National Institute for Health and Care Excellence

Final

Cerebral palsy in adults

Health economic literature review

NICE guideline NG119

Supplementary Material D

January 2019

Final

Supplementary materials were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

Health economic literature review

A literature search was carried out across all guideline topics for any health economic studies relating to cerebral palsy in adults. This supplement contains details of this evidence search and the systematic review process.

Information sources and eligibility criteria

The following databases were searched for economic evidence relevant to the PICO: MEDLINE, EMBASE, COCHRANE, NHS EED and HEED. Studies were selected for inclusion in the evidence review if the following criteria were met:

- both cost and health consequences of interventions reported (that is, true cost-effectiveness analyses)
- conducted in an OECD country
- incremental results are reported or enough information is presented to allow incremental results to be derived
- studies that matched the population, interventions, comparators and outcomes specified in PICO
- studies that meet the applicability and quality criteria set out by NICE, including relevance to the NICE reference case and UK NHS.

Note that studies that measured effectiveness using quality of life based outcomes (for example, quality adjusted life years [QALYs]) were desirable but, where this evidence was unavailable, studies using alternative effectiveness measures (for example, life years) were considered.

Literature search for economic evidence

Multifile search strategy

Full methods of the literature search are available in Supplementary material C: Health economics search literature.

Date of initial search: 20 March 2017

Date of re-run search: 22 March 2018

Table 1: Health economics

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.	health economics/ use oemezd
11.	exp economic evaluation/ use oemezd

1.	exp Cerebral Palsy/ use prmz
12.	exp health care cost/ use oemezd
13.	exp fee/ use oemezd
14.	budget/ use oemezd
15.	funding/ use oemezd
16.	or/10-15
17.	exp Economics/ use prmz
18.	Value of life/ use prmz
19.	exp "Costs and Cost Analysis"/ use prmz
20.	exp Economics, Hospital/ use prmz
21.	exp Economics, Medical/ use prmz
22.	Economics, Nursing/ use prmz
23.	Economics, Pharmaceutical/ use prmz
24.	exp "Fees and Charges"/ use prmz
25.	exp Budgets/ use prmz
26.	or/17-25
27.	(economic* or pharmaco?economic*).ti.
28.	(price* or pricing*).ti,ab.
29.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
30.	(financ* or fee or fees).ti,ab.
31.	(value adj2 (money or monetary)).ti,ab.
32.	budget*.ti,ab.
33.	cost*.ti.
34.	or/27-33
35.	16 or 26 or 34
36.	9 and 35

Database(s): Embase 1974 to 2017 March 20

Table 2: Economics Scoping Search for Embase

#	Searches
1	cerebral palsy/
2	((cerebral or brain or central) adj2 (pal* or paralys#s or pares#s)).tw.
3	little? disease.tw.
4	((hemipleg* or dipleg* or quadripleg* or unilateral*) adj5 spastic*).tw.
5	((hemipleg* or dipleg* or quadripleg* or unilateral*) adj3 ataxi*).tw.
6	or/1-5
7	limit 6 to (adult <18 to 64 years> or aged <65+ years>)
8	limit 7 to english language
9	health economics/
10	exp economic evaluation/
11	exp health care cost/
12	exp fee/
13	budget/

#	Searches
14	funding/
15	budget*.ti,ab.
16	cost*.ti.
17	(economic* or pharmaco?economic*).ti.
18	(price* or pricing*).ti,ab.
19	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
20	(financ* or fee or fees).ti,ab.
21	(value adj2 (money or monetary)).ti,ab.
22	or/9-21
23	8 and 22

Database(s): Ovid MEDLINE(R)

Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Table 3: Economics Scoping Search for Medline

#	Searches
1	Cerebral Palsy/
2	((cerebral or brain or central) adj2 (pal* or paralys#s or pares#s)).tw.
3	little? disease.tw.
4	((hemipleg* or dipleg* or quadripleg* or unilateral*) adj5 spastic*).tw.
5	((hemipleg* or dipleg* or quadripleg* or unilateral*) adj3 ataxi*).tw.
6	or/1-5
7	limit 6 to "all adult (19 plus years)"
8	limit 7 to english language
9	Economics/
10	Value of life/
11	exp "Costs and Cost Analysis"/
12	exp Economics, Hospital/
13	exp Economics, Medical/
14	Economics, Nursing/
15	Economics, Pharmaceutical/
16	exp "Fees and Charges"/
17	exp Budgets/
18	budget*.ti,ab.
19	cost*.ti.
20	(economic* or pharmaco?economic*).ti.
21	(price* or pricing*).ti,ab.
22	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
23	(financ* or fee or fees).ti,ab.
24	(value adj2 (money or monetary)).ti,ab.
2	or/9-24

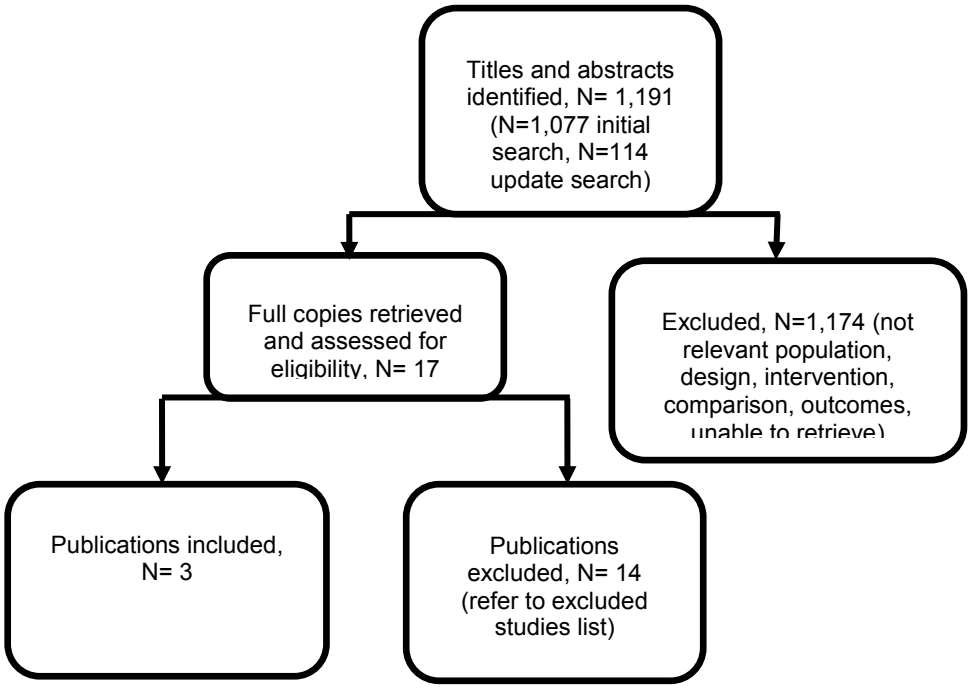
#	Searches
26	8 and 25

Economic evidence study selection

A single search was undertaken for all health economic content in the guideline.

Figure 1 below provides an illustration of the process used to select those papers and presents the number of papers identified for all the guideline topics. Full details of the search strategies are presented in the section titled 'Literature search for economic evidence' above.

Figure 1: Flow diagram of selection for economic evaluations



Three economic evaluations were included for this review: one cost-utility analysis (cost per additional QALY), one cost effectiveness analysis (cost per successful treatment), and one cost-benefit analysis that translated clinical outcomes into resource use and costs (see evidence review [A2] for summary). All 3 evaluations compared intrathecal baclofen to other standard treatment protocols. No economic evaluations were identified that assessed selective dorsal rhizotomy (SDR).

No other economic studies were identified which matched any other review question.

Table 4: Number of included economic studies by clinical area covered in the guideline

Area	Include
A2 Neurosurgical Procedures for Spasticity	3

Area	Include
Total	3

The methods and results for each of the 3 economic evaluations are presented in the health economic evidence tables and health economic evidence profiles sections below.

Economic evidence tables

Table 5: Sampson et al., 2002

Bibliographic reference	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
Full citation	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
Economic study type	Cost-utility
Country(ies) where the study was done	UK
Perspective & Cost Year	UK NHS perspective Cost year 1999
Source of funding	Not reported
Study dates	Systematic review of the literature included studies from 1985 to 1997
Intervention	Intrathecal baclofen
Comparison(s)	Less invasive treatments (only intrathecal baclofen side of studies meta-analysed, comparator not discussed in detail)
Source of effectiveness data	17 trials were included in meta-analysis, identified from a systematic review of the literature Benefits were assumed to last 5 years, the procedure needs to be repeated at between 5 and 7 years because of the device's limited battery life
Source of cost data	• A separate literature search was performed to identify existing economic analyses or cost studies relating to continuous ITB • Key cost elements were identified from the literature and from semi structured interviews with clinicians • Cost estimates were derived from 1999 data from three centers within the United Kingdom in which the operation was performed • This included the cost of the pre-screening evaluation, test dose procedure, implantation procedure, and follow-up costs
Other data sources e.g. transition probabilities	Not applicable

Time horizon and discount rate	Time horizon: 5-year expected life of the pump. Costs and benefits were discounted at 6% per annum.
Method of eliciting health valuations (if applicable)	• Used the EQ-5D, examined the impact of continuous ITB for 3 categories of patients with different levels of disability • Baseline health-related QOL estimates for each dimension were scored for each of these patient categories • Data from the literature review were used to estimate the improvements that would be expected in each of the five dimensions of the EQ-5D, and the proportion of patients who would be likely to experience these benefits • Categories and improvements supported by clinical opinion
Modelling approach	No decision analytical model built. QoL estimated from meta-analysis. Three different patient groups were considered seperately: • 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 per patient per alternative	• The cost of continuous ITB was estimated to be £11,700 for the assessment, test dose, and implantation procedure • Follow-up costs of £580 to £1160 per annum, based on an average of 4 to 8 refills per annum • Total discounted cost over a 5-year period is estimated at £15,420
Effectiveness per patient per alternative	Baseline QOL Value (EQ-5D); Changes in QOL measured by EQ-5D; **Improvement** • Category 1 - 0.594 (33333); 1) 11% no change (33333) 0.50 2) 23% reduction in pain (33323) 3) 66% reduction in pain, able to sit in wheelchair, reduction in anxiety & depression scores (23322); **0.50** • Category 2 - 0.208 (33313); 4) 34% no change (33313) 0.27 5) 66% able to sit in wheelchair, reduction in anxiety & depression scores (23312); **0.27** • Category 3 - 0.079 (23322); 6) 11% no change (23322) 0.43 7) 73% reduction in pain, improved ability to care for self & perform ADL (22212) 8) 16% reduction in pain only (23312); **0.43**
Incremental cost-effectiveness	ICER cost per QALY • Category 1 £6,900 • Category 2 £12,790 • Category 3 £8,030
Other reporting of results	Not applicable
Uncertainty	• A 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 • The cost effectiveness of continuous ITB will rise above the notional limit of £20,000 per QALY if the average annual QALY gain is less than approximately 0.15 or if the cost of continuous ITB is above £19,000 for the 5-year period

Limitations	• Meta-analysis included non-comparative studies • Potentially out-of-date practice used to inform the model • Sensitivity analysis was limited
Other information	• Categories: 1, bedbound patients experiencing severe spasm-related pain; 2, bedbound patients who were not in pain; 3, wheelchair users with moderate spasm related pain • Trials and reviews of the use of ITB were included if the people studied had the following conditions: cerebral palsy, multiple sclerosis, spinal cord injury, traumatic brain injury, or hypoxic brain injury. • Considered functional benefits as the measure of effect • Included studies must report or be able to calculate the proportion of patients who achieved at least one of the following outcomes: 1) bedbound patients becoming able to sit in a wheelchair; 2) patients who had severe difficulty sitting in a wheelchair becoming able to sit comfortably; 3) wheelchair users improving their wheelchair mobility; 4) wheelchair users improving their ability to transfer; 5) wheelchair-bound patients becoming ambulatory; 6) ambulatory patients improving their ability to walk; 7) improved ability to perform ADL; 8) improved ease of nursing care; 9) patients with skin integrity problems who showed improvements in these symptoms; and 10) reduction in spasm-related pain • Trials in which only measurements of patient impairment were recorded, such as the Ashworth score, spasm score, or reflex score, were not included as those measures provide some indication of the physiological effect of the intervention, but do not necessarily relate to improvements in function or QOL

Table 6: Bensmail et al., 2009

Bibliographic reference	**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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009**
Full citation	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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009
Economic study type	Cost effectiveness analysis
Country(ies) where the study was done	France
Perspective & Cost Year	Direct medical costs measured in 2006 Euros

Table 6: Bensmail et al., 2009

Bibliographic reference	**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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009**
Source of funding	Not reported
Study dates	Not reported
Intervention	Intrathecal baclofen
Comparison(s)	Defined as a package of specific current treatments based on the most established treatment pattern in France at the time of model development, namely: physical treatment only; oral antispastic agents; focal spasticity treatments; neurosurgical interventions; nursing care; and ITB (+ ITB potential adjustment dose + potential pump explantation).
Source of effectiveness data	An expert panel was used to define the treatment sequences (model structure) and review parameters estimates of the historical databases. However, the databases used are not specified.
Source of cost data	• 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. • Physical treatment costs include physiologist fees and transport costs. Oral treatment costs include drug costs using standard dosage and physical treatment. Neurosurgery costs include hospital and physical treatment costs. • ITB explantation costs include hospital and nursing costs. • Focal spasticity treatment costs include hospital, transport, and physical treatment costs. • ITB adjustment costs include specialist visits, hospital, and transport costs. • ITB costs include device, hospital, and drug refilling costs, as well as physical treatment costs for 30% of patients, plus potential complication costs. Nursing costs include home care for all treatments strategy. • ITB system costs for complications have been integrated in the model. • Direct medical costs were based on a French retrospective cost survey at Raymond Poincaré Hospital. • Total medical cost data were analysed for 170 patients followed in the R. Poincaré Hospital, Garches, France, for whom resource utilization was recorded.
Other data sources e.g. transition probabilities	Not applicable

Table 6: Bensmail et al., 2009

Bibliographic reference	**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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009**
Time horizon and discount rate	Time horizon 2 years, no discount rate applied.
Method of eliciting health valuations (if applicable)	Not applicable
Modelling approach	• 2 comprehensive decision trees were developed to represent the different treatment patterns and the corresponding outcomes, transition probability distribution, and cost distributions. • Each strategy to be assessed and compared was composed of different treatment patterns used successively following an inadequate response to the previous one. • Each event tree used the following set of parameters: success rate over 2 years and confidence interval (CI); total medical costs over 2 years; CI, mean cost-effectiveness ratios (mean costs divided by mean effectiveness); and CI. <u>Conventional medical treatment</u> • Composed of 54 health states (branches) and 46 transition probabilities • Began with physical treatment only and moved on to oral treatment in the event of failure • If this proved unsuccessful, 3 therapeutic strategies were proposed: (1) neurosurgery followed by nursing; (2) ITB (with potential dose adjustment if necessary); or (3) focal spasticity treatment (botulinum toxin, phenol, or neurotomy) followed by neurosurgery if necessary • Finally, nursing care was the last option in the strategy. <u>ITB first-line strategy decision tree</u> • Began with ITB and, in the case of treatment failure, was followed by ITB dose adjustment and then pump explatation, if necessary • Pump explantation would be carried out in case ITB is discontinued. • After potential pump explantation, oral treatment (followed by neurosurgery, focal spasticity treatment, or nursing), neurosurgery (followed by nursing), nursing (followed by neurosurgery), or focal spasticity treatment (followed by nursing) were prescribed in specific sequence
Cost per patient per alternative	Despite the fact that ITB acquisition costs were the highest among antispastic treatments, the ITB treatment regimen (when used as a first option strategy) resulted in a significantly lower total medical cost (€59 391 vs €88 272; P < .001)

Table 6: Bensmail et al., 2009

Bibliographic reference	**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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009**
	<u>Total Direct Medical Costs of Main Therapeutic Regimen Over 6 Months</u> Minimum Cost to Maximum Cost • Physical treatment €11 620 to €18 886 • Oral treatment €19 354 to €34 216 • Neurosurgery €23 326 to €45 490 • Focal spasticity treatment €19 036 to €34 674 • ITB semester 1 €26 901 to €30 292 • ITB semester 2, 3, 4 €8093 to €11 484 • ITB dose adjustment €5230 to €7760 • ITB pump explanting €5133 to €6388 Costs at 2 years are only presented graphically and cannot be interpreted accurately.
Effectiveness per patient per alternative	Using ITB as a first line strategy in severely impaired patients with disabling spasticity had a significantly higher success rate than conventional medical management (78.7% vs 59.3%; P < .001)
Incremental cost-effectiveness	ITB was considered to be the dominant strategy providing greater effectiveness at a lower cost. The mean cost-effectiveness ratios show a significantly lower average cost per success with ITB as a first-line strategy (€75 204/ success vs €148 822/success; P < .001).
Other reporting of results	Not applicable
Uncertainty	Mean PSA values using 5,000 iterations presented as the base case, no further analysis of uncertainty is performed.
Limitations	• Databases used to inform clinical effectiveness in the model are not reported • The probabilities of "success" and "no success" are not reported and it is not described how they were estimated from the historical databases • Model inputs are not sufficiently reported • No comparative clinical trials were used to inform the model (given that none were published at the time of model development)
Other information	• The decision trees were designed as simulation models and programmed to take into account the entire distribution costs and distribution effectiveness for each predefined parameter. • Deterministic results are not reported.

Table 6: Bensmail et al., 2009

Bibliographic reference	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 (Structured abstract), Neurorehabilitation and Neural Repair, 23, 546-552, 2009
	• The population included poorly functioning patients who were disabled by their spasticity and dependent for activities of daily living, such as: tetraplegic patients; very dependent patients with multiple sclerosis, traumatic brain injury, cerebral palsy, or stroke; adults with a modified Barthel score <10 or children with level V Gross Motor Function Classification scale (GMFCS); or nonambulatory patients.

Table 7: Saulino et al., 2015

Bibliographic reference	Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J., Medical cost impact of intrathecal baclofen therapy for severe spasticity, Neuromodulation, 18, 141-149, 2015
Full citation	Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J., Medical cost impact of intrathecal baclofen therapy for severe spasticity, Neuromodulation, 18, 141-149, 2015
Economic study type	Cost-benefit
Country(ies) where the study was done	US
Perspective & Cost Year	Third party payer perspective, only direct costs appear to be included.
Source of funding	Funded by Medtronic, Inc.
Study dates	Each pump implant date was adjusted so that the midpoint of the implant month was aligned to July1,2007
Intervention	Intrathecal baclofen
Comparison(s)	Using a pre–post cohort methodology, the control group is the actuarial projection of a conventional treatment protocol had the patients not been implanted
Source of effectiveness data	Patient utilization and eligibility experience were extracted from OptumInsight's nationally consolidated database containing integrated medical and prescription drug claims from fully insured holders of private commercial and Medicaid policies.
Source of cost data	• Each patient's experience was priced to an allowed charge level based on national average reimbursement information for calendar year 2007 derived from OptumInsight's database

Bibliographic reference	Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J., Medical cost impact of intrathecal baclofen therapy for severe spasticity, Neuromodulation, 18, 141-149, 2015
	• Separate average 2007 discount rates (i.e., discount from billed charges) were calculated for inpatient facility and outpatient facility services and then applied to the billed charge information at a detailed claim level • Physician claims were priced based on a 2007 allowed-charge fee schedule • If a procedure code was supplied on the patient's claim or if the procedure code was not on the fee schedule, a 39% discount was applied to the billed charge for that claim • Prescription drug claims were priced at the standard 2007 average wholesale ingredient cost of the prescription, including its per-prescription dispensing fee
Other data sources e.g. transition probabilities	Not applicable
Time horizon and discount rate	Time horizon 30 years 3% discount rate applied
Method of eliciting health valuations (if applicable)	Not applicable
Modelling approach	A DAM was not developed. <u>Actuarial Cost Projections: Future Implantation Cycles</u> • Based on the device registration system, the average operating life of an implantable pump was assumed to be 6 years • After approximately 6 years, additional medical procedures, including explant and reimplantation, are required • More rarely, the device may need to be replaced owing to mechanical failure • Pump survival rates have been reported to range from 92.4% to 96.5% at 6 years • The reimplant is replicated five times over the 30-year projection period (i.e., reimplantation at years 6, 12, 18, 24, and 30) • It was assumed that future implant episodes, or cycles, would be similar in shape and characteristic to the initial implant cycle, but at increased cost levels to reflect inflationary trends • That is, the same incline in pre implant expenses was not carried into future episodes. Rather, expenses were trended using published industry trend rate • The annual net medical trend rate was projected as follows: 10.0% in year 1, 8.8% in year 2, 7.6% in year 3, 6.4% in year 4, 5.2% in year 5, and 4.0% for all subsequent years • The trend rates reflect healthcare industry average expectations
Cost per patient per alternative	<u>Mean cost/savings per patient (US$)</u> Month of implant; 1 year post-implant; 3 years post-implant

Bibliographic reference	Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J., Medical cost impact of intrathecal baclofen therapy for severe spasticity, Neuromodulation, 18, 141-149, 2015
	• Number of patients 409; 294; 54 • Inpatient facility Pump implantation 18,422; 21,508; 22,799 • All other hospitalizations 677; (9,359); (50,988) • Outpatient facility Pump implantation 7,800; 8,549; 8,970 • Refill and programming –; 5; 5 • Emergency room (1); (241); (864) • Physiotherapy (25); 218; (2,327) • Surgery/ambulatory surgery center 364; 1,546; 2,926 • Pharmacy (7); (28); 107 • Other 56; 1,272; 2,122 • Professional physician Pump implantation 2,447; 3,023; 3,375 • Refill and programming 18; 2,092; 5,976 • Acupuncture/blocks/ chiropractic care (12); (100); (320) • Onabotulinumtoxin A injections (11); (68); (221) • Emergency room 1; (79); (545) • Injections 34; (97); (386) • Physiotherapy (43); (257); (972) • Office visits 23; (156); (1,141) • Other 357; (903); (6,375) • Prescription drugs 7; (550); (2,082) • Subtotal 30,107; 26,375; (19,941) • Standard error 24,556; 140,593; 527,57 Projection assumes an annual discount rate of 3% and annual medical trend rates of 10.0%, 8.5%, and 7.0% for years 1, 2, and 3, respectively. Values not in parentheses are costs. Values in parentheses are savings.
Effectiveness per patient per alternative	• Cost-benefit type of analysis, hence improvement are translated into monetary benefits: savings are produced from reduced utilization, reduced intensity of medical services, or reduced need for prescription drug medication, and vice versa for losses • The cost projection includes device-related complications and postoperative infection • During the first year post-implant, 23 patients (5.6%) experienced at least one complication, and 56 patients received revisions (13.7%).Two to three years post-implant, the prevalence of revisions decreased to 3.0%
Incremental cost-effectiveness	At 30 years, ITB provides an annual saving per-patient of $8,009 compared with conventional treatment, or a saving of $240,272 over 30 years.
Other reporting of results	Not applicable
Uncertainty	Sensitivity analyses were carried out using different values of three variables likely to have a meaningful impact on our results: 1) the drug delivery system's battery life, 2) the length of the preimplant experience period used to establish average starting cost for projection purposes, and 3) the medical cost trend assumptions (i.e., both initial and ultimate rates).

Bibliographic reference	Saulino, M., Guillemette, S., Leier, J., Hinnenthal, J., Medical cost impact of intrathecal baclofen therapy for severe spasticity, Neuromodulation, 18, 141-149, 2015
	Sensitivity test of pre-implant experience period (for projection) • Baseline (36-month period) (8,009) • 12-month period (21,833) • 6-month period (25,438) **Sensitivity test of implant cycle length (time to reimplant)** • Baseline (8,009) • 3-year cycle 1,311 • 4-year cycle 189 • 5-year cycle (3,430) • 6-year cycle (8,009) • 7-year cycle (13,053) • 8-year cycle (18,724) • 9-year cycle (16,080) **Sensitivity test of medical cost trend rate assumptions** • Baseline (initial trend 10.0%; ultimate trend 4.0%) (8,009) • Initial trend 8.0%; ultimate trend 2.0% (5,965) • Initial trend 12.0%; ultimate trend 6.0% (10,835) Analysis assumes an annual discount rate of 3% and annual medical trend rates of 10.0%, 8.5%, 7.0%, 5.5%, and 4.0% for years 1, 2, 3, 4, and 5+, respectively. *Values not in parentheses are costs. Values in parentheses are savings. When the cost trend assumptions were altered, the respective rates were increased or decreased uniformly.
Limitations	• no control group was observed relative to the intervention group • survival was not considered as part of the analysis which will overestimate survival • potential conflict of interest
Other information	32% had cerebral palsy, 30% had multiple sclerosis <u>Actuarial Cost Projections: Initial Implantation Cycle</u> • An actuarial cost projection was made based on the patient's pre implantation experience to determine expected future patient costs • The actuarial cost projection, intended to simulate an ITB-free treatment protocol, was compared with the patient's actual post-implant claim experience to determine the difference in outcomes • The projection assumed that no pump implantation would occur and that the patient's average pre-implant costs would continue to increase according to industry-standard trends • Projected costs for years following the month of implantation relied on the patient's annual claim cost distribution prior to the pump implant month as inputs to extrapolate future costs • It was assumed that future costs would follow a reasonable trend rate based on healthcare industry standards • Incremental differences between the patient's actuarial cost projection and his or her actual post-implant claim experience reflect expected losses or savings for a conventional protocol relative to ITB therapy

Excluded studies for economic evidence

Table 8: Economic studies

Study	Reason for Exclusion
Abogunrin, S., Hortobagyi, L., Remak, E., Dinet, J., Gabriel, S., Bakheit, A. M. O., Budget impact analysis of botulinum toxin a therapy for upper limb spasticity in the United Kingdom, ClinicoEconomics and Outcomes Research, 7, 185-193, 2015	Not a cost-effectiveness analysis - benefits not assessed
Butler, C., Campbell, S., Adams, R., Abel, M., Chambers, H., Goldstein, M., Leach, J., Darrah, J., Msall, M., Edgar, T., McLaughlin, J., Damiano, D., Susan Stott, N., Samson-Fang, L., Logan, L., Albright, L., Armstrong, R., O'Donnell, M., Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy, Developmental medicine and child neurology, 42, 634-645, 2000	Not a cost-effectiveness analysis - only measure clinical effects
Calvert, J, Kelly, J, What is the clinical and cost effectiveness of dynamic elastomeric fabric orthoses (DEFOs) for cerebral palsy? (Structured abstract), Health Technology Assessment Database, 2013	No cost effectiveness analysis conducted or identified from their review of the literature. Report unit costs of DEFOs.
Catsman-Berrevoets, C. E., Bussmann, J. B. J., Pangalila, R. F., Becher, J. G., Polinder, S., Steyerberg, E., Stam, H. J., Schasfoort, F. C., Treatment with botulinum toxin of children with cerebral palsy has no added therapeutical value or cost-effectiveness for gross motor function, everyday physical activity levels or quality of life when combined with intensive functional physiotherapy, European Journal of Paediatric Neurology, 19, S11, 2015	Population - children (4 to 12 years)
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	Population - children (health state valuations on children aged 11 and clinical effectiveness from studies with participants less than 18 years)
Health Quality, Ontario, Intrathecal baclofen pump for spasticity: an evidence-based analysis, Ontario Health Technology Assessment Series, 5, 1-93, 2005	Population - not specific to CP. No economic evaluation

Study	Reason for Exclusion
	conducted or identified.
Houltram,J., Noble,I., Boyd,R.N., Corry,I., Flett,P., Graham,H.K., Botulinum toxin type A in the management of equinus in children with cerebral palsy: an evidence-based economic evaluation, European journal of neurology : the official journal of the European Federation of Neurological Societies, 8 Suppl 5, -202, 2001	Population - children (clinical effectiveness taken from papers with average ages of 4.6, 37 and 5.6 years)
Hoving, M A, Evers, S M, Ament, A J, Raak, E P, Vles, J S, Intrathecal baclofen therapy in children with intractable spastic cerebral palsy: a cost-effectiveness analysis (Provisional abstract), Developmental Medicine and Child Neurology, 50, 450-455, 2008	Population - children (aged from 7 to 17 years)
Ruiz,F.J., Guest,J.F., Lehmann,A., Davie,A.M., Guttler,K., Schluter,O., Dreiss,G., Costs and consequences of botulinum toxin type A use: Management of children with cerebral palsy in Germany, European Journal of Health Economics, 5, 227-235, 2004	Population - children (mean age 9 years)
Symington, D. C., Lewis, M. P., Cost-benefit analysis of a hospital and university based prevocational program, Archives of Physical Medicine & Rehabilitation, 54, 341-7, 1973	Only 11% CP. Out of date (1973). Include productivity costs.
Ugrekhelidze, D., Yagudina, R., Kulikov, A., Cost analysis of intrathecal baclofen therapy for the treatment of spastic cerebral palsy in the Russian Federation, Value in Health, 19 (7), A537, 2016	Conference abstract with insufficient detail. Not a full cost-effectiveness analysis. Include indirect costs.
Walczak , Jozwiak, Jasinska, Garbacka, Obrzut, Dardzinski, A cost-effectiveness analysis of programmable baclofen pump therapy in children with spastic cerebral palsy , Journal of Health Policy & Outcomes Research, 1, 8188, 2012	Population - children (model starts at age 12 and continues for 6 years)
Yagudina, R., Kulikov, A., Ugrekhelidze, D., Cost-Effectiveness Analysis of Botulinum Toxin Type a Treatment for Cerebral Palsy, Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research, 18, A734, 2015	Population - children inferred from conference paper

Health economic evidence profiles

Table 9: Health economic evidence profiles for [A2]

Study	Limitations	Applicability	Other comments	Costs	Effects	Inc. cost-effectiveness	Uncertainty
Bensmail 2009	Potentially serious[a]	Partially[b]	A decision tree was developed, but transition probabilities, costs and probabilties used to inform the model are not reported.	ITB therapy was cheaper than other established treatment patterns (€59 391 vs €88 272; P < .001)	Using ITB as a first line strategy in severely impaired patients with disabling spasticity had a significantly higher success rate than conventional medical management (78.7% vs 59.3%; P < .001)	ITB was considered to dominate other established treatment patterns by providing greater effectiveness at a lower cost. The mean cost-effectiveness ratios show a significantly lower average cost per success with ITB as a first-line strategy (€75 204/ success vs €148 822/success; P < .001).	Mean PSA values using 5,000 iterations presented as the base case, no further analysis of uncertainty is performed.
Sampson 2002	Potentially serious[c]	Partially[d]	DAM not developed. Category 1, bedbound patients experiencing severe spasm-related pain; Category 2, bedbound patients who were not in pain; Category 3,	The cost of ITB was estimated to be approximately £11,700 for the assessment, test dose, and implantation procedure, with follow-up costs of	Patient category: baseline EQ-5D value (score); improvement (score) 1: -0.594 (33333); 0.50 (23322) 2: -0.208 (33313); 0.27 (23312) 3: 0.079 (23322); 0.43 (23312)	Category: cost per additional QALY for ITB 1: £6900 2: £12,790 3: £8030	Threshold sensitivity analysis performed to examine the annual gains in QALYs required to provide specific ICERs between £5000 and £25,000 per QALY

Study	Limitations	Applicability	Other comments	Costs	Effects	Inc. cost-effectiveness	Uncertainty
			wheelchair users with moderate spasm related pain.	£580 to £1160 per annum, based on an average of 4 to 8 refills per annum. The total discounted cost over a 5-year period is estimated at £15,420.			
Saulino 2015	Potentially serious[e]	Partially[f]	Using a pre–post cohort methodology, the control group is the actuarial projection of a conventional treatment protocol had the patients not been implanted. After 6 years, a proportion of patients who received	Cumulative cost savings per patient 30 years post-ITB implant US$240,272 Cost savings per patient per year 30 years post-ITB implant US$8,009	NA	NA	Sensitivity analyses carried out on 3 variables likely to have a meaningful impact: 1) the drug delivery system's battery life, 2) the length of the pre-implant experience period used to establish average starting cost for projection purposes, and 3) the medical cost trend assumptions (i.e., both initial and ultimate rates).

Study	Limitations	Applicability	Other comments	Costs	Effects	Inc. cost-effectiveness	Uncertainty
			ITB pumps are assumed to undergo additional medical procedures, including explant and reimplantation, reflecting health-care industry average expectations.				

(a) Bensmail 2009 limitations: time horizon may not be long enough to capture all differences between treatments, databases used to inform clinical effectiveness in the model are not reported, model inputs such as the probabilities of "success" and "no success" are not reported and it is not described how they were estimated from the historical databases, no comparative clinical trials were used to inform the model (given that none were published at the time of model development), sensitivity analysis not explored.

(b) Bensmail 2009 applicability: analysis included people with spasticity other than cerebral palsy, QALY not used as outcome measure.

(c) Sampson 2002 limitations: meta-analysis included non-comparative studies but changes in HRQoL (EQ-5D) were based on additional assumptions, sensitivity analysis was limited.

(d) Sampson 2002 applicability: potentially out-of-date trials used to inform the model, not all papers included in the meta-analysis included people with cerebral palsy, costs and benefits were discounted at 6% as opposed to 3.5%.

(e) Saulino 2015 limitations: no control group was observed relative to the intervention group, survival was not considered as part of the analysis which will overestimate survival, potential conflict of interest

(f) Saulino 2015 applicability: US setting may not be generalizable to UK practice, not all patients included in the analysis had cerebral palsy