto, Y., Oshino, S., Maruo, T., Tani, N., Khoo, H. M., Hosomi, K., Hirata, M., Yoshimine, T., Respiratory Function Under Intrathecal Baclofen Therapy in Patients With Spastic Tetraplegia, Neuromodulation, 19, 650-654, 2016	N=2 with CP
Kita, M., Goodkin, D. E., Drugs used to treat spasticity, Drugs, 59, 487-495, 2000	Expert review
Knapp, M. E., Cerebral palsy. 2, Postgraduate Medicine, 47, 247-252, 1970	Expert review

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Kolaski,K., Logan,L.R., A review of the complications of intrathecal baclofen in patients with cerebral palsy, NeuroRehabilitation, 22, 383-395, 2007	Systematic review
Krach, L., Intrathecal baclofen and motor function in cerebral palsy, Developmental Medicine and Child Neurology, 53, 391-391, 2011	Commentary on Motta 2011
Krach,L.E., Pharmacotherapy of spasticity: Oral medications and intrathecal baclofen, Journal of Child Neurology, 16, 31-36, 2001	Expert review
Krach,L.E., Intrathecal baclofen use in adults with cerebral palsy, Developmental Medicine and Child Neurology, 51, 106-112, 2009	Expert review
Krach,L.E., Kriel,R.L., Day,S.M., Strauss,D.J., Survival of individuals with cerebral palsy receiving continuous intrathecal baclofen treatment: a matched-cohort study, Developmental Medicine and Child Neurology, 52, 672-676, 2010	SDR in childhood CP
Krach,L.E., Kriel,R.L., Gilmartin,R.C., Swift,D.M., Storrs,B.B., Abbott,R., Ward,J.D., Bloom,K.K., Brooks,W.H., Madsen,J.R., McLaughlin,J.F., Nadell,J.M., GMFM 1 year after continuous intrathecal baclofen infusion, Pediatric Rehabilitation, 8, 207-213, 2005	Median age 10.6 years
Krach,L.E., Kriel,R.L., Gilmartin,R.C., Swift,D.M., Storrs,B.B., Abbott,R., Ward,J.D., Bloom,K.K., Brooks,W.H., Madsen,J.R., McLaughlin,J.F., Nadell,J.M., Hip status in cerebral palsy after one year of continuous intrathecal baclofen infusion, Pediatric Neurology, 30, 163-168, 2004	Median age 10
Krach,L.E., Kriel,R.L., Nugent,A.C., Complex Dosing Schedules for Continuous Intrathecal Baclofen Infusion, Pediatric Neurology, 37, 354-359, 2007	Median age at treatment < 15 years
Krach,L.E., Nettleton,A., Klempka,B., Satisfaction of individuals treated long-term with continuous infusion of intrathecal baclofen by implanted programmable pump, Pediatric Rehabilitation, 9, 210-218, 2006	Median age not reported (range 5 to 42 years)
Langerak, N. G., Lamberts, R. P., Fieggen, A. G., Peter, J. C., van der Merwe, L., Peacock, W. J., Vaughan, C. L., A prospective gait analysis study in patients with diplegic cerebral palsy 20 years after selective dorsal rhizotomy, Journal of Neurosurgery. Pediatrics., 1, 180-6, 2008	Childhood SDR (at median 5 years)
Langerak, N. G., Vaughan, C. L., Peter, J. C., Fieggen, A. G., Peacock, W. J., Long-term outcomes of dorsal rhizotomy, Journal of Neurosurgery-Pediatrics, 12, 664-665, 2013	Reply to comment on article
Langerak,N.G., Tam,N., Vaughan,C.L., Fieggen,A.G., Schwartz,M.H., Gait status 17-26 years after selective dorsal rhizotomy, Gait and Posture, 35, 244-249, 2012	SDR in childhood
Langerak,N.G., Lamberts,R.P., Fieggen,A.G., Peter,J.C., Peacock,W.J., Vaughan,C.L., Functional Status of Patients With Cerebral Palsy According to the International Classification of Functioning, Disability and Health Model: A 20-Year Follow-Up Study After Selective Dorsal Rhizotomy, Archives of Physical Medicine and Rehabilitation, 90, 994-1003, 2009	Childhood SDR

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Lapeyre, E., Kuks, J. B. M., Meijler, A. J., Spasticity: Revisiting the role and the individual value of several pharmacological treatments, NeuroRehabilitation, 27, 193-200, 2010	Expert review
Latash,M.L., Penn,R.D., Changes in voluntary motor control induced by intrathecal baclofen in patients with spasticity of different etiology, Physiotherapy Research International, 1, 229-246, 1996	N=2 with CP
Lazorthes, Y. R., Continuous Intrathecal Baclofen Infusion in the treatment of spastic cerebral palsy: A prospective multicenter study, Neurosurgery, 59, 484-484, 2006	Abstract only, age 6-8 years
Lazorthes,Y., Sallerin-Caute,B., Verdie,J.C., Bastide,R., Carillo,J.P., Chronic intrathecal baclofen administration for control of severe spasticity, Journal of Neurosurgery, 72, 393-402, 1990	1/18 had CP
Leary, S. M., Gilpin, P., Lockley, L., Rodriguez, L., Jarett, L., Stevenson, V. L., Intrathecal baclofen therapy improves functional intelligibility of speech in cerebral palsy, Clinical Rehabilitation, 20, 228-231, 2006	Case report
Leland Albright, A., Barry, M. J., Shafron, D. H., Ferson, S. S., Intrathecal baclofen for generalized dystonia, Developmental Medicine and Child Neurology, 43, 652-657, 2001	median age 13
Levy, R. M., The Failed and Future Promise of Intraspinal Drug Administration for Neurologic Disorders, Neuromodulation, 15, 165-170, 2012	Expert review
McCormick, Z. L., Chu, S. K., Binler, D., Neudorf, D., Mathur, S. N., Lee, J., Marciniak, C., Intrathecal Versus Oral Baclofen: A Matched Cohort Study of Spasticity, Pain, Sleep, Fatigue, and Quality of Life, PM and R, 8, 553-562, 2016	10/62 had CP - results not reported separately
McLaughlin, J., Motor function after dorsal rhizotomy, Developmental Medicine and Child Neurology, 54, 389-390, 2012	Editorial
McLaughlin, J. F., Bjornson, K. F., Astley, S. J., Hays, R. M., Hoffinger, S. A., Roberts, T. S., Selective Dorsal Rhizotomy in Spastic Cerebral-Palsy - Critical-Evaluation of a Prospective Series, Pediatric Research, 35, A383-A383, 1994	Abstract only, SDR in children
McLaughlin, Jf, Bjornson, Kf, Astley, Sj, Hays, Rm, Hoffinger, Sa, Armantrout, Ea, Roberts, Ts, The role of selective dorsal rhizotomy in cerebral palsy: critical evaluation of a prospective clinical series, Developmental Medicine and Child Neurology, 36, 755-69, 1994	Expert review
Mess,S.A., Kim,S., Davison,S., Heckler,F., Implantable baclofen pump as an adjuvant in treatment of pressure sores, Annals of Plastic Surgery, 51, 465-467, 2003	Case report
Meythaler,J.M., Guin-Renfroe,S., Hadley,M.N., Continuously infused intrathecal baclofen for spastic/dystonic hemiplegia: a preliminary report, American Journal of Physical Medicine and Rehabilitation, 78, 247-254, 1999	Not CP
Misbahuddin, A., Warner, T. T., Dystonia: an update on genetics and treatment, Current Opinion in NeurologyCurr Opin Neurol, 14, 471-5, 2001	Expert review

Excluded studies - A2 Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?	
Study	**Reason for Exclusion**
Mohammed,I., Hussain,A., Intrathecal baclofen withdrawal syndrome-a life-threatening complication of baclofen pump: a case report, BMC Clinical Pharmacology, 4, 6-, 2004	Case report
Mooney, J. F., Koman, L. A., Smith, B. P., Pharmacologic management of spasticity in cerebral palsy, Journal of Pediatric Orthopaedics, 23, 679-686, 2003	Expert review
Morota,N., Abbott,R., Kofler,M., Epstein,F.J., Cohen,H., Residual spasticity after selective posterior rhizotomy, Child's Nervous System, 11, 161-165, 1995	Mean age 6
Morr, S., Heard, C. M., Li, V., Reynolds, R. M., Dexmedetomidine for Acute Baclofen Withdrawal, Neurocritical Care, 22, 288-292, 2015	Case report
Nakou, V., Perides, S., Lundy, C., Mackin, G., Tustin, K., Gimeno, H., Baker, L., Lumsden, D. E., Selway, R., Ashkan, K., Bassi, S., Lin, J. P., Kaminska, M., Heterogeneity of movement disorders in hypomyelination with atrophy of the basal ganglia (H-ABC) syndrome and their management with Deep Brain Stimulation (DBS) or Intrathecal Baclofen Pump (ITB), Developmental Medicine and Child Neurology, 59, 11-12, 2017	Not CP
Neville, B. G., Selective dorsal rhizotomy for spastic cerebral palsy, Developmental Medicine & Child NeurologyDev Med Child Neurol, 30, 395-8, 1988	Expert review
O'Donnell,M., Armstrong,R., Pharmacologic interventions for management of spasticity in cerebral palsy, Mental Retardation and Developmental Disabilities Research Reviews, 3, -211, 1997	Expert review
Olree,K.S., Engsberg,J.R., Ross,S.A., Park,T.S., Changes in synergistic movement patterns after selective dorsal rhizotomy, Developmental Medicine and Child Neurology, 42, 297-303, 2000	mean age 6.7
Oppenheim, W. L., Selective Posterior Rhizotomy for Spastic Cerebral-Palsy - a Review, Clinical Orthopaedics and Related Research, 20-29, 1990	Expert review
Park, T. S., Cost-Analysis of Continuous Intrathecal Baclofen Versus Selective Functional Posterior Rhizotomy in the Treatment of Spastic Quadriplegia Associated with Cerebral-Palsy - Editorial Comment, Pediatric Neurosurgery, 22, 265-265, 1995	Cost effectiveness of ITB in children
Peacock, W. J., Arens, L. J., Selective Posterior Rhizotomy for the Relief of Spasticity in Cerebral-Palsy, South African Medical Journal, 62, 119-124, 1982	SDR in children
Peacock, W. J., Staudt, L. A., Spasticity in Cerebral-Palsy and the Selective Posterior Rhizotomy Procedure, Journal of Child Neurology, 5, 179-185, 1990	SDR in children
Peacock,W.J., Arens,L.J., Berman,B., Cerebral palsy spasticity. Selective posterior rhizotomy, Pediatric Neuroscience, 13, 61-66, 1987	Expert review
Penn,R.D., Gianino,J.M., York,M.M., Intrathecal baclofen for motor disorders, Movement Disorders, 10, 675-677, 1995	N=2 with CP
Perez-Arredondo, A., Cazares-Ramirez, E., Carrillo-Mora, P., Martinez-Vargas, M., Cardenas-Rodriguez, N., Coballase-Urrutia, E.,	Expert review

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Study	**Reason for Exclusion**
Alemon-Medina, R., Sampieri, A., Navarro, L., Carmona-Aparicio, L., Baclofen in the Therapeutic of Sequele of Traumatic Brain Injury: Spasticity, Clinical Neuropharmacology, 39, 311-319, 2016	
Peter,J.C., Arens,L.J., Selective posterior lumbosacral rhizotomy for the management of cerebral palsy spasticity. A 10-year experience, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde. 83, 745-747, 1993	Median age < 12 years
Peter,J.C., Arens,L.J., Selective posterior lumbosacral rhizotomy in teenagers and young adults with spastic cerebral palsy, British Journal of Neurosurgery, 8, 135-139, 1994	Median age < 15 years
Pin, T. W., McCartney, L., Lewis, J., Waugh, M. C., Use of intrathecal baclofen therapy in ambulant children and adolescents with spasticity and dystonia of cerebral origin: a systematic review, Developmental Medicine & Child Neurology, 53, 885-95, 2011	Systematic review (checked for relevant studies)
Plassat, R., Verbe, B. P., Menei, P., Menegalli, D., Mathe, J. F., Richard, I., Treatment of spasticity with intrathecal baclofen administration: long-term follow-up, review of 40 patients, Spinal Cord, 42, 686-693, 2004	3/41 had CP
Rappaport, Z. H., Limited (L4-S1, L5-S1) selective dorsal rhizotomy for reducing spasticity in cerebral palsy - Comment, Acta Neurochirurgica, 141, 751-752, 1999	Comment on Lazareff 1999
Rawicki,B., Treatment of cerebral origin spasticity with continuous intrathecal baclofen delivered via an implantable pump: long-term follow-up review of 18 patients, Journal of Neurosurgery, 91, 733-736, 1999	3/18 had CP
Rawlins,P., Intrathecal baclofen for spasticity of cerebral palsy: project coordination and nursing care, Journal of Neuroscience Nursing, 27, 157-163, 1995	Describes nursing organisation
Rawlins,P.K., Intrathecal baclofen therapy over 10 years, Journal of Neuroscience Nursing, 36, 322-327, 2004	Mean age at implant 13.3 years, N=18
Remy-Neris,O., Tiffreau,V., Bouilland,S., Bussel,B., Intrathecal baclofen in subjects with spastic hemiplegia: Assessment of the antispastic effect during gait, Archives of Physical Medicine and Rehabilitation, 84, 643-650, 2003	N=1 with CP
Russman, B. S., Intrathecal baclofen, Developmental Medicine and Child Neurology, 52, 601-602, 2010	Includes > 50% of patients without CP (including MS and degenerative disease)
Salame,K., Ouaknine,G.E., Rochkind,S., Constantini,S., Razon,N., Surgical treatment of spasticity by selective posterior rhizotomy: 30 years experience, Israel Medical Association Journal: Imaj, 5, 543-546, 2003	60/152 had CP - not reported separately
Saltuari,L., Kronenberg,M., Marosi,M.J., Kofler,M., Russegger,L., Rifici,C., Bramanti,P., Gerstenbrand,F., Long-term intrathecal baclofen treatment in supraspinal spasticity, Acta Neurologica, 14, 195-207, 1992	Not CP

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Study	**Reason for Exclusion**
Sampson, F. C., Hayward, A., Evans, G., Morton, R., Collett, B., Functional benefits and cost/benefit analysis of continuous intrathecal baclofen infusion for the management of severe spasticity, Journal of Neurosurgery, 96, 1052-1057, 2002	Cost effectiveness study - not CP
Sansone,J.M., Mann,D., Noonan,K., Mcleish,D., Ward,M., Iskandar,B.J., Rapid progression of scoliosis following insertion of intrathecal baclofen pump, Journal of Pediatric Orthopedics, 26, 125-128, 2006	N=4, case series
Saulino, M., Anderson, D. J., Doble, J., Farid, R., Gul, F., Konrad, P., Boster, A. L., Best Practices for Intrathecal Baclofen Therapy: Troubleshooting, Neuromodulation, 19, 632-641, 2016	Consensus guideline
Saval,A., Chiodo,A.E., Intrathecal baclofen for spasticity management: a comparative analysis of spasticity of spinal vs cortical origin, Journal of Spinal Cord Medicine, 33, 16-21, 2010	7/57 had CP
Saval,A., Chiodo,A.E., Effect of intrathecal baclofen concentration on spasticity control: case series, Journal of Spinal Cord Medicine, 31, 394-397, 2008	1/3 had CP, case reports
Schijman,E., Erro,M.G., Meana,N.V., Selective posterior rhizotomy: Experience of 30 cases, Child's Nervous System, 9, 474-477, 1993	Insufficient detail about the population
Schmidt, E., DiMario, F. J., Efficacy profile for anti-spasticity therapies in cerebral palsy, Journal of Investigative Medicine, 47, 165A-165A, 1999	Abstract only, paediatric study
Schmit,B.D., Gaebler-Spira,D., Mechanical measurements of the effects of intrathecal baclofen dosage adjustments in cerebral palsy: a pilot study, American Journal of Physical Medicine and Rehabilitation, 83, 33-41, 2004	Case series, N=6
Shilt, Js, Lai, Lp, Cabrera, Mn, Frino, J, Smith, Bp, The impact of intrathecal baclofen on the natural history of scoliosis in cerebral palsy, Journal of pediatric orthopedics, 28, 684-7, 2008	Mean age 9.8
Siegfried,J., Rea,G.L., Intrathecal application of baclofen in the treatment of spasticity, Acta Neurochirurgica - Supplementum, 39, 121-123, 1987	1/9 had CP
Silva, S., Nowicki, P., Caird, M. S., Hurvitz, E. A., Ayyangar, R. N., Farley, F. A., Vanderhave, K. L., Hensinger, R. N., Craig, C. L., A comparison of hip dislocation rates and hip containment procedures after selective dorsal rhizotomy versus intrathecal baclofen pump insertion in nonambulatory cerebral palsy patients, Journal of Pediatric Orthopedics, 32, 853-6, 2012	Mean age <10
Sindou, M., Limited (L4-S1, L5-S1) selective dorsal rhizotomy for reducing spasticity in cerebral palsy - Comment, Acta Neurochirurgica, 141, 751-752, 1999	SDR in children < 12 with CP.
Sindou,M., Mifsud,J.J., Boisson,D., Goutelle,A., Selective posterior rhizotomy in the dorsal root entry zone for treatment of hyperspasticity and pain in the hemiplegic upper limb, Neurosurgery, 18, 587-595, 1986	Not CP
Speelman,J.D., Treatment strategies in movement disorders, Journal of Inherited Metabolic Disease, 28, 441-444, 2005	Case report

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Study	**Reason for Exclusion**
Spiegel,D.A., Flynn,J.M., Evaluation and Treatment of Hip Dysplasia in Cerebral Palsy, Orthopedic Clinics of North America, 37, 185-196, 2006	Expert review
Steinbok, P., Outcomes after selective dorsal rhizotomy, Developmental Medicine and Child Neurology, 57, 214-215, 2015	Comment on another study (Josenby 2015)
Steinbok,P., 10-year follow-up after selective dorsal rhizotomy in cerebral palsy, Developmental Medicine and Child Neurology, 53, 678-678, 2011	Comment on another study (Tedroff 2011)
Stempien,L., Tsai,T., Intrathecal baclofen pump use for spasticity: A clinical survey, American Journal of Physical Medicine and Rehabilitation, 79, 536-541, 2000	Age < 9
Stokic, D. S., Yablon, S. A., Hayes, A., Vesovic-Potic, V., Olivier, J., Dose-response relationship between the H-reflex and continuous intrathecal baclofen administration for management of spasticity, Clinical Neurophysiology, 117, 1283-1289, 2006	4/34 had CP
Sweetser, P. M., Badell, A., Schneider, S., Badlani, G. H., Effects of Sacral Dorsal Rhizotomy on Bladder Function in Patients with Spastic Cerebral-Palsy, Neurourology and Urodynamics, 14, 57-64, 1995	Median age < 10
Taira, T., Hori, T., Intrathecal baclofen therapy, Neurological Surgery, 36, 573-590, 2008	Japanese language
Tasseel-Ponche, S., Intrathecal baclofen in cerebral palsy. A retrospective study of 25 wheelchair-assisted adults, Annals of Physical and Rehabilitation Medicine, 54, e16, 2011	Abstract only - see Tasseel 2010 for full text
Thakur, S. K., Rubin, B. A., Harter, D. H., Long-term follow-up for lumbar intrathecal baclofen catheters placed using the paraspinal subfascial technique, Journal of Neurosurgery: Pediatrics, 17, 357-360, 2016	Insufficient detail about the population
Tichy,M., Kraus,J., Horinek,D., Vaculik,M., Selective posterior rhizotomy in the treatment of cerebral palsy, first experience in Czech Republic, Bratislavske Lekarske Listy, 104, 54-58, 2003	Median age < 16
Trost,J.P., Schwartz,M.H., Krach,L.E., Dunn,M.E., Novacheck,T.F., Comprehensive short-term outcome assessment of selective dorsal rhizotomy, Developmental Medicine and Child Neurology, 50, 765-771, 2008	Mean age 7 years
Vogt, T., Urban, P. P., Optimising therapy for spastic syndrome by combining baclofen with botulinumtoxin, Nervenarzt, 71, 1007-1011, 2000	Case report, German language
Walker, R. H., Danisi, F. O., Swope, D. M., Goodman, R. R., Germano, I. M., Brin, M. F., Intrathecal baclofen for dystonia: Benefits and complications during six years of experience, Movement Disorders, 15, 1242-1247, 2000	Not CP
Xu,L., Hong,Y., Wang,A.Q., Wang,Z.X., Tang,T., Hyperselective posterior rhizotomy in treatment of spasticity of paralytic limbs, Chinese Medical Journal, 106, 671-673, 1993	Mean / median age of subjects not reported
Zierski,J., Muller,H., Dralle,D., Wurdinger,T., Implanted pump systems for treatment of spasticity, Acta Neurochirurgica - Supplementum, 43, 94-99, 1988	3/30 had CP

CP: cerebral palsy; ITB: intrathecal baclofen; N: number of participants in study; SDR: selective dorsal rhizotomy

Economic studies

See supplementary material D for the excluded clinical studies.

Appendix L – Research recommendations

Research recommendations for review question A2: What is the effectiveness and cost effectiveness of selective dorsal rhizotomy compared to continuous intrathecal baclofen pump to reduce spasticity in adults with cerebral palsy?

Table 16: Research recommendation rationale

Research question	What is the effectiveness and cost effectiveness of selective dorsal rhizotomy compared to continuous intrathecal baclofen pump to reduce spasticity in adults with cerebral palsy?
Importance to 'patients' or the population	Minimise further surgery Minimise follow up Reduce complications
Relevance to NICE guidance	Ability to make firm recommendations according to functional level
Relevance to the NHS	Reduce costs of ongoing ITB therapy Reduce costs of further surgery
National priorities	Ensure equal access to treatments Reduce variations in treatment practice Ensure validity of SDR in adult population
Current evidence base	Current evidence not available or not applicable to adult population
Equality	Applies to all patients with cerebral palsy and spasticity regardless of functional (GMFCS) level

Table 17: Research recommendation modified PICO table

Criterion	Explanation
Population	Adults (18 or over) with generalised spasticity not managed by physical means and oral medication causing problems with pain, posture or function
Intervention	Selective dorsal rhizotomy
Comparator	Intrathecal baclofen
Outcome	Reduction in spasticity Functional gains Goal achievement Patient satisfaction HRQoL Complications Cost
Study design	Randomised, open label
Timeframe	5 years
Additional information	Need to stratify by: Age GMFCS level

GMFCS, Gross Motor Function Classification System (GMFCS), HRQoL, health-related quality of life

Appendix M – Health Economic Quality Assessment

Health economic quality assessment for review question A2: Are neurosurgical procedures (intrathecal baclofen pump and selective dorsal rhizotomy) effective in adults aged 19 and over with cerebral palsy to reduce spasticity and or dystonia?

Table 18: Health economic quality assessment

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
Guidance topic: Cerebral palsy in adults		Question no: A.2
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Partly	Patients with disabling spasticity and functional dependence caused by any neurological disease
1.2 Are the interventions appropriate for the review question?	Yes	Intrathecal baclofen (ITB) therapy compared with conventional medical treatments
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	France
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Only direct costs of treatment included according to French Guidelines for economic evaluations
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon 2 years
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Successful treatment (defined as a combination of: the increased patient and caregiver satisfaction as assessed by goal attainment scaling (GAS), and a decrease of at least 1 point on the Ashworth score)
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Decision tree structure. An expert panel was used to define the treatment sequences (model structure) and review parameters estimates of the historical databases.
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon 2 years
2.3 Are all important and relevant outcomes included?	Yes	See 2.1
2.4 Are the estimates of baseline outcomes from the best available source?	Unclear	Clinical effectiveness data is included in the model but sources and values are not reported
2.5 Are the estimates of relative intervention effects from the best available source?	Unclear	See 2.4
2.6 Are all important and relevant costs included?	Yes	Treatment costs were calculated based on hospital costs in France including drug costs, physician visits, procedure costs, hospitalization, nursing care, physical treatments, surgery, transportation services, device acquisition costs (ITB), complication costs of ITB treatment, cost of managing pressure sores, and severe muscle contractions.
2.7 Are the estimates of resource use from the best available source?	Unclear	Not all cost sources reported. Direct medical costs were measured in Euros (2006) and based on a French retrospective cost survey at Raymond Poincaré Hospital.
2.8 Are the unit costs of resources from the best available source?	Unclear	See 2.7
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA (5,000 iterations)
2.11 Is there any potential conflict of interest?	No	Not reported
2.12 Overall assessment: Potentially serious limitations		
Other comments:		
Study identification Sampson, F. C., Hayward, A., Evans, G., Morton, R., Collett, B. Functional benefits and cost/benefit analysis of continuous intrathecal baclofen infusion for the management of severe spasticity. Journal of Neurosurgery 2002		
Guidance topic: Cerebral palsy in adults		Question no: A.2

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Partly	Severe spasticity, not all papers included in the meta-analysis included participants with CP
1.2 Are the interventions appropriate for the review question?	Yes	Continuous intrathecal baclofen infusion
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Only direct costs of treatment included.
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Partly	Time horizon 5 years. Costs and benefits were discounted 6% per annum (NICE reference case 3.5%).
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	DAM not developed
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon 5 years (the lifespan of ITB equipment)
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Estimation of benefits identified from a systematic review of the literature
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	See 2.4

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
2.6 Are all important and relevant costs included?	Yes	A separate literature search was performed to identify existing economic analyses or cost studies relating to continuous intrathecal baclofen infusion. Key cost elements were identified from the literature and from semi structured interviews with clinicians from hospitals in the UK.
2.7 Are the estimates of resource use from the best available source?	Yes	See 2.6
2.8 Are the unit costs of resources from the best available source?	Yes	See 2.6
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	No	One threshold sensitivity analysis was performed to examine the annual gains in health state values (QALYs) required to provide specific cost-effectiveness ratios of between £5000 and £25,000 per QALY
2.11 Is there any potential conflict of interest?	No	Not reported
2.12 Overall assessment: Potentially serious limitations		
Other comments:		
Study identification Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J. Medical cost impact of intrathecal baclofen therapy for severe spasticity. Neuromodulation 2015		
Guidance topic: Cerebral palsy in adults		Question no: A.2
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	Informed by data that included participants with multiple sclerosis (N=124), cerebral palsy (N=131) and spinal cord injury (N=40)
1.2 Are the interventions appropriate for the review question?	Yes	Intrathecal baclofen compared to continued conventional medical management (pre-pump implantation)
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	No	US
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Partly	US third party payer. Indirect costs are not reported but the perspective is not explicitly stated.

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon 30 years. 3% annual discount rate applied (note slight deviation from NICE's preferred 3.5%)
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	DAM not developed. Cost-benefit analysis.
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon 30 years
2.3 Are all important and relevant outcomes included?	Partly	It was assumed that future costs would follow a reasonable trend rate based on healthcare industry standards. Device-related complications were included.
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	Model informed by retrospective analysis of commercial administrative claims data. A systematic review of the literature was not undertaken.
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	See 2.4
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	See 2.4
2.8 Are the unit costs of resources from the best available source?	Yes	See 2.4
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	

Study identification **Bensmail, D, Ward, Ab, Wissel, J, Motta, F, Saltuari, L, Lissens, J, Cros, S, Beresniak, A. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. Neurorehabilitation and Neural Repair 2009**		
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	SA for different values of three variables: 1) the drug delivery system's battery life, 2) the length of the pre implant experience period used to establish average starting costforprojectionpurposes,and3)the medical cost trend assumptions. PSA not undertaken
2.11 Is there any potential conflict of interest?	Yes	Funded by Medtronic, Inc.
2.12 Overall assessment: Potentially serious limitations		
Other comments:		