
# WORKING GROUP ON ACUTE PURCHASING

# The Effectiveness of Intrathecal Baclofen in the Management of Patients with Severe Spasticity

**January 2000**

# GUIDANCE NOTE FOR PURCHASERS 00/01

## Series Editor: Nick Payne

**InterTASC No: 6/2000**

# Trent Development and Evaluation Committee

The purpose of the Trent Development and Evaluation Committee is to help health authorities and other purchasers within the Trent Region by commenting on expert reports which evaluate changes in health service provision. The Committee is comprised of members appointed on the basis of their individual knowledge and expertise. It is chaired by Professor Sir David Hull.

The Committee recommends, on the basis of evidence provided, priorities for:

- the direct development of innovative services on a pilot basis;
- service developments to be secured by health authorities.

The statement that follows was produced by the Development and Evaluation Committee at its meeting on 11 January 2000, at which this Guidance Note for Purchasers (in a draft form) was considered.

## THE EFFECTIVENESS OF INTRATHECAL BACLOFEN IN THE MANAGEMENT OF PATIENTS WITH SEVERE SPASTICITY

**AUTHORS:** Sampson F C, Hayward A, Evans G, Touch S, Morton R, Vloeburghs M, Playford D, Collett B J, Critchley P. Trent Institute for Health Services Research, Universities of Leicester, Nottingham and Sheffield 2000. Guidance Note for Purchasers: 00/01.

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*(The recommendations made by the Committee may not necessarily match the personal opinions expressed by the experts)*

**DECISION: The Committee recommended that Continuous Intrathecal Baclofen Infusion (CIBI) be made available only to those patient groups in which there is evidence of benefit (patients who are bedbound due to severe spasticity, patients who cannot be seated appropriately in a wheelchair due to severe extensor spasms, and other wheelchair-bound patients in whom spasm-related pain or skin breakdown is a severe problem). The Committee considered it important to establish regional or national trials to collect further information on outcomes for these patients. Children receiving CIBI should be offered treatment within the**

**context of a national study. Other patient groups should only receive treatment in the context of high quality trials to enable data about efficacy to be collected.**

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## EXPIRY DATE

The conclusions reached in this Guidance Note are likely to be relevant for a period of approximately two years.

**January 2000**

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InterTASC No: 6/2000

Published by the Trent Institute for Health Services Research



ISBN 1 900 733 36 6

Referencing information:
Sampson F C, Hayward A, Evans G, Touch S, Morton R, Vloeburghs M, Playford D, Collett B J, Critchley P. *The Effectiveness of Intrathecal Baclofen in the Management of Patients with Severe Spasticity*. Sheffield: Trent Institute for Health Services Research, Universities of Leicester, Nottingham and Sheffield, 2000. Guidance Note for Purchasers: 00/01.

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## ABOUT THE TRENT INSTITUTE FOR HEALTH SERVICES RESEARCH

The Trent Institute for Health Services Research is a collaborative venture between the Universities of Leicester, Nottingham and Sheffield with support from NHS Executive Trent.

The Trent Institute:

- undertakes Health Services Research (HSR), adding value to the research through the networks created by the Institute;
- provides advice and support to NHS staff on undertaking HSR;
- provides training in HSR for career researchers and for health service professionals;
- provides educational support to NHS staff in the application of the results of research;
- disseminates the results of research to influence the provision of health care.

The Directors of the Institute are: Professor R L Akehurst (Sheffield); Professor H Williams (Nottingham); and Professor M Clarke (Leicester).

Professor Clarke currently undertakes the role of Institute Co-ordinator.

A Core Unit, which provides central administrative and co-ordinating services, is located in Regent Court within The University of Sheffield in conjunction with The School of Health and Related Research (ScHARR).

## FOREWORD

The Trent Working Group on Acute Purchasing was set up to enable purchasers to share research knowledge about the effectiveness and cost-effectiveness of acute service interventions and determine collectively their purchasing policy. The Group is facilitated by The School of Health and Related Research (ScHARR), part of the Trent Institute for Health Services Research, the ScHARR Support Team being led by Professor Ron Akehurst and Dr Nick Payne, Consultant Senior Lecturer in Public Health Medicine.

The process employed operates as follows. A list of topics for consideration by the Group is recommended by the purchasing authorities in Trent and approved by the Health Authority And Trust Chief Executives (HATCH) and the Trent Development and Evaluation Committee (DEC). A public health consultant from a purchasing authority leads on each topic assisted by a support team from ScHARR, which provides help including literature searching, health economics and modelling. A seminar is led by the public health consultant on the particular intervention where purchasers and provider clinicians consider research evidence and agree provisional recommendations on purchasing policy. The guidance emanating from the seminars is reflected in this series of Guidance Notes which have been reviewed by the Trent DEC, chaired by Professor Sir David Hull.

In order to share the work on reviewing the effectiveness and cost-effectiveness of clinical interventions, The Trent Institute's Working Group on Acute Purchasing has joined a wider collaboration, InterTASC, with units in other regions. These are: The Wessex Institute for Health Research and Development and The University of Birmingham Department of Public Health and Epidemiology.

**Professor R L Akehurst**
**Chairman, Trent Working Group on Acute Purchasing**

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## SUMMARY

Severe spasticity is a significant problem for many patients with spinal cord injury, multiple sclerosis and cerebral palsy, causing a loss of independence and mobility, pain, sleep problems, difficulties in nursing care and aggravating other problems such as skin breakdown and urinary incontinence.

Description of Proposed Service

Continuous Intrathecal Baclofen Infusion (CIBI) is used in the treatment of patients whose spasticity is refractory to other treatments for the management of spasticity (including physical therapies and oral treatments), or for patients who experience unacceptable side-effects with oral drug therapy.

Although CIBI has been shown to reduce severe spasticity of spinal origin and to a lesser degree spasticity of cerebral origin, its effect on patient function and quality of life is less clear.

Number and Quality of Studies and Direction of Evidence

Studies which reported outcomes related to function or quality of life were identified and reviewed. The majority of these were small, open, uncontrolled, follow-up studies with subjective outcome measures.

Summary of Benefits

Functional improvements included improvements in ability to sit out of bed or to sit more comfortably in a wheelchair, improved ease of nursing care and moderate improvements in activities of daily living.

The extent of benefit is likely to be greatest in those with the most severe restriction in mobility. For example, around 70% of bed-bound patients may become able to sit out of bed and 90% of patients who find it difficult to sit in wheelchairs because of severe spasticity may be able to sit much more comfortably. Wheelchair users who already have a reasonable degree of function may experience moderate improvements in ability to perform activities of daily living, but they are likely to continue to need help with most activities. The effect on patients who are already ambulatory has not been researched adequately, but the available evidence suggests that around 30% of such patients may show moderate improvements in their ability to walk and in around 10% of patients walking may deteriorate.

Improvements in ease of nursing care will occur with most patients, although the extent of

improvement has not been quantified. Nursing care may be reduced greatly by improvements in skin integrity and the healing of chronic decubital ulcers. Patients who require help in dressing are likely to need less help, but it is unlikely that they will become independent. Some patients may no longer need help feeding themselves. It has been reported that a few patients have been able to live in community settings, with support.

Approximately 90% of patients with spasm related pain may benefit from a reduction in pain, although few studies reported objective pain measures. Approximately 82% of patients with urinary problems showed some improvements, including decreased nocturia, ability to self-catheterise and becoming continent between catheters.

Minor complications are not uncommon, but major complications are rare. Improvements in pump design and experience in their use are thought to have reduced complication rates.

Costs/QALY

The cost of the pump and implantation procedure is estimated at around £11,800, with further annual costs of £500 - £900 for follow-up and refill. The battery life of the pump is around 5-7 years, with a further procedure required after this time.

No studies reported improvements in quality of life in terms of standard quality of life measures (QoL), thus making conventional estimates of cost-utility impossible. Use of threshold analysis suggested that, assuming five years of benefit are obtained, a benefit of around 0.16 quality adjusted life years (QALY)s would equate to a cost-utility ratio of £20,000. This is in the same range of cost-effectiveness as interventions such as home haemodialysis, coronary artery bypass graft (CABG) or continuous ambulatory peritoneal dialysis (CAPD). Clinical opinion and Index of Health Related Quality of Life (IHQL) analysis suggested this scale of QoL improvement to be realised.

Moreover, the high initial cost of CIBI implantation could be offset substantially by reductions in pressure sores, other admissions related to spasticity, orthopaedic procedures and reductions in requirements for orthoses or other aids and adaptations.

The report identifies a number of possible options for purchasers. In all options CIBI should be administered only within the context of an appropriately resourced and organised service, including an appropriately trained multi-disciplinary team with an ability to provide good follow-up care. The options recommend the need for further research at least in some patient groups.

## ABBREVIATIONS

| | |
|---|---|
| **ABI** | Acute Brain Injury |
| **ADL** | Activities of Daily Living |
| **CIBI** | Continuous Intrathecal Baclofen Infusion |
| **CNS** | Central Nervous System |
| **CP** | Cerebral Palsy |
| **CSF** | Cerebrospinal Fluid |
| **EMG** | Electro Myography |
| **IHQL** | Index of Health Related Quality of Life |
| **MS** | Multiple Sclerosis |
| **PICU** | Paediatric Intensive Care Unit |
| **QALY** | Quality Adjusted Life Year |
| **QoL** | Quality of Life |
| **SCI** | Spinal Cord Injury |
| **SDR** | Selective Dorsal Rhizotomy |
| **TBI** | Traumatic Brain Injury |

## 1. AIMS OF THE REVIEW

Spasticity has been defined as 'a motor disorder characterised by velocity-dependent increase in the tonic stretch reflex (muscle tone) with exaggerated tendon jerks resulting from hyperexcitability of the stretch reflexes, as one component of the upper motor neurone syndrome'.[1] Increased tone and spasms reduce a patient's mobility and independence and interfere with activities of daily living, continence and sleep patterns. Spasticity may also be associated with significant pain, skin breakdown, contractures, sleep disorders and dyspnoea as well as making transfers more difficult. Spasticity that is not effectively managed can lead to severe disability and loss of independence.[2,3,4]

Spasticity is a significant problem for the majority of patients with multiple sclerosis (MS), spinal cord injury (SCI)[4,3] cerebral palsy (CP) and acute brain injury (ABI). It is complex, but can be broadly defined into two causes, cerebral lesions and spinal lesions. Spasticity relating to cerebral lesions may be more complex and complicated by other motor disorders.

Most patients with mild to moderate spasticity can be managed effectively with combinations of physical therapies or oral medication.[5] However, a significant number of patients with more severe or generalised spasticity experience unacceptable side-effects or fail to improve with conventional oral drug therapy.[6] Increasingly, Botulinum Toxin is being used to treat spasticity in individual muscle groups, but cannot be used for general spasticity. Prior to the development of implantable drug delivery systems, the only alternative for alleviation of severe generalised spasticity was through destructive, irreversible surgical or neurolytic procedures. These are often considered unacceptable alternatives by patients and doctors[2] and, indeed, are rarely performed within the UK. However, the use of Continuous Intrathecal Baclofen Infusion (CIBI) now offers an alternative to patients with intractable spasticity refractory to more conservative management methods.

The use of baclofen as an oral treatment for spasticity is well established. However, penetration into the cerebrospinal fluid (CSF) is poor with oral administration, so high doses may be needed to achieve a therapeutic response. These high doses can result in unacceptable side-effects.[7] The administration of the drug intrathecally (directly into the CSF) has been shown to be effective in reducing spasticity in patients with severe spasticity, using concentrations of the drug of less than one hundredth of those used orally.[8]

This technique has the attraction of allowing a gradual increase in the rate of infusion until the appropriate level of spasticity control is achieved. Some patients need some residual spasticity, for example, in leg extensor muscles to aid standing. The technique is, thus, more acceptable to many patients than irreversible destructive surgery.

The technique is now being used to treat patients with SCI and MS and is being considered increasingly in the UK for some children with CP in conjunction with the conventional treatments of physiotherapy and orthoses.

Uncertainty surrounding the benefits and complications associated with intrathecal baclofen, along with the considerable costs of pump implantation, has limited the extent to which the procedure is being used within the UK.

The effects of CIBI are difficult to quantify, as improvements in function are highly individualised due to the differing expectations and experiences of each patient. However, a large number of case reports and small trials reporting the benefits and complications associated with the procedure have been published since the benefits of the intervention were first reported in 1984.[9] The treatment has been reported to improve the function and quality of life of many carefully selected patients, although improvements have not been systematically reported. However, there are a number of concerns currently limiting the extent to which the pump is being used within the UK. The cost of providing a patient with intrathecal baclofen is considerable; the pump itself costs around £5,800 with significant additional resources for the implantation procedure and follow-up for refill. Also, many complications associated with the implantation have been reported, notably concerning problems with the pump, risk of infection and problems with the catheter. The likelihood of experiencing complications appears to vary considerably depending upon the experience of the clinician and the type of pump used. Recent experience abroad, especially in North America, has reduced the rate of complications leading to pump removal to an acceptable 5% of procedures.[10]

Uncertainty surrounding the benefits and complications associated with intrathecal baclofen, along with the considerable costs of pump implantation, have limited the extent to which the procedure is being used within the UK. Thus, there are a number of patients who are not yet receiving the treatment who potentially could benefit from doing so.

The purpose of this Guidance Note is to identify and review the evidence-base for the use of intrathecal baclofen in the treatment of spasticity and to outline the potential cost implications of providing the treatment for all patients who may benefit.

## 2. DESCRIPTION OF UNDERLYING DISEASE

### 2.1 CEREBRAL PALSY

Cerebral spasticity in children (aged 18 or under) is largely due to cerebral palsy, with acquired encephalopathy such as head injury accounting for a small number. Cerebral palsy is present at birth or soon after and is the name given to a variety of conditions causing non-progressive damage to the developing brain, causing mainly but not exclusively, motor problems such as spasticity. Cerebral Palsy occurs in 2-3/1000 children, around half of whom have generalised spasticity.

Quadriplegia (loss of movement and sensation in both the arms and legs) accounts for around only 7% of CP, but the severity of the condition leads to considerable distress both in the child and his/her carers, and care is very expensive. In these patients CIBI has the potential to lead to improvements in nursing care, reductions in hip dislocation and reductions in the onset of scoliosis.

Children with diplegic CP (loss of movement and sensation in corresponding limbs on both sides of the body) account for 44% of those with CP and are usually able to walk, even if only a little and with aids. Around the age of eight years, however, their mobility fails to improve and often subsequently deteriorates, leading in some cases to wheelchair confinement.[11] This is due partly to an increasing mismatch between weight and strength, but also to muscle contractures developing as a result of spasticity. Orthopaedic surgery is needed for contractures to elongate the muscle at the tendons and, increasingly, all muscles are operated upon together - so called multilevel surgery, usually around the plateau stage.[11]

In these patients, CIBI may have the potential to improve mobility, reduce spasticity and defer the onset of muscle contractures, in some cases avoiding the need for such extensive orthopaedic surgery.

It should be remembered, however, that any improvement due to spasticity reduction would only be relative, as CP involves other motor problems including weakness, poor co-ordination and immature movement patterns.

## 2.2 MULTIPLE SCLEROSIS

MS is characterised by an autoimmune process within the central nervous system (CNS) resulting in demyelination with secondary axonal loss. The primary trigger or triggers are not known. There are foci of inflammatory cell infiltration around venules predominantly in peri-ventricular white matter, called plaques. The pathological changes are progressive whilst the clinical picture is usually relapsing and remitting at first, and later becoming secondarily progressive.

The clinical pattern is both variable in severity and unpredictable. People with MS develop a range of symptoms and signs including fatigue, memory and attention difficulties, bowel and bladder problems, weakness, numbness, pain and increased muscle stiffness (increased tone or spasticity). People with young age at onset and sensory symptoms do relatively well whilst those with primary progressive MS have a poor prognosis. Approximately one third will need assistance to walk, or be dependent within 15 years of diagnosis.[12,13,14]

The prevalence of MS in the UK is around 100 in 100,000,[15,16] thus, within an average health district of 500,000 there will be 500 people with MS of whom approximately 160-180 will have significant disability.

Increased tone or spasticity may be important contributors to disability, causing pain, difficulty in walking and transferring, and cause significant problems in the management of perineal hygiene. It may prevent comfort with seating, predispose to pressure sores and cause difficulty with transfers as the patients adopt an extensor posture. Tone management should ideally be multi-disciplinary starting with the prevention of unpleasant and painful stimuli and a stretching programme and progressing to adequate trials of oral therapy. Focal spasticity may be treated adequately with motor point blocks using botulinum, and phenol nerve blocks.

The group of MS patients most likely to benefit from CIBI is that with non-focal spasticity and spasms unresponsive to conventional oral treatment including an adequate trial of baclofen, dantrolene, nocturnal diazepam and tizanidine.[17,18] In general, this group is unable to walk, but patients are able to use powered or self propelled wheelchairs. No studies have yet identified the proportion of MS patients who fall into this group, but it is estimated that perhaps 3-4% of the MS population could benefit, that is 15 to 20 per health district of 500,000 population.

## 2.3 SPINAL CORD INJURY

Spinal cord injury (SCI) occurs as a result of road traffic accidents, violence, falls, diving accidents and work or sports related injuries. Patients are predominantly males in the 16-30 year age group. The majority of SCI patients will expect a normal life span. Around 55% of SCI patients will be affected by paraplegia (loss of movement and sensation in the lower body) while 44% are affected by quadriplegia (loss of movement and sensation in both the arms and legs) (paralysis website - http://paralysis.apacure.org/progress/facts.html).

Spasticity has been reported to develop within one year of injury in 67% of patients[19]. Soni[20] estimates that around 5-10% of SCI patients will require intrathecal drug delivery systems to treat their excessive spasticity.

## 2.4 ACUTE BRAIN INJURY

Acute brain Injury (ABI) due to traumatic brain injury (TBI), hypoxic brain injury or trauma is a further cause of cerebral spasticity which has been treated with CIBI.

## 2.5 SIZE OF PROBLEM IN AN AVERAGE HEALTH AUTHORITY

Table 1 provides an indication of the number of prevalent and incident cases in a health authority (HA) of 500,000 population.

**Table 1 Estimated Incidence and Prevalence of Spasticity In Conditions Potentially Amenable to Treatment with CIBI**

| Disease Area | Incidence per 100,000 per year | Prevalence per 100,000 | % Who May be Considered for CIBI | Prevalent Cases who may Benefit from CIBI in a HA of 500,000 | Incident Cases who may Benefit from CIBI in a HA of 500,000 per annum |
|---|---|---|---|---|---|
| **SCI** | 1.7[21] | 72[22] | 5-10%[20] | 18 - 36 | 0.4 - 0.8 |
| **CP** | 2.6* | 50 | 10% | 25† | 1.3† |
| **MS** | 3.5 | 100[16] | 3-4% | 15 - 20 | 1-1.3 |
| **Total** | | | | 58 - 81 | 2.7 – 3.4 |

* Based on CP birth rate of 2 per 1,000 and overall birth rate of 1,300 per 100,000 population.[23]

† These figures relate mainly to severe quadriplegic and diplegic CP with limited mobility. If CIBI were considered for those with mild diplegic CP also, then the prevalent cases and incident cases could be doubled.

Although these analyses are extremely approximate, they suggest that there may be a large 'backlog' of prevalent cases which could potentially benefit, but that at steady state around three procedures per year might be expected in each district.

# 3. CURRENT SERVICE PROVISION

The use of CIBI is not standard in the UK and there are a small number of centres which have set up services for the use of CIBI. Many health authorities are currently not funding the treatment for patients with cerebral palsy due to uncertainty surrounding the benefits of the intervention. To date, a small number of children with cerebral palsy have received the treatment in England and Wales. The Trent regional centre for SCI (The Spinal Cord Injuries Unit, Northern General Hospital, Sheffield) sees around 100 new patients per annum. Around 36 intrathecal baclofen pumps have been implanted within the past six years, the majority of patients having had SCI, but only a few having MS.

In 1998, approximately 200 patients in Britain were implanted with pumps for intrathecal baclofen (Medtronic). Approximately 60% were SCI patients, 30% had MS and the remaining 10% had an underlying cause of spasticity due to other causes, such as CP, traumatic brain injury and metabolic disorders.[24]

## 3.1 CURRENT TREATMENT OPTIONS FOR THE MANAGEMENT OF SPASTICITY

The management of spasticity for all patients, regardless of the underlying cause, follows a rational treatment plan, starting with the most conservative therapy and advancing as needed to a more invasive approach. Once patients begin to require the more aggressive methods, then the cause and degree of the spasticity, generalised or local, has an effect on which treatment is most beneficial.

### 3.1.1 Initial Treatments

Initial attention should be paid to eliminating noxious or external stimuli which could encourage the development of, or exacerbate, spasticity. This is followed by a routine of passive range-of-motion exercises, including physiotherapy, occupational therapy, hydrotherapy, applications of heat and ice and various physical interventions.

### 3.1.2 Oral Treatments

Once this line of treatment has been exhausted, oral drug therapy is considered. Single doses or combinations of a number of drugs may be tried, including baclofen (Lioresal), diazepam, dantrolene sodium (Dantrium), tizanidine and benzodiazepines. Baclofen is the

drug of choice for spinal cord spasticity, but 25-30% of SCI patients still fail to respond.[25] The major drawbacks with oral drug therapy are the side-effects. Many patients find them intolerable when the medications are given at the dosage level required to be effective. The main side-effects are lethargy, weakness, somnolence, dizziness and mental confusion, which is reported to occur in approximately 10-20% of patients.[25] Other side-effects include hallucinations, hypotonia and ataxia.

### 3.1.3 Botulinum Toxin

Intramuscular injection of botulinum toxin to reduce spasticity has been used increasingly in the past five years in adults and children suffering from MS,[26] stroke[27] and CP.[28] It can easily be given as an out-patient procedure, sometimes with mild sedation. However, because of the limited amount that can be given safely at one time, only a small number of muscles can be treated on a 4-6 monthly basis. Its use, therefore, tends to be restricted to certain muscle groups, for example the hip adductors in quadriplegic CP. Knowledge of this technique is still incomplete, especially the benefits from repeated use as some patients may develop a resistance to botulinum.[29]

Apart from reducing spasticity, weakness is also created, although this is rarely a practical problem. There is a maximal total dose according to body weight for each course of treatment, beyond which toxin escapes into the systemic circulation in significant amounts to cause general fatigue. This limits the number of muscles which can be treated at any one time (four in the lower limb or eight in the upper limb) and current practice dictates a minimum of around four months between treatments to avoid resistance due to antibody formation.[30]

The major indications for botulinum are in the relief of spasticity in the calves in children with hemiplegic CP (loss of movement and sensation in the right or left half of the body) and the calves, hamstrings and hip adductors in diplegics. The plan, as for other anti-spasticity treatments, is to defer the time for orthopaedic surgery, and perhaps avoid some procedures. Botulinum can also be used to good effect in quadriplegics, especially in the hip adductors,[31] although it has not yet been established as to whether this is sufficient to avoid hip dislocation. It is likely to become established as a primary treatment in many children with CP. However, it is not usually considered for SCI patients as the treatment is not really appropriate in generalised spasticity.

### 3.1.4 Selective Dorsal Rhizotomy

This technique has been popular abroad in reducing cerebral spasticity in children but continues to be less popular in the UK.[32] A laminotomy is performed (L1 - L5) and selective dorsal roots are cut under the guidance of intraoperative electro-myography (EMG), involving the sacral roots, but avoiding those affecting the bladder.[33] Dramatic reductions in spasticity can result, leading to improvements in gait in diplegics,[34] although most patients still need orthopaedic surgery within four years.[35] Post-operative complications still occur in 17% of procedures,[36] although most are temporary. Abnormal perineal sensation can persist, and spinal complications also occur,[31] but probably will be reduced by the modern practice of replacing the boney arches after rhizotomy. Its use in quadriplegics already at risk of scoliosis remains contentious.

The major debate around Selective Dorsal Rhizotomy (SDR) concerns whether documented functional benefits result from the spasticity reduction it produces, or simply the intensive physiotherapy needed for a year or more afterwards. Three recent blinded and controlled trials have been unable to sort this out. Each compared two matched groups of diplegic children, one receiving SDR and intensive physiotherapy and the other intensive physiotherapy alone, measuring outcome with a validated scale of motor function in children.[37] Two studies showed a significant improvement in the SDR group up to one year,[38,39] but the third showed no difference at two years.[40] The indications for SDR in the UK remain uncertain, although the invasiveness of the procedure, together with its complications, continue to make it unpopular with many clinicians here, despite it being probably cheaper overall than CIBI.[41]

### 3.1.5 Therapeutic Nerve Blocks

Therapeutic nerve blocks tend to be used to treat MS or SCI patients. Nerve blocks can either be administered peripherally, in order to manage localised spasticity, or be given to motor points, known as motor point blocks, which are areas of muscle which produce maximum contractions when stimulated. Passive range of movement exercises, splinting and devices to maintain proper joint positioning are recommended in conjunction with nerve block therapy.

Intraneural or perineural 2-5% phenol injection is one of the most common types of peripheral nerve block. Phenol acts by protein denaturation of nerve fibres. In

concentrations of <1%, phenol has local anaesthetic effects which are fully reversible. Percutaneous phenol injections are relatively simple procedures, but a thorough knowledge of peipheral neuroanatomy, kinesiology and electrodiagnostic techniques is essential to perform these procedures safely. Common sites injected are the obturator nerve in adductor spasticity, posterior tibial nerve for the relief of calf spasticity and ankle clonus, musculocutaneous nerve for elbow spasticity causing flexion deformity in hemiplegia, and median and ulnar nerves for wrist and finger spasticity. Alcohol is also injected locally, with its mechanism of action thought to be dehydration effect on nerve tissue, resulting in sclerosis of nerve fibres and myelin sheath destruction.

For the motor point block, 5% phenol is used and effects may last for a month or for as long as two years. The motor points of individual muscles can be identified by the manipulation of a stimulating Teflon-coated needle and then destroyed by the injection. The technique is time consuming but effective.[42] Motor point injections can be used on the hip adductors and calf muscles, which may prevent scissoring and deformity respectively.

The complications of phenol or alcohol injections include post-block pain when injected into a mixed motor sensory nerve or due to an incomplete block. This occurs with a frequency of 2-10%.[43] Other complications include dysaesthesia, cardiac arrhythmia, variable duration of effect and incomplete recovery.

# 4. DESCRIPTION OF NEW INTERVENTION

Following the standard multidisciplinary management of patients with spasticity, some patients whose spasticity is uncontrolled by alternative therapies may be considered suitable for CIBI.

## 4.1 PRE-SCREENING ASSESSMENT

If these patients fulfil selection criteria, have no contraindications to the insertion of an intrathecal catheter (such as anti-coagulant therapy, coagulopathy, local or systemic infection, anatomical abnormality of the spine) and are in agreement, then a trial of intrathecal baclofen may proceed.

The technique is fully discussed with the patient. It will be explained that bolus test doses of baclofen will be given on a daily basis and that initially a temporary catheter will be inserted intrathecally for this procedure. Response to the bolus doses will be assessed on the Ashworth Scale. Informed consent is obtained from the patient before proceeding.

## 4.2 TEST PROCEDURE

An intrathecal catheter is inserted under local anaesthesia and light sedation, if necessary, using an aseptic technique in the operating theatre and using X-ray screening. A general anaesthetic is not normally required. Baclofen is given intrathecally and the patient returned to the ward for observation. Monitoring of vital signs and change in spasticity is undertaken by ward nurses and doctors trained in the identification and treatment of baclofen toxicity. The dose of baclofen is titrated upwards in 25 microgram per day aliquots until the patient responds. If the patient does not react to 100 microgrammes intrathecally he/she is considered not to have an adequate response and should not undergo implantation. Following an adequate reaction the catheter is removed.

For children with CP, a general anaesthetic will be administered. While under anaesthetic, tests for orthopaedic problems that will contraindicate the use of CIBI are undertaken and used as part of the assessment of patient suitability, i.e. ankles no longer movable, knees unable to bend, decreased tone in lower limbs.

## 4.3 PUMP IMPLANTATION

Following a positive response with a test dose and discussion of the potential benefits with the patients (and parent(s) in the case of children), the decision as to whether an implant should go ahead is made. For the implant, the patient is admitted to hospital the night before surgery is planned. Insertion of the pump is performed using an aseptic technique under general anaesthesia, radiological control and antibiotic cover. The catheter is fixed, the pump pocket formed and the pump prepared according to the manufacturer's instruction and filled with the correct volume of baclofen. The pump is then connected to the catheter, inserted into the pocket and the incisions sutured. The volume of the catheter must be calculated accurately to ensure the correct programming of the pump. This is done by measuring accurately the catheter left at the end of the surgical procedure.

## 4.4 POST-OPERATIVE MONITORING

The patient is returned to the ward and undergoes routine post-operative monitoring and also observation for signs of baclofen overdose (light-headedness, drowsiness, unconsciousness, infusion, depressed respiration, coma). Nurses on the ward should be fully acquainted with the programmer and should be able to perform an 'emergency stop' procedure.

If no complications are experienced, the patient may be discharged after 5-10 days.
Potential post-operative complications comprise:

1. Heamatoma/seroma
2. Infection
3. CSF leakage.

Patients will receive antibiotics two weeks post-operatively.

## 4.5 FOLLOW-UP

Following discharge from hospital, patients will require regular follow-up visits for monitoring and pump refills. Training of carers, hospital staff and specialised nurses is important as it will be these people primarily who are required to monitor the patients and observe any vital changes in their conditions. Specialist baclofen nurses are required for the follow-up visits

and pump refills after implantation. Typically, these visits take place within an out-patient clinic or office setting, but may take place in a rehabilitation facility or in the home of the patient, as transport of severely affected patients is very difficult.

A protocol needs to be developed for trouble-shooting any problems and for re-filling the pump at appropriate time intervals. Ward nurses and junior doctors in the ward area need to undergo a training programme. This needs to be an ongoing programme to cover changes of staff. The education of GPs, out-reach nurses and district nurses should also be arranged. There should be senior doctor cover for emergencies.

### 4.6 PERSONNEL AND SETTING

Due to the need for follow-up and the possibility of complications, CIBI requires an appropriately trained multi-disciplinary team. A specialist surgical team may include a neurosurgeon, anaesthetist, and general surgeon for implanting the pump and attending to any complications, although not all three will be required. The pump should be implanted at a specialist centre, after which the patient should be referred to a local centre to be managed. Local clinicians should be involved in monitoring the pump in association with appropriately trained nurses.

### 4.7 LENGTH OF TREATMENT

The length of time that the treatment will be administered depends upon the nature of the underlying disease. For a progressive disease such as MS, the length of time CIBI will be beneficial will be dependent upon the progression of the disease. For other conditions such as SCI or CP, where life expectancy is not generally reduced or progression does not affect the spasticity, there is no defined limit as to how long the treatment will be required. Long-term use of CIBI has not been reported as the intervention was only introduced in 1984. However, Albright has reported the successful use of CIBI in patients for over 10 years.[10]

Due to limited battery life, the initial pump procedure will need to be repeated every 5-7 years depending upon the type of pump used. The dosage of baclofen may be increased due to increased tolerance of the drug, but the optimal dose often levels out after one year.

# 5. METHODS

A literature search of Medline, Embase, DARE and Cochrane Collaboration databases was carried out, using the search terms ‘Intrathecal’ and ‘Baclofen’. All abstracts identified were reviewed and articles requested if they met suitable criteria.

## 5.1 RESULTS

Due to the considerable yield of trials (94 studies) identified from the literature search, further criteria for inclusion were agreed upon. Trials and reviews on the use of intrathecal baclofen were considered if they investigated patients with the following conditions: cerebral palsy, multiple sclerosis, spinal injury, traumatic brain injury or hypoxic brain injury. Further inclusion criteria specified trials, which sought to measure patient outcomes in terms of:

- Function;
- Quality of life;
- Pain;
- Subjective patient/carer report of effectiveness; or
- Health service use.

Trials measuring the effect of intervention on the carer’s quality of life or perceived ease of patient care were also considered. Trials seeking only to record measurements of patient impairment such as the Ashworth score, spasm score or reflex score were not included. These measures provide some indication of the physiological effect of the intervention, but do not necessarily relate to improvements in function or quality of life.

Further inclusion criteria specified that trials must include more than one patient and have an average follow-up period of at least six months. Further papers were requested if they reported any major complications due to the treatment.

For the purpose of economic analysis, references with keywords ‘costs’ or ‘economic’ were also obtained.

Reference lists of review articles and of the papers included in this review were also scanned to identify further papers.

A standard data form was used as the data extraction strategy to extract information from the relevant papers identified.

## 5.2 QUALITY OF EVIDENCE

Most studies were before-and-after observational trials. Only one employed a blinded randomised controlled methodology for part of the trial, and this randomised part lasted only 13 weeks.

The number of patients in most trials is small, although there are several larger trials.

Many trials did not describe the methodology they had used to measure the functional outcomes they described, and it appeared possible that they had made qualitative judgements rather than used quantified measures. For example, some trials stated that, post-treatment, some patients were easier to care for, but gave no indication of how this had been assessed. A minority of trials used validated outcome measures, but other trials used outcomes measures which had not necessarily been demonstrated as being reliable and valid for the purpose.

The majority of reports provided no statistical analysis.

# 6. RESULTS

## 6.1 QUANTITY AND QUALITY OF RESEARCH AVAILABLE

### 6.1.1 Quantity and Type of Evidence Available

94 studies were identified of which 68 were excluded. The primary reasons for exclusion are shown in Table 2.

**Table 2 Exclusion of Trials**

| Reason for Exclusion | Number of Papers Excluded |
|---|---|
| Reports of complications only | 21 |
| Wrong outcomes measured (usually confined to Ashworth +/- spasm/reflex scores) | 17 |
| Case reports | 9 |
| Health economics outcomes only (included in economics review) | 7 |
| Trial of bolus dose only | 6 |
| Follow-up less than 6 months | 6 |
| Preliminary reports of data presented elsewhere | 2 |

26 original studies met the criteria for inclusion in the review of effectiveness. One meta-analysis was also used in the review of effectiveness.

Only one randomised controlled trial of CIBI was identified, with a randomisation phase of three months. All the other trials related to the uncontrolled follow-up of patients with continuous intrathecal baclofen.

- 8 studies only included patients with spasticity of spinal origin (See Appendix A);
- 6 studies only included patients with spasticity of cerebral origin (See Appendix B);
- 12 studies either included patients with spasticity of cerebral origin and patients with spasticity of spinal origin, or it was not clear whether the origin of spasticity was spinal or cerebral in some patients (See Appendix C).

### 6.1.2 Outcome Measures

Most studies used either the Ashworth score,[44] or a modified version[45] of this to measure the level of spasticity. This is a five-point scale as described below. Both the original scale and the modified version have been shown to have good inter-rater reliability.[46,47]

*The Ashworth Scale:*

0. No increase in muscle tone;
1. Slight increase in muscle tone giving a catch when the limb is moved;
2. More marked increase in tone, but limb is easily moved;
3. Considerable increase in tone-passive movement difficult;
4. Limb rigid in flexion or extension (abduction/adduction).

The main problem with the scale is that, although it gives an indication of the degree of spasticity, it gives no indication of how that spasticity affects the patient's function or quality of life.

The Penn spasm score is also often used in studies. This measures the frequency of spasms, but again provides no indication of how this affects function or quality of life.

A large variety of measures relating to function or quality of life have also been used, however, most studies do not use any formal scales to measure these outcomes.

These include:

- Outcomes related to mobility e.g. ability to sit out of bed, ability to transfer, wheelchair mobility, ability to walk. Most studies relate to improved ability in these areas, but do not use any scales to quantify these improvements.
- Activities of daily living (ADLs) – many studies mention ADLs, but do not appear to use any formal scales to assess these.
- Level of nursing – many studies report on improved ease of nursing care, but do not quantify this.
- Pain – several studies report decreases in pain, but do not use formal scoring systems.

A few studies have used formal scores to measure function or quality of life. Scores used include:

- The Sickness Impact Profile (2 studies)[48,49,50]
- The Functional Independence Measure (1 study)[51]
- The Hopkins Symptom Checklist (1 study)[50]
- The Barthel score (1 study)[52]
- Ferrans and Powers Quality of life index[49]
- The Functional Disability score[53]

The best validated of these scores is the Sickness Impact Profile. The score aims to measure the impact of the patient's condition on performance (rather than on capacity for performance). The behaviours included are designed to represent limitations that may be affected by any disease. The score consists of 136 questions grouped into different areas. It has a physical sub-score (including ambulation, mobility, body care and movement) and psychological sub-score (including social interaction, alertness, emotional behaviour and communication). Scores are standardised and reported on a 0-100 scale. The scale is designed to be reported either as separate physical and psychological scores or as an overall score. The score has been shown to have good repeatability, inter-rater reliability, and validity (when compared with other scores). Its sensitivity to clinical change has varied in different studies. The score has been used in a wide variety of different conditions.

The Functional Independence Measure (FIM), described below, is a seven point scale for measuring the level of independence in self-care, sphincter control, mobility, locomotion, communication and social cognition.

1 = total assistance
2 = maximal assistance
3 = moderate assistance
4 = minimal assistance
5 = supervision or prior preparation
6 = modified independence
7 = complete independence

The score has been shown to have good inter-rater reliability and has been used in a wide variety of patient groups requiring rehabilitation.

## 6.2 EVIDENCE OF EFFECTIVENESS OF CIBI

### 6.2.1 Meta-analysis of Intrathecal Baclofen (Creedon et al. 1997)[54]

A meta-analysis of English language trials of CIBI published prior to June 1996 included 27 studies. (490 patients, 206 spinal cord injury, 162 multiple sclerosis, 59 cerebral palsy, 64 other causes of severe spasticity). The average patient was 36 years old, seven years post-onset of CNS disorder, and had undergone follow-up evaluations for 18 months after implantation of the pump.

- 91% of patients who were screened had a positive response to screening;
- 92% of patients who had a pump implanted had a positive response to the pump;
- 92% of patients who had a pump implanted were still using the pump at one year follow-up.

The overall effect on Ashworth and spasm scores and the effect in different patient groups is shown in table 3 below.

**Table 3 Overall Effect on Ashworth and Spasm Scores**

| Condition | Ashworth Score pre-CIBI | Ashworth Score post-CIBI | N* | p | Spasm Score pre-CIBI | Spasm Score post-CIBI | N* | p |
|---|---|---|---|---|---|---|---|---|
| All patients | 3.9 | 1.6 | 134 | <0.001 | 3.2 | 0.6 | 51 | <0.001 |
| Multiple Sclerosis | 4.2 | 1.3 | 43 | <0.001 | 3.2 | 0.4 | 18 | <0.001 |
| Cerebral Palsy | 2.9 | 2.0 | 23 | 0.34 | - | - | 0 | - |
| Spinal Cord Injury | 4.0 | 1.7 | 49 | <0.001 | 3.4 | 0.8 | 21 | <0.001 |
| Other | 4.3 | 1.7 | 19 | <0.001 | 3.2 | 0.8 | 11 | <0.001 |

* Number of patients on which estimate is based.

The dosage of baclofen required to achieve spasticity reduction increased during follow-up. The greatest increase in dose tended to be in the first month. The average starting dose

was around 150 micrograms per day and after 16 months this was likely to have increased by 250%.

The meta-analysis demonstrates that CIBI successfully reduces spasticity and spasm scores in around 92% of patients who have a pump implanted. The effect on spasticity in patients with cerebral palsy was less marked than in other patients. This needs to be interpreted in the light of the fact that the meta-analysis did not include many patients with cerebral palsy and that these patients tended to have less severe spasticity at baseline than other patients.

Although Ashworth and spasm scores provide a useful way of monitoring spasticity they do not tell us anything about how spasticity affects patients' quality of life. In view of this, and the fact that the meta-analysis has already summarised the data on Ashworth and spasm scores, the subsequent descriptions of trials included in this review do not include further description of the effect of CIBI on these measures.

### 6.2.2 Likely Effects of CIBI in Patients with Spasticity of Spinal Origin

Eight studies which included only patients with spasticity known to be of spinal origin fulfilled the inclusion criteria (160 patients in total; including 78 SCI and 65 MS). These studies are summarised in Appendix A.

It is clear from the meta-analysis that CIBI is likely to have a dramatic effect on the degree of spasticity in at least 92% of patients with spasticity of spinal origin.[54] However, the only randomised controlled trial of CIBI demonstrated no significant difference between placebo and baclofen groups in quality of life/functional measures at three months.

The only large case series of CIBI in spinal spasticity is difficult to interpret, because of subjective outcome measures and a failure to report the numbers of patients improving.[55]

The following statements concerning the effect of CIBI on function or quality of life need to be treated with caution as they are based on uncontrolled, open follow-up studies, mainly using subjective outcome measures and usually involving relatively small numbers of patients.

Patients with spinal spasticity are likely to show modest improvements on the physical dimension of the Sickness Impact Profile. Middel et al.[50] reported a reduction of 41.5 to 31.5 and Gianino et al.[49] recorded a fall of 38.5 to 31.0. Gianino et al.[49] also showed improvements on the psychosocial sub-scale (20.8 to 13.0), but no significant improvement at one year was shown in the study by Middel.[50]

Patients with spinal spasticity who are very severely disabled are likely to benefit from improved ability to sit in a wheelchair and from improved nursing care.[56,53] Patients with less severe disabilities may have some improvements in their ability to transfer, dress and mobilise.[50,53,49,56]

Patients with pain related to spasticity are likely to benefit from CIBI[53,57] and urinary problems may be improved.[58,59]

### 6.2.3 Likely Effects of CIBI in Patients with Spasticity of Cerebral Origin

Six studies which only included patients with spasticity of cerebral origin fulfilled the inclusion criteria (111 patients including 63 with cerebral palsy, the majority of the remaining patients had traumatic or hypoxic brain injury). These studies are summarised in Appendix B.

The meta-analysis suggests that CIBI may be less effective in reducing spasticity in patients with spasticity of cerebral origin than in patients with spasticity of spinal origin.

The following statements concerning effect on function or quality of life need to be treated with caution, because they are based on uncontrolled open follow-up studies mainly using subjective outcome measures and usually only involving relatively small numbers of patients.

Bed-bound patients with cerebral spasticity are likely to benefit in terms of being able to sit out of bed and be pushed in a wheelchair. Ease of nursing is also likely to improve in these patients. Such patients are unlikely to show a measurable improvement in activities of daily living.[7,60]

Children with severe extensor posturing are likely to find it easier to sit in a wheelchair, be easier to nurse and may be able to participate more in activities of daily living.[11]

Patients who are wheelchair bound may become able to walk in therapy sessions, but the available evidence does not suggest that they would be likely to become able to walk independently.[7,60,61] Wheelchair mobility may improve, probably mainly due to improved upper limb function.[7,60,61]

Those who can already walk independently to some extent may improve their walking ability, although most are unlikely to improve sufficiently to enable them to walk outside the home.[62] It should also be noted that walking ability may deteriorate in a proportion of ambulatory patients.[62]

### 6.2.4 Likely Effect of CIBI on Different Outcome Measures

Many different outcome measures were used in different studies. Outcome measures were often subjective. Many studies did not provide denominator data, for example they may report that two patients had decreased pain, but not say how many patients suffered from pain before treatment. Tables 4-8 have attempted to summarise outcomes related to mobility, activities of daily living, dependency and the need for nursing care, and other quality of life issues. Only studies where appropriate denominator data were provided have been included. Each entry also describes the patient group studied. 'Mixed adults' means the study included patients with spasticity of cerebral origin and patients with spasticity of spinal origin. 'Cerebral' means the study only included patients with spasticity of cerebral origin and 'spinal mainly adults'; means the study only included patients with spasticity of spinal origin, most of whom were adults.

### 6.2.5 Outcomes Related to Mobility

Because CIBI has an effect on the degree of spasticity, it can have an important effect on mobility. The proportion benefiting will clearly depend on patient selection, but the following figures are the best estimates available of the percentage of patients likely to benefit (rounded to the nearest 10%).

- Around 70% of bed-bound patients may become able to sit out of bed in a chair.[7,63,64,65]
- 90% of wheelchair users who have difficulty sitting in a wheelchair, because of severe spasticity may become able to sit more comfortably[66,53,52] and 70% of wheelchair users might improve their wheelchair mobility.[7,65] Nearly all patients who can transfer report

improvements in ease of doing this.[66,56,53] There have been a few reports of wheelchair-bound patients who have become able to walk with aids, but this is a rare occurrence.[61,64,67]

- The effect of CIBI on ambulation in those who can already walk to some extent has not been studied in many patients. The available evidence suggests that only around 30% of those who are already able to walk will improve their ability to do this and 10% may have a deterioration in walking ability.[56,62,65,67,68]
- The extent of benefit is generally likely to be greatest in those with the most severe restrictions in mobility e.g. bed-bound patients and patients who find it difficult to sit in wheelchairs because of severe spasticity.
- Most papers were not specific about the size of the improvements seen, so it is difficult to gauge how important these effects on mobility are.

### 6.2.6 Effect on ADLs

A number of papers report subjective improvements in ADLs.

- Around 80% of patients may show some improvements in abilities to perform ADLs.[60,62,63] The extent of improvement is generally not quantified, making it difficult to know how important the changes are.
- Patients who are bed-bound with severe spasticity are unlikely to show any improvement in ADLs.[7,56,60,65,69]

### 6.2.7 Effect on Dependency Levels and Nursing

- One study has shown that some patients may improve their ability to live in community settings.[66]
- In most patients ease of nursing care will improve, however no studies quantify the improvement in ease of nursing care.[6,7,53,66,52,69]
- Patients who require help in dressing are likely to need less help, but it is unlikely they will become independent.[64] Some patients who require help in feeding themselves may become independent in this.[64,70]
- A number of studies have shown improvements in skin integrity.[7,70,71] Chronic decubital ulcers may heal.[7] This may be a very important outcome as ulcers may increase greatly the need for nursing care.

### 6.2.8 Other Outcomes which have an Impact on Quality of Life

- Pain related to spasms is an important problem for some patients. CIBI appears to be effective in reducing or removing spasm-related pain. Approximately 90% of patients with spasm-related pain may benefit from a reduction in pain.[26,57,53,65,69,72] Few studies had objective pain outcome measures or attempted to quantify the reduction in pain, so it is difficult to tell how important this may be.
- Urinary function was reported to have improved in a number of studies. Improvements included decreased nocturia, becoming able to self-catheterise and becoming continent between catheters. Approximately 82% of patients with urinary problems showed some improvements.[58,61,67,68,70,72] There are rare reports of patients being able to take up employment[55,73] or go on holiday[74] following CIBI.
- Sexual functioning was reported to be improved in a very small minority of patients e.g. Ordia et al.[55] reported improvements in four women out of 59 patients.

### 6.2.9 Scoring Systems

- A number of different scoring systems have been used to assess the effect of CIBI on function and quality of life, with differing results.[49,50,52,53,56]
- The Sickness Impact Profile (the best validated of these scores) has been used in two studies.[49,50] On long-term follow-up, both studies showed an improvement in physical dimensions of the score, however only one showed an improvement in psychosocial aspects of the score.[49] The improvements seen were statistically significant, but of modest size.
- Significant improvements have also been seen on the Functional Disability Score[53] and the Functional Independence Measure.[56]
- No significant changes have been observed in the Hopkins Symptoms Checklist,[50] the Barthel score[52] or the Ferrans and Powers Quality of Life Index.[49]
- Some of the scores used may not be sensitive to change in these patient groups.

**Table 4 Outcomes Related to Mobility**

| **BEDRIDDEN PATIENTS BECOMING ABLE TO SIT IN WHEELCHAIR** | | |
|---|---|---|
| Becker[7] | Cerebral adults | 8/12 |
| Stewart-Wynne[63] | Mixed adults | 6/6 |
| Ochs[64] | Mixed adults | 22/38 |
| Zierski[65] | Mixed adults | 14/20 |
| **Overall 50/76 (66%) bedridden patients became able to sit in a chair.** | | |

| **IMPROVED ABILITY TO SIT COMFORTABLY** | | |
|---|---|---|
| Becker[66] | 6 MS patients | On a 0-5 scale – average 3 point improvement in ability to sit |
| Mertens[53] | Spinal adults | 15/15 improved ability to sit comfortably |
| Patterson[52] | Mixed adults | 16/21 improved ability to sit comfortably |
| **Overall 31/36 (86%) had improved ability to sit comfortably.** | | |

| **IMPROVED WHEELCHAIR MOBILITY** | | |
|---|---|---|
| Becker[7] | Cerebral adults | 3/6 |
| Zierski[65] | Mixed adults | 10/12 |
| **Overall 13/18 (72%) improved wheelchair mobility.** | | |

| **ABILITY TO TRANSFER IMPROVED** | | |
|---|---|---|
| Becker[66] | Mixed adults | 8/9 major improvement |
| Azouvi[56] | 12 Adults with thoracic/lower cervical lesions | Average improvement from 3.5 to 6.5 on a 1-7 scale. |
| Mertens[53] | Spinal adults | 17/17 improved ability to transfer |
| **Overall 25/26 (96%) had improved ability to transfer.** | | |

| WHEELCHAIR BOUND PATIENTS BECOMING AMBULATORY (with aids) | | |
|---|---|---|
| Concalves[61] | Cerebral adults | 1/4 wheelchair bound developed 'handicapped walking' |
| Ochs[64] | Mixed adults | 1/27 |
| Penn[67] | Mixed adults | 2/5 |
| **Overall 4/36 (11%) had developed 'handicapped walking'.** | | |

| AMBULATORY PATIENTS IMPROVING THEIR CAPACITY TO AMBULATE | | |
|---|---|---|
| Broseta[68] | Mixed adults | 1/7 |
| Azouvi[56] | Adults with lower cervical /thoracic lesions | 5/12 (including 2/12 who became able to climb stairs) |
| Zierski[65] | Mixed adults | 3/5 |
| Penn[67] | Mixed adults | 1 of 2 ambulatory patients lost ability to walk |
| Gerszten[75] | Cerebral mean age 18 | 6/21 improved walking ability including 4/7 who only walked in therapy became able to walk at home<br>2/6 who only walked at home who became able to walk in the community<br>(note 3 patients also had deterioration in walking ability) |
| **Overall 15/47 (32%) ambulatory patients improved their ability to walk and 4/47 (9%) had deterioration of their ability to walk.** | | |

| PATIENTS BECOMING ABLE TO DRIVE | | |
|---|---|---|
| Parke[70] | Mixed adults | 1/8 |
| Patterson[52] | Mixed adults | 2/21 |
| **Overall 3/29 (10%) became able to drive.** | | |

**Table 5 Subjective Assessments of ADLs**

| **ACTIVITIES OF DAILY LIVING IMPROVED (subjective impression - no scoring systems used)** | | |
|---|---|---|
| Albright[60] | Cerebral mainly children | 19/25 self caring patients<br>0/7 non-self caring patients |
| Gerszten[75] | Cerebral mainly children | 20/24 (deteriorated in 2/24) |
| Stewart-Wynne[63] | Mixed adults | 6/6 |
| **Overall 45/62 (73%) showed some improvement in ADLs. Improvements in ADLs were usually not seen in bed-bound patients.** | | |

**Table 6 Outcomes Related to Dependency Levels and Nursing**

| **PLACE OF RESIDENCE** | | |
|---|---|---|
| Becker[66] | Mixed adults | Of the 3 patients who were hospitalised prior to CIBI, 2 became able to live in the community and 1 in a group home. Of 3 patients in chronic care institutions prior to CIBI, 2 were able to move to a group home and one moved to hospital (due to comorbidities and progression of MS). |

| **NEED FOR PERSONAL ATTENDANT SERVICES** | | |
|---|---|---|
| Nance[8] | Mixed adults | 2/7 had decreased need for personal attendants. |

| **ABILITY TO DRESS** | | |
|---|---|---|
| Ochs[64] | Mixed adults | 8/12 patients who required major help in dressing required only a little help in dressing 6 months after CIBI.<br>1/4 patients who required a little help became able to dress without help. |

| **EATING ALONE** | | |
|---|---|---|
| Ochs[64] | Mixed adults | 2/9 who required help became able to eat alone. |
| Parke[70] | Mixed adults | 5/7 who required help became able to eat alone. |

| **DEPENDENCY LEVEL** | | |
|---|---|---|
| Stewart-Wynne[63] | Mixed adults | 6 adults – no measurable change in dependency levels. |

| **IMPROVED EASE OF NURSING CARE** | | |
|---|---|---|
| Albright[60] | Cerebral – mainly children | 6/7 non-self caring patients. |
| Becker[7] | Cerebral adults | 18/18 |
| Becker[66] | Mixed adults | 8/9 |
| Patterson[52] | Mixed adults | 16/21 |
| Lazorthes[69] | Mixed – mainly adults | 18/18 |
| Mertens[53] | Spinal adults | 17/17 |
| **Overall 83/90 (92%) had improved ease of nursing care.** | | |

| **SKIN INTEGRITY** | | |
|---|---|---|
| Becker[7] | Cerebral adults | Of 11 chronic decubital ulcers, 5 healed, 5 improved. |
| Becker[66] | Mixed adults | 6/9 improved skin condition. |
| Parke[70] | Mixed adults | 3/3 with skin problems had resolution of problems. |
| **Overall 19/23 (83%) of patients with skin integrity problems showed improvements.** | | |

**Table 7 Other Outcomes Related to Quality of Life**

| **PAIN** | | |
|---|---|---|
| Broseta[68] | Mixed adults | 9/10 with pain became pain free. |
| Lazorthes[69] | Mixed | 14/16 resolution of painful spasms. |
| Loubser[57] | Spinal injury adults | 6/6 with musculo-skeletal pain had complete resolution.<br>6/6 with neurogenic pain had no resolution. |
| Mertens[53] | Spinal - adults | 9/9 with spasm related pain became pain free. |
| Sahuquillo[72] | Mixed adults | 8/8 with spasm related pain had relief. |
| Zierski[65] | Mixed | 13/17 with spasm related pain became pain free. |
| **Overall 59/66 (89%) of patients with spasm related pain had relief of complete resolution.** | | |

| **SLEEPING** | | |
|---|---|---|
| Becker[66] | Mixed adults | On a 0-5 scale sleep improved an average of 2.9 points, from 1.6 to 4.5. |
| Penn[67] | Mixed adults | 7/7 had improved sleep. |

| **SEXUAL FUNCTIONING** | | |
|---|---|---|
| Ordia[55] | Spinal adults | 4/59 resumed sexual activity (all females). |
| Loubser[74] | Spinal injury adults | 1/7 improved sexual functioning. |

| **SOCIAL** | | |
|---|---|---|
| Patterson[52] | Mixed adults | 2/21 improved social life. |
| Penn[67] | Mixed adults | 3/7 returned to work. |
| Middel[50] | | At 1 year no change on psychosocial dimensions of SIP score. |
| Ordia[55] | Spinal adults | 2/59 became employed. |
| Loubser[74] | Spinal injury adults | 3/7 became able to take vacations. |

| **URINARY FUNCTION** | | |
|---|---|---|
| Broseta[68] | Mixed adults | 5/9 bladder function improved. |
| Parke[70] | Mixed adults | 2/4 who were dependent became independent. |
| Penn[73] | Mixed adults | 4/4 who were incontinent between catheters became continent between catheters. |
| Nanninga[58] | Spinal adults | 4/4 who were incontinent between catheters became continent between catheters.<br>3/3 patients with indwelling catheters became able to self catheterise. |
| Concalves[61] | Cerebral adults | 2/2 with bladder dysfunction showed improvement. |
| Sahuquillo[72] | Mixed adults | Of 3 with indwelling catheters, 2 had minimisation of leaks and 1 became able to self catheterise.<br>4/4 with voluntary voiding had decreased nocturia. |
| **Overall 27/33 (82%) had improved urinary function.** | | |

**Table 8 Studies Using Scoring Systems**

| **SCORING SYSTEMS** | | |
|---|---|---|
| Azouvi[56] | Spinal adults | **Functional improvement measure**. 7 point scale. Overall improvement in motor, but not cognitive domains. Minimum 2 point improvement in bathing, dressing lower body, transfers, and locomotion. 18 patients. |
| Gianino[49] | Spinal adults | **Ferrans and powers Quality of life index** – no improvements. **Sickness Impact Profile** (0-100 scale) improved from 29.7 to 21.7. Physical sub-score improved from 38.5 to 31.0. Psychological sub-score improved from 20.8 to 13.0. Changes were measured at 12 months in 16 patients and were statistically significant ($p<0.005$). |
| Mertens[53] | Spinal Adults | **Functional Disability Score** - composite score measuring pain, spasms, wheelchair use, transfers and washing/dressing each on a 4 point scale decreased from 13.4 to 5.8 ($p<0.0001$). (17 patients). |
| Middel[50] | Spinal adults | **Hopkins Symptom Checklist and Sickness Impact Profile** - no difference between placebo and intervention group at 3 months. At 12 months physical sub-score of sickness impact profile improved from 41.5 to 31.5. No change on psychosocial sub-score. |
| Patterson[52] | Mixed adults | 0/21 showed improvements in **Barthel score.** |

### 6.2.10 Complications Associated with CIBI

The studies included in the review were also examined to extract data on side-effects. Studies that systematically reported side-effects and in which the type of pump used was know, were summarised in Table 9.

**Table 9 Complications Associated with CIBI**

| | Type of Pump | | |
|---|---|---|---|
| **Complication** | **Medtronic (222)** | **Cordis Secor (30)** | **Infusaid (43)** |
| Death due to pulmonary embolus (Unknown if related to pump) | 2 (0.9%) | 0 | 1 (2.3%) |
| Deep vein thrombosis | 0 | 2 (7%) | 0 |
| Meningitis | 1 (<1%) | 6 (20%) | 2 (5%) |
| Overdose | 5 (2%) | 4 (13%) | 2 (5%) |
| Pump removal due to complication | 16 (7%) | 9 (30%) | 1 (2%) |
| Catheter problems requiring surgery | 37 (17%) | 0 | 7 (16%) |
| Local infection | 9 (4%) | 7 (23%) | 0 |
| Constipation | 13 (6%) | | |
| Erectile Dysfunction | 7 (3%) | | |
| Urinary retention | 6 (3%) | | |
| CSF leaks | 5 (2%) | | |
| Skin erosions over pump | 3 (1%) | | 1(2%) |
| Pseudomeningocoele | 1 (<1%) | | |
| Epileptic seizure | 1 (<1%) | | |
| Pocket seroma | 1 (<1%) | | |

Deep vein thrombosis and pulmonary embolism are likely to occur more frequently in this patient group because of poor mobility. Therefore, it is unlikely that the reported incidents of

these conditions were directly related to use of the pump. Serious complications such as meningitis or overdose appear to be rare when the Medtronic pump is used. Up to 7% of pumps may be removed because of complications. Problems with the catheter, e.g. blockage or kinking requiring minor surgical intervention, are the most common problems with the procedure.

### 6.2.11 Summary of Effectiveness of CIBI

Continuous intrathecal baclofen infusion has been shown to produce a major reduction in severe spasticity of spinal origin in most patients. The effect on spasticity in patients with severe spasticity of cerebral origin is likely to be less, but useful changes are also seen in this group.

The quality of the evidence to demonstrate the effectiveness of CIBI is generally poor (consisting almost entirely of small, open, uncontrolled follow-up studies with subjective outcome measures and a failure to report results separately in different patient groups). However, the quantity of the evidence is now quite large and many studies show important effects in some patients.

Decisions about whether or not to use CIBI need to be based on an understanding of the likely benefits in patients with different levels of function:

- Patients with very severe spasticity who are bed-bound and difficult to nurse are likely to benefit from being able to sit out of bed. Nursing care is also likely to be easier. Such patients are very unlikely to have improvements in ADL.

- Patients who use wheelchairs but have great difficulty in being seated in the chair are likely to benefit by being able to sit much more comfortably.

- Patients with a reasonable degree of remaining function may show some improvements in their ability to perform important functions such as transfers, feeding, dressing or wheelchair mobility. Most studies do not quantify the level of improvement, so it is difficult to judge from the literature how great that improvement may be. Failure to show large improvements in functional measures, such as the Sickness Impact Profile, suggest that such improvements may be modest. It is very unlikely that patients will show dramatic improvements in function, although there are a few reports where this

has occurred. The vast majority of patients will still need help to perform many of their activities. However, in severe disability even modest improvements in function may be very important to patients.

The evidence for using CIBI to improve walking ability is very limited. Up to one third of ambulatory patients may show some improvements in ambulation, but these improvements are unlikely to be dramatic. Some patients may find that the loss of tone makes walking more difficult.

Significant pain related to spasms and problems with skin integrity strengthen the case for using CIBI. CIBI may also improve urinary function, but patients are still likely to need to self-catheterise.

The benefits need to be weighed against the risk of complications (major complications appear to be rare when the Medtronic pump is used), the inconvenience of needing regularly to have the pump refilled, and the cost of the procedure.

## 6.3 ECONOMIC ANALYSIS

### 6.3.1 Estimation of Net Benefits

Estimation of the benefits of CIBI is not straightforward as there is no standard outcome measure used to quantify the benefits. CIBI does not aim to provide a ‘cure’ for spasticity, but aims to manage the condition in terms of easing pain, ability to transfer and patients' quality of life. Although the Ashworth scale is the most commonly reported scale, this is not considered meaningful in terms of reflecting a patient’s quality of life. None of the studies identified reported standard quality of life (QoL) measures for patients using CIBI, although a number reported improvements in patients' quality of life. As such, it has not been possible to estimate the benefits in terms of quality adjusted life year (QALY)s gained. Potential cost-utility results are discussed later, using threshold analysis to examine the QoL benefits required to produce a cost-utility estimate within acceptable limits.

### 6.3.2 Estimation of Net Costs

Intrathecal baclofen is considered only for patients with spasticity that have not responded sufficiently to any other forms of treatment or in whom side-effects of oral treatments were

considered unacceptable. These patients are functionally dependent and require almost constant care. Patients with severe spasticity use a variety of health and social service resources, receiving care at home and within hospital or care home setting.

The use of CIBI has been shown to reduce spasticity and improve the functional outcomes for patients, increasing their independence, comfort and facilitating the job of the carer. Despite a high cost of initiating therapy, the costs may be offset by reductions in future costs for the management of spasticity. There may be potential for cost savings in other areas, such as a reduction in bed days used for the management of spasticity and reductions in the number of orthopaedic procedures required.

It is difficult to quantify benefits for CIBI in terms of improvements to the quality of life of both the patient and the carer. Therefore, the authors have not considered the cost-utility of CIBI, but compared the cost of CIBI with the healthcare costs of alternative interventions. No formal economic analysis of CIBI incorporating consideration of benefits has been identified from the existing literature, although a number of cost analyses are identified and discussed.

### 6.3.3 NHS Costs of Intrathecal Baclofen

The costs of intrathecal baclofen arise from the cost of the procedure, costs of follow-up, support and costs of potential complications. The initial high cost of CIBI therapy arises from screening, the cost of the pump and the hospitalisation required to establish dose requirements. Following the initial hospitalisation, the costs are reduced considerably. The pumps will require a refill every two to three months, and this will normally take place on an out-patient basis.

The cost of hospitalisation reported within the literature varies depending upon whether complications are experienced. The cost studies identified include substantial costs associated with the management of side-effects. However, costs of complications should be less significant than those reported in many of the studies due to improvements of the pump itself and the experience of the surgeons.

The typical length of stay in an acute care facility after an uncomplicated implant has been reported to be between 3 and 10 days.[76,77,78] The average length of stay within an in-patient ward for the UK is considered to be around five days.

Screening costs will be incurred for all patients who may be considered suitable for CIBI therapy, including those who do not respond to the bolus dose. The test dose CIBI is given before the pump is implanted to establish the patient's responsiveness to the drug. The test dose is either by means of lumbar puncture or using an indwelling catheter. This requires hospitalisation of around two to three days, with patients usually observed on a general ward, but with access to intensive care, if required (due to the potential of an anaphylactic response). Around 70%-80% of children tested for response to intrathecal baclofen will undergo implantation.[79]

The batteries in the CIBI pumps have a limited lifetime after which the pump must be replaced. In the older pumps battery life is approximately 4-5 years and in the most recent pumps the battery life is seven years (SynchroMed Infusion System, Medtronic). Replacing the pump involves a procedure similar to the initial implant. However, optimally, the pump is removed without affecting the catheter, in which case the procedure is less lengthy and requires less time in hospital. The procedure may be associated with an increased risk of infection, as is the initial pump implantation.

Further costs will be incurred due to training requirements for carers, hospital staff and specialised nurses. There will also be further educational requirements for the GP, patient and family. This is an ongoing process consisting of an initial introduction to CIBI therapy, further information once therapy has been chosen, and then advice on the follow-up procedure and the degree of commitment required. Information will need to be provided on the delivery system, frequency of pump refills, methods to assess improvements and potential complications, such as, adverse skin reactions, overdose and so on. Intensive in-patient rehabilitation for some patients is also necessary so that the patient can learn new living techniques in order to maximise the benefit of CIBI.

The question as to whether the need for physiotherapy increases or decreases following CIBI is debated.[41,75] Albright[80] suggests that the frequency of physical therapy after pump insertion depends on the goal of the treatment; if the goal is to improve gait, therapy is often given three times a week. If the aim is to facilitate care, patients may need therapy once a week to maintain range of motion, or not at all.

The costs associated with CIBI have been estimated using costs from the Queen's Medical Centre (Nottingham) and the Leicester Royal Infirmary. The cost of administering the test

dose, pump implantation and equipment is estimated at between £10,500 and £12,900. Additional annual costs of around £580 to £870 were estimated for follow-up and refill.

The costs are broken down as follows:

- Pre-screening costs (including 30 minutes neurosurgeon time and out-patient clinic visit) £330 - £556
- Test dose (including lumbar puncture, lumbar catheter, procedure (HRG A452 – injection of therapeutic substance), 2 days' hospitalisation, drug costs and physiotherapist and nursing time for patient observation) £940 - £1,570
- Cost of pump and catheter £7,000
- Cost of implantation procedure (including cost of procedure, drugs, 5 day in-patient stay £8,730 - £10,260
- Other costs (tests, pathology, radiology, microbiology, excluding potential transport costs) £550
- Cost of follow-up (including refill kit, drug costs, physiotherapist assessment and out-patient visit) £140 - £150

Further details of the cost breakdown are provided in Appendix E.

These assume no costs related to complications. The Paediatric Intensive Care Unit (PICU) may be needed when CIBI is administered to children with CP, due to potential anaphylactic response. The cost of the PICU at the Queen's Medical Centre is currently £1,500 per day and, thus, will, increase costs considerably. However, the potential for incurring these costs is difficult to estimate and has not been reported within any published UK study.

The majority of complications will occur within the first few months following implantation, with further complications potentially arising from inappropriate dosage. The potential for error depends upon the experience of the surgeon, cognitive function of patients (related to patient selection) and carers.

### 6.3.4 NHS Savings from Use of New Intervention

Following CIBI therapy, patients experience a decrease in spasticity which can lead to improved mobility and ease of care, and consequently they require fewer resources for management of the spasticity. The reduction in spasticity may lead to fewer carers being

needed for an individual patient and reductions in the requirement for institutional care, orthopaedic surgery, orthoses and other supporting aids. Reductions in the number of bed days required for the management of spasticity have been reported, notably due to the decreased likelihood of developing pressure sores following reductions in spasticity. In addition, savings may be realised from the reduced need for oral drugs or other interventions to treat spasticity.

The potential savings are not well quantified in the literature, although there are a number of articles which examine the potential savings resulting from reductions in bed days and one which reports upon the reduced need for orthopaedic surgery. There are no UK studies of costs or savings relating to the use of CIBI.

**a) Reductions in Hospital Stay**

Patients with severe spasticity frequently require hospitalisation for the treatment of problems related to the spasticity. Patients often require hospital stays of several months for the management of bedsores due to long-term immobility resulting from the spasticity. Other patients will require hospitalisation for periods when the spasticity is so severe that the burden of care is too much for them to be looked after within the community.

The impact on hospitalisation requirements following CIBI have been reported for the US,[55] Canada[8,66] and the Netherlands.[81] The conclusions of these studies are detailed in Appendix F.

The savings reported by Nance et al.[8] and Becker et al.[66] refer only to hospitalisation days related to spasticity. Nance reports a 40 day average reduction in the number of bed days used over two years and Becker reports a 55 day average reduction in the number of bed days used over one year. The difference in numbers could be due to a greater degree of disability in the population reported by Becker, as there were patients suffering skin breakdown who had considerable resource requirements.

The savings reported by Ordia et al.[55] do not relate specifically to spasticity and there is no information provided as to the reason for hospitalisation prior to or post CIBI. Further information would be required in order to consider the use of the results of this analysis.

Postma et al.[81] provide a detailed cost analysis of the costs and savings of CIBI in the Netherlands. The study showed no significant difference in the number of hospital days used by patients undergoing CIBI and the control group in the year following CIBI. For the implantation year there were 18.7 days used on average by the control group compared to an estimated average of 20.7 days related to the CIBI procedure and no further days related to spasticity for the CIBI group.

These papers provide three estimates of bed days used for patients without or prior to CIBI; 19 days,[37] 32 days (63 days over 2 years)[8] and 84 days.[66] The differences are due to different patient selection and care settings. Assuming an average cost per in-patient day of £211,[82] this represents costs of £4,000, £6,800 and £17,700 respectively.

The number of bed days used during the year of implantation ranges from 21 days[81] to 29 days.[66] This corresponds to costs of £4,400 to £6,100 for the hospitalisation related to the CIBI procedure.

**b) Pressure Sores / Decubitus Ulcers**

Pressure sores are a considerable risk for patients who are bed bound due to spasticity. The cost of treating pressure sores is substantial, as they require either long periods of hospitalisation or intensive community nursing care. It is estimated that the total national cost in the UK for the treatment of pressure sores is approximately £755 million a year.[83] For example, a full thickened sacral ulcer extends hospital stay by over 25 weeks at a cost of £26,000 including extra staffing, drugs, dressings and hospital overheads.[83] Costs for pressure ulcers differ depending on the ulcer stage, and also vary depending on care setting. One US study found the mean costs varied from US$1.55 per day for a stage 1 ulcer to US$6.03 per day for a stage 4 ulcer in 1992.[84] Local estimates of costs for treating pressure sores are around £17,000 for a grade 4 pressure sore and £5,000 for grade 3/4.[85] Research is lacking in many areas of pressure ulcer prevention and treatments with regards to cost-effectiveness.

**c) Orthopaedic Surgery**

The use of CIBI in patients with spasticity due to CP may defer the onset of muscle contractures, hip dislocations and potentially reduce the onset of scoliosis.[86] The resulting reduction in the need for orthopaedic surgery for patients undergoing CIBI has been

reported.[75] This paper suggests a reduction of 66% in orthopaedic operations needed following CIBI. While it is not clear whether these procedures have been avoided or merely delayed, there is clearly potential for cost savings.

Neither the actual operations avoided, nor the costs associated with these procedures is documented within the article. Local costings[86] report the costs of common orthopaedic procedures for this patient group as follows:

| | |
|---|---|
| Adductor releases | £2,000 |
| Open or closed adductor tenotomy | £1,500 - £2,000 (excl. physiotherapy) |
| Hamstring release | £2,500 |
| Salter's osteotomy or Chiari osteotomy (for hip dislocation) | £5,000 |

The number of orthopaedic procedures avoided depends upon the age of the child. When the child is treated within the early stages, it is considered likely that orthopaedic procedures may be avoided altogether. In the older child (7-10 years) further orthopaedic work, e.g. Achilles tendons and hamstring releases, may be necessary.

**d) Reductions in Oral Treatments or Other Interventions**

The cost of the drug for CIBI should be offset by reductions in oral treatments, which are prescribed in considerably higher doses. The use of CIBI may also reduce the need for interventions such as therapeutic nerve blocks.

**e) Orthoses and Other Aids or Adaptations**

Patients with severe spasticity require considerable resources. Improved management of spasticity may lead to a reduction in seating aids, wheelchairs, spinal jackets (due to scoliosis) and orthoses.[86] Reductions in spasticity have also been reported to decrease the need for specially designed wheelchairs designed to accommodate extended legs due to spasticity and allow patients to switch to less expensive compact models.[76,78] The compact wheelchair means there is no need for remodelling of the home hallway and fewer adaptations are required.

There are currently no data available to quantify these potential savings, although anecodotal evidence suggests the savings will be realised. Examples of potential cost savings from the reduced need for home adaptions are as follows:

| | |
|---|---|
| Redesign bathroom: | £1,925 (median)[82] |
| Redesign kitchen: | £2,282 (median).[82] |

### f) Reductions in Care Resources

One area of potentially significant savings following CIBI, which is not well documented within the literature, is the potential reduction in carers' time and the need for nursing home care following a reduction in spasticity. Due to the intensity of care required for patients with severe spasticity, any reductions in care requirements will represent considerable cost savings.

The use of CIBI to manage spasticity may reduce carers' time significantly as improved sleep may lead to reductions in night care and patients will be able to be seated and dressed more easily, sometimes reducing the number of carers required to assist one person. Although reductions in the caregiving time required and the ease of care are frequently reported[8,66,76,87] there is no quantification of the potential savings which may be realised.

Similarly, savings have been reported in terms of reductions in the need for institutional care,[66,81] but the potential scale of the cost reduction is not quantified.

### g) Indirect costs

Further potential impact on costs may be achieved through indirect costs, as some patients have been reported to return to employment following CIBI[8,81] or been able to further their education due to reductions in spasticity. Again, these costs are not quantified within the literature.

## 6.3.5 Estimation of Cost-effectiveness and/or Cost-utility

The central cost estimate of CIBI is estimated at around £11,700 per patient for the screening and initial implantation, including £6,770 for the cost of the pump. This is based upon a hospital stay of two days for the test dose and five days for the implantation phase. Costs were obtained from the Queen's Medical Centre (Nottingham), Leicester Royal Infirmary and Central Sheffield University Hospitals NHS Trusts, using an average of the in-patient costs per day. Costs per day varied depending upon the type of ward used (i.e. paediatric neurosurgery or neurology ward). The cost of refills and follow-ups are estimated at around £867 per annum, again using an average of costs from the three Trusts and assuming six refills per year. This gives a total cost of around £15,900 for a five year period

and £17,600 for a seven year period, depending upon the type of pump used. The number of years of benefit received depends upon the type of pump used and the condition of the patient. Some severely disabled MS patients may have a reduced life expectancy when undergoing implantation for CIBI.

Gross costs were used as there is no evidence available quantifying the potential savings. Also, the potential to achieve savings and to shift resources is not always realisable.

Discounting costs at a rate of 6%, gives a total current value of £15,400 for a five year period and £16,700 for a seven year period.

As there is no quantified measure by which the QALYs gained by the use of CIBI can be measured, it is not possible to provide an estimate of the cost per QALY for the treatment. However, by performing threshold sensitivity analyses, an indication of the potential cost-effectiveness can be provided.

*Scenario 1: Using Average Costs per Year Over the Period of Treatment*

Assuming total costs of £17,600 for seven years' treatment, i.e. an average cost per year of £2,500, a benefit of 0.13 QALYs per year (i.e. 0.88 QALYs for the seven year period) would produce a cost-effectiveness ratio of £20,000.

Assuming total costs of £15,800 for five years' treatment, i.e. an average cost per year of £3,200, a benefit of 0.16 QALYs per year (i.e. 0.79 QALYs for the seven year period) would produce a cost-effectiveness ratio of £20,000.

*Scenario 2: Discounting Costs and Benefits to Account for Different Costs in Each Year*

Assuming a cost of £11,870 in year one and £870 in following years, and discounting both costs and benefits at 6%, the number of QALYs gained over the seven year period would be 0.83 to produce a cost-effectiveness ratio of £20,000, i.e. 0.14 QALYs for year one. Assuming the pump lasts for five years, and discounting costs and benefits at 6%, the number of QALYs gained over the period would have to be 0.77 to produce a cost-effectiveness ratio of £20,000, i.e. 0.17 QALYs in year one.

### 6.3.6 Sensitivity Analyses

This section will examine the impact of altering assumptions surrounding different parameters upon the cost estimates and results of the cost-effectiveness analyses.

#### a) Ranges in Costs

The costs used for CIBI may vary between centres and costs will vary depending upon the care setting, with paediatric neurosurgery wards being generally more expensive than neurology wards. The cost of the intervention is dependent upon assumptions made relating to the number of in-patient days required for the test dose, the implantation procedure, the management of potential complications and the number of follow-up visits required. Discussion with clinicians suggested that the range of days for the test dose was 2-5, with the mean in-patient stay for implantation procedure of between five and seven days. The number of refills per year ranged from four to 10, with an average of six. Extreme sensitivity analyses using our ranges of costs and parameter estimates suggest the cost of implantation of a CIBI pump could range between £10,500 and £15,700. These estimates are based upon the range of days listed above, using cost per day of £245 - £551 and do not include the cost of follow-up or refills. The cost of follow-up is estimated to range from £578 to £1,400 per annum, using a range of 4-10 visits per annum.

There may be a small risk of PICU requirement for patients with CP and occasional complications may require additional resources, although clinical opinion suggests that complications are rare, with the exception of catheter related problems which can be fixed easily and do not require extensive hospitalisation. Postma et al.[81] reported a mean additional length of stay of 8.4 days for the management of complications related to the procedure. The necessity for PICU is not quantified within the literature and has not been quantified by clinical opinion.

#### b) Sensitivity of Cost per QALY Assumption to QALY Gains and Treatment Costs

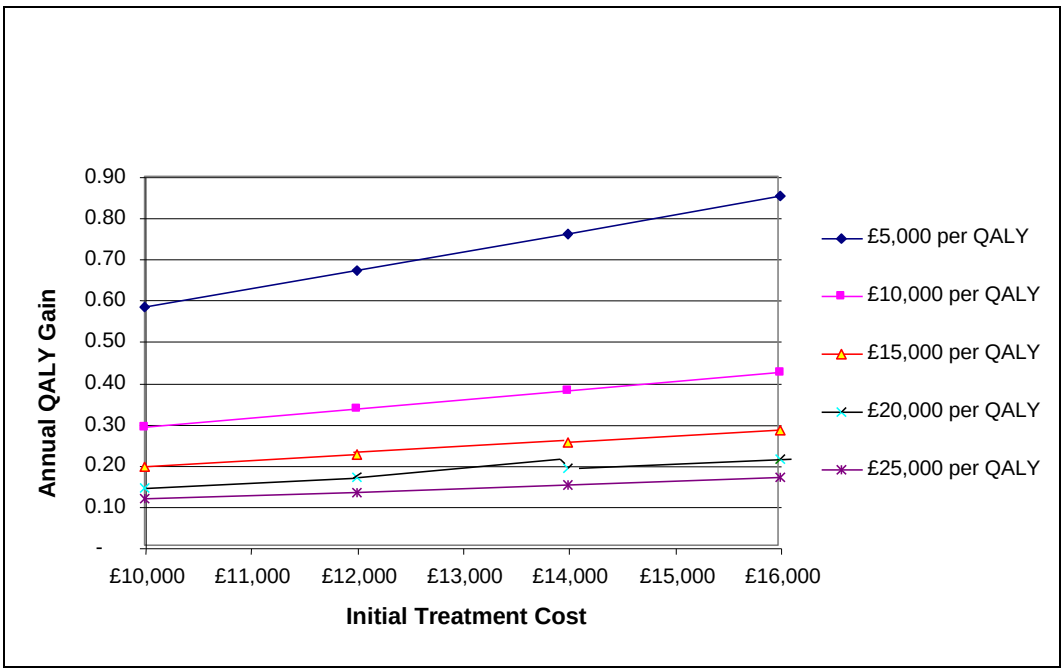
In order to demonstrate the relationship between variance in cost, cost-utility ratio and QALY gains, the following graph (Figure 1) tracks the annual gains in health state values (QALY gains) required to provide cost-effectiveness ratios of between £5,000 and £25,000 per QALY. The following tables and graphs assume that five years of benefit are derived.

Table 10 presents the number of QALYs that the treatment would need to provide per annum to achieve different levels of cost-effectiveness, based upon variance in the initial cost of the treatment and discounting costs and benefits at 6% per annum. As the cost of the pump and the in-patient stay for implantation are the largest cost elements, variance in the initial cost will have the greatest effect upon cost-effectiveness. The impact of altering the cost of refill/follow-up depending upon the number of refills per year is significantly lower.

**Table 10** **Annual Gains in Health State Values (QALY Gains) Required per Year of Treatment for Different Cost-Utility Ratios and Initial Treatment Costs. Costs and Benefits Discounted at 6% per Year Over a 5 Year Period.**

| 5 Year Scenario Only | | | | |
|---|---|---|---|---|
| DISCOUNTED | Initial Cost of Treatment | | | |
| Cost per QALY ratio | £10,000 | £12,000 | £14,000 | £16,000 |
| £5,000 | 0.58 | 0.67 | 0.76 | 0.85 |
| £10,000 | 0.29 | 0.34 | 0.38 | 0.43 |
| £15,000 | 0.19 | 0.22 | 0.25 | 0.28 |
| £20,000 | 0.15 | 0.17 | 0.19 | 0.21 |
| £25,000 | 0.12 | 0.13 | 0.15 | 0.17 |

**Figure 1** **Sensitivity of Annual QALY Gains to Initial Treatment Cost and Cost per QALY Assumptions**



This graph suggests that a likely QALY gain of between 0.10 and 0.20 per annum would be expected to provide a cost-utility of around £20,000 per QALY. Clinical opinion (meeting of the Trent Working Group on Acute Purchasing) suggested that this scale of improvement in QoL would be achievable.

### c) Example of Equivalent Health States Providing QoL Utilities of 0.1 – 0.2

There are no quality of life studies reported for CIBI and, thus, it is not possible to estimate the cost per QALY using conventional cost-utility analysis. In order to indicate the potential changes in health state which would provide a change in health state utility of between 0.1 and 0.2 QALYs, the authors referred to the Index of Health Related Quality of Life measure (IHQL) to estimate potential QoL indices for patients utilising CIBI. The classification of these health states are provided in Appendix G. If it is assumed that a patient pre-CIBI is confined to bed (state D7), has severe pain (state P3) and is moderately distressed (anxious and depressed most of the time, but happy and relaxed some of the time) (state E3), the patient will be associated with a utility of 0.449. If post-CIBI the patient has the same distress and disability, but a reduction in pain to slight pain, then he/she will be associated with a utility score of 0.675. The QALY utility gain will be 0.226. If the pain were reduced only to moderate pain, the QALY utility gain would reduce to 0.149. If CIBI resulted in an improvement in pain to moderate pain levels and the patient also experienced a reduction in disability to state D6 (confined to a chair, only able to get out with assistance, very limited ability to perform role functions), he/she would experience a QALY utility gain of 0.199.

These examples are not based upon real-life experience of benefits from CIBI, but are indicative of the relevant QALY utilities gained from reductions in pain and disability. Similarly, the IHQL was used as an indicative QoL utility score and may not be the most relevant QoL indicator for this evaluation.

### d) Consideration of Potential Savings

The potential savings due to reduced resource requirements for the management of spasticity are detailed below.

i) Hospitalisation

Reductions in the need for hospitalisation were reported within the literature. These studies considered patients with SCI, head injury or MS. The reduction in bed days has been reported as between 20 days[8] and 55 days[66] per year.

This equates to savings of between £11,020 and £30,300 per annum, based upon costs of £551 per day (Queen's Medical Centre). This may be an over-estimate as this cost per day is based upon stay on a paediatric neurosurgery ward. Assuming average in-patient costs per day of £211,[82] this would equate to savings of between £4,220 and £11,600 per annum.

Assuming the lower cost estimate, costs could be saved for each year of therapy; savings could range from £21,000 to £58,000 for five years of therapy (£18,800 to £51,800 discounted at 6% per year).

ii) Pressure Sores

The reduction in bed days may be due partially to the reduced need for the management of pressure sores. None of the cost studies related to CIBI examined the cost consequences or nursing requirements related to a reduction in pressure sores, although the cost consequences of pressure sores have been reported elsewhere.[83,84,85] The cost of treating a grade 4 pressure sore has been reported at between £17,000 and £26,000. Assuming patients with MS or SCI have a 50% chance of developing a grade 4 pressure sore over the five year period, this could result in an average saving of £8,500 - £13,000 per patient.

iii) Orthopaedic Surgery

The costs of orthopaedic surgical procedures have been estimated at between £1,500 and £5,000 depending upon the operation required. Assuming all patients with CP will avoid at least one orthopaedic procedure within five years of implantation, orthopaedic surgery costs of between £1,500 and £5,000 may be avoided. These figures may be an under-estimate as patients frequently undergo multiple orthopaedic procedures.

**Table 11 Summary Table of Potential Savings**

| | | |
|---|---|---|
| Reductions in hospitalisation (MS & SCI) | Avoidance of 20 days' hospitalisation | £4,220 |
| | Avoidance of 55 days' hospitalisation | £11,605 |
| | | |
| Orthopaedic surgery (CP) | Avoidance of 1 adductor release | £2,000 |
| | Avoidance of 1 open or closed tenotomy | £1,500 |
| | Avoidance of 1 hamstring release | £2,500 |
| | Avoidance of hip dislocation | £5,000 |
| | | |
| Pressure sore (MS & SCI) | 50% chance of avoiding pressure sore – using cost of pressure sore of £26,000[83] | £13,000 |
| | 50% chance of avoiding pressure sore – using cost of pressure sore of £17,000[85] | £8,500 |

*Savings per year based upon cost per in-patient day of £211[82]

### 6.3.7 Summary of Economic Analysis

The cost of CIBI is estimated at around £11,700 for the initial assessment, test procedure, implantation procedure and equipment. In addition, there will be further costs of around £870 per annum for refill and follow-up. The treatment may last for up to seven years, depending upon the type of pump used, although life expectancy may be less than this period for some patients, notably MS patients. There are no studies reporting upon QoL utilities for CIBI. Assuming five years of benefit are obtained from the pump implantation, an average annual QoL utility gain of around 0.16 would result in a cost-utility ratio of £20,000. Clinical opinion and IHQL analysis suggested this scale of QoL improvement to be possible.

Moreover, the high initial cost of CIBI implantation could be offset substantially by reductions in pressure sores, other admissions related to spasticity, orthopaedic procedures and reductions in requirements for orthoses or other aids and adaptations.

## 7. OPTIONS FOR PURCHASERS/COMMISSIONERS

Due to problems with the methodology of most trials of CIBI, it is not possible to make a definitive statement about the recommended option for purchasers. Whilst it is likely that CIBI would be of benefit to selected groups of patients, especially those most disabled by their spasticity, very little is known about the cost-effectiveness of the intervention.

**Option 1 Do nothing and await further evidence**

Rigorous, large, multi-centre randomised controlled trial/s with long-term follow-up, appropriate outcome measures and good quality information on costs would be required to progress the current state of knowledge.

**Option 2 Provide CIBI only in the context of high quality trials**

A nationwide multi-centre controlled trial, ideally randomised, could provide better evidence of the effectiveness and cost-effectiveness of this procedure and the groups who might benefit. However, the study would need to have a long follow-up period, use appropriate functional outcome measures and be sufficiently large to allow estimation of the effects in different pathological and disease-severity groups. It might not be considered ethical to withhold CIBI from groups where there is already some evidence of benefit.

**Option 3 Provide CIBI only in those patient groups in which there is most evidence of benefit. Provide CIBI in other patient groups only in the context of high quality trials**

Groups for which there is reasonable evidence of likely benefit include:-

- Patients who are bedbound due to severe spasticity;
- Patients who cannot be seated appropriately in a wheelchair due to severe extensor spasms;
- Other wheelchair bound patients in whom spasm related pain or skin breakdown is a severe problem.

It would be valuable to set up a nationwide multi-centre scheme to collect further information on outcomes in these patients. It is recommended that all children receiving CIBI should be part of a well co-ordinated national research study.

Groups for which the evidence of benefit is less clear include:-

- Wheelchair users who already have a reasonable degree of function;*
- Ambulatory patients.

(* excepting patients experiencing severe frequent spasm related pain or skin breakdown which cannot be managed with other interventions.)

The evidence is insufficient to justify routine use in these patients. Thus, CIBI should only be provided in the context of a high quality RCT with long-term follow up using appropriate functional outcome measures.

**Option 4 Provide intrathecal baclofen for all patients with severe spasticity whom clinicians judge to be likely to benefit, but ensure that good quality data are collected on outcomes.**

This is unlikely to advance significantly the state of knowledge on this procedure, and could lead to some patients in whom there is minimal evidence of effectiveness receiving treatment.

## 8. DISCUSSION AND CONCLUSIONS

Many studies describe the benefits of CIBI in patients with spinal and cerebral spasticity. However, most of these studies fail to report functional outcome measures and concentrate on less clinically meaningful measures such as the Ashworth scale. Almost all studies are open follow-up studies with no control groups. The one reported randomised controlled trial of CIBI demonstrated no significant difference between the treatment and placebo group in functional or QoL outcomes at three months. However, it is possible that the measures used were not sufficiently sensitive to detect clinically important differences.

Despite the methodological drawbacks, the range of benefits and the proportion of patients benefiting was reasonably consistent across studies. In particular, it was reported consistently that bed-bound patients often became able to sit out of bed, wheelchair users who were unable to sit comfortably because of spasticity were able to sit more comfortably, spasm related pain was decreased and ease of nursing care was increased.

Patients who are likely to obtain the most benefit from CIBI are those who are bed-bound or are unable to sit comfortably in a wheelchair due to severe spasticity. In patients who are wheelchair-bound, but have a reasonable degree of functional ability, the benefits are likely to be less marked, although those with severe spasm related pain or problems with skin integrity may benefit more. There has been insufficient research on the effects of CIBI in ambulatory patients. The available research suggests that only a minority of such patients will benefit and some will deteriorate.

The estimate of cost-effectiveness of CIBI is difficult due to the lack of trials examining QoL measures. The treatment is estimated to cost around £15,000 and will provide benefit for around 5-7 years. Savings may be incurred due to reductions in hospitalisations related to spasticity, pressure sores and orthopaedic procedures. Threshold analysis suggests that the cost-utility is likely to be in the same range as coronary artery bypass surgery, peritoneal dialysis or home haemodialysis, even for gross cost-utility, excluding potential savings.

The use of CIBI should be considered only after patients have undergone a full assessment to ensure any potential underlying aggravating factors have been eliminated and all other potential avenues for treatment have been explored. Patients should be given realistic descriptions of the benefits which are likely to be achieved and the possible adverse effects.

CIBI should be initiated by specialist teams which are able to assess the suitability of the patient, fit the pump and arrange regular follow-up.

If such a service is to be commissioned, it should work to clear guidelines detailing which patients are suitable for treatment and which patients should only be treated in the context of high quality research studies.

## ACKNOWLEDGEMENTS

The authors would like to acknowledge gratefully the help and advice of the following people: Professor Ian Whittle (Forbes Professor in Surgical Neurology, Lothian University Hospitals NHS Trust, Edinburgh), Dr M R McLelland (Consultant in Spinal Injuries, Northern General Hospital, Sheffield), Professor C D Ward (Consultant in Rehabilitation Medicine, Derbyshire Royal Infirmary), Dr A Holton (Paediatric Neurologist, Leicester Royal Infirmary), Dr E McClement (Consultant in Rehabilitation Medicine, Community Rehabilitation Centre, Lincoln), Dr T Stephan (Consultant in Rehabilitation Medicine, Mansfield Community Hospital), Dr E B Knight-Jones (Consultant Paediatrician, Nottingham City Hospital), Ms L Jarrett (Nurse Practitioner ITB, National Hospital for Neurology, London).

We would also like to thank the following people for providing costing data to inform this report; Jessica Sealy (Queen's Medical Centre, Nottingham), Linda Hodgson (Central Sheffield University Hospitals), and Jane Parker (Leicester Royal Infirmary).

Grateful acknowledgements are also due to Suzy Paisley and Margaret Kilner (Information Resources, ScHARR) for their help with literature searching and obtaining articles. Also, Gill Rooney, Pat Holmes and Mike Jacobs for their invaluable help in the editing, formatting and proofreading of this document.

## CONFLICT OF INTEREST

None of the authors of this document has any financial interests in the drug or product being evaluated here.

**APPENDIX A STUDIES INCLUDING PATIENTS WITH SPASTICITY OF SPINAL ORIGIN**

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow-Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Azouvi 1996[56] | **I** - Severe and disabling spasticity, ineffectiveness of oral drugs, positive response to bolus.<br>**E** - infectious problems, bedsores, psychiatric disorders. | **18 patients**<br><br>12 SCI,<br>4 MS,<br>1 Syringomyelia,<br>1 tropical paraplegia.<br><br>All non-ambulatory<br><br>Mean age 38 (21-59) | 37.4 months (9-72)<br>17 programmable<br>1 mechanical | **Functional Improvement Measure** (composite score measuring different functions on a 7 point scale). Overall score improved for motor domains of score, but not cognitive domains.<br><br>Most dramatic improvements were in 12 patients with thoracic or lower cervical lesions. (At least 2 point improvement in bathing, dressing lower body, transfers and locomotion aspects of FIM.<br>2/12 became able to sit in chair, 5/12 walking ability improved, including 2 who became able to climb stairs)<br><br>Improvements in the 6 most severely disabled patients was confined to improvements in sitting position and ease of nursing care. | Patients with useful upper limb function likely to show measurable improvements in ADLs. Patients without upper limb function are unlikely to show improved function, but may benefit from improved sitting position and ease of nursing care. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Gianino 1998[49] | **I** - Intractable spasticity of spinal origin | **25 patients**<br><br>MS 15<br>SCI 7<br><br>Mean age 39 (21-70) | 12 month follow-up available for 16 patients.<br><br>Synchromed | Ferrans and Powers Quality of life index – no change between baseline and 12 months.<br>Sickness Impact profile (0-100 scale) improved from 29.7 to 21.7 p 0.0082. (14/16 patients had improved score). Physical subscore 38.5 to 31.0 p=0.001. (13/16 improved). Psychological subscore 20.8 to 13.0 p=0.025.(12/16 improved).<br>Subjects identified the following features of their disease as important, difficulty in dressing, walking, standing, transferring, moderate to severe pain, reduced independence, decreased social interaction and stress on relationships. | Use of 2 measures led to 'questionnaire fatigue'. Researchers felt that 1 year follow-up may not be enough to demonstrate changes. Measures used may not be very sensitive in this group. |
| Loubser 1991[74] | **I** - Spinal injury, severe spasticity, failure to respond to oral treatment, response to test dose.<br>**E** - Myelography showing scarring of intrathecal space | **7 patients**<br><br>Spinal injury and severe spasticity.<br><br>Mean age 42 (22-61) | Medtronic 8611H<br>16 months (5-24) | 3/7 who were previously unable to travel became able to take vacations.<br>1/7 reported improved sexual function. | Limited outcome data |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Loubser 1996[57] | **I** - Spinal injury, severe spasticity, failure to respond to oral treatment, response to test dose.<br>**E** - psychological co-morbidity | **12 patients**<br><br>Spinal injury and severe spasticity.<br><br>Mean age 43 (21-63) | Medtronic 8611H<br>12 months | 6 patients with musculoskeletal pain became pain free.<br>None of the 9 patients with neurogenic pain became pain free. | Series includes 7 patients from previous publication. |
| Mertens 1995[53,88] | **I** - Severe chronic disabling spasticity due to a spinal lesion. Refractory to oral treatment, Response to test dose, Favourable environment for rigorous out-patient follow-up, Age 18-65. Cognitive capacity to give informed consent. | **17 patients**<br><br>5 SCI<br>7 MS<br>1 Friedrich's Disease<br>1 Cervical myelopathy<br>1 Dorsal myelopathy<br>1 Syringomyelia<br>15 wheelchair dependent/ bedbound,<br>Age 25-61 | Medtronic 8615<br>37.5 months (5-69) | Mean functional disability score (composite score measuring pain, spasms, wheelchair use, transfers and washing/dressing each on a 4 point scale) decreased from 13.4 +/-2.7 to 5.8 +/-2.7 ($p<0.0001$)<br>Sitting position, transfers and nursing care became easier in all patients.<br>1/15 wheelchair bound patients became able to walk with crutches.<br>2/2 ambulatory patients improved walking distance, one of whom became able to walk alone outside his/her home.<br>9/9 patients with spasm related pain became - pain free.<br>1 patient became able to self-catheterise. Urinary urgency was ameliorated in 2 patients. | Functional improvement was greater in paraparetic and paraplegic patients with spinal cord injury than in tetraplegic patients with a progressive disease. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Middel 1997[50] | **I** -18yrs+, chronic disabling spasticity of spinal origin inhibiting personal care, sitting, lying and transfers accompanied by pain and stiffness, or disturbed sleeping. Insufficient response to oral treatment. Sufficient understanding of consequences of treatment. Response to a test dose. **E** - Pregnancy, supraspinal spasticity. | **22 patients**<br><br>13 MS, 9 SCI<br><br>All were non-ambulatory<br><br>Mean age 48 | Placebo controlled RCT of intrathecal baclofen for 3 months. All patients received intrathecal baclofen after 3 months. Both groups were followed up for 12 months after starting intrathecal baclofen.<br><br>Synchromed. | No significant difference between placebo and intervention groups BUT at 3 months the intervention group showed modest improvements in the physical and psychosocial dimensions of the Sickness Impact Profile and the mental health component of the Hopkins Symptoms Checklist compared to baseline.<br><br>At 1-year follow-up there were modest improvements in the physical dimension of the Sickness Impact Profile (41.5 to 31.5 – on a 0-100 scale), but not on psychosocial aspects of the score. | Only RCT of continuous infusion of intrathecal baclofen.<br><br>Failure to demonstrate significant differences in placebo and intervention group, but sample size may have been too small.<br><br>Statistically significant, but relatively modest changes in the SIP score were seen at 1 year. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Nanninga 1989[58] | **I** - Response to bolus dose, failure to respond to oral treatment, bladder dysfunction associated with spasticity. | **7 patients**<br><br>6 SCI,<br>1 transverse myelitis.<br>Adults | Medtronic 8601<br>1–4 years | 4 patients who were incontinent between catheterisations became continent between catheterisations.<br>3 patients with indwelling catheters became able to use intermittent catheterisation.<br>1 patient who was impossible to catheterise became possible to catheterise. | Only bladder function outcomes were measured |
| Ordia 1996[55] | **I** - Intractable spasticity of spinal cord origin, failed medical management, response to test dose Ashworth 3 or higher or spasm score 2 or higher.<br>**E** - Pregnancy or not using birth control, baclofen allergy. | **59 patients**<br><br>27 SCI<br>26 MS<br>2 Familial Spastic paraparesis<br>1 spinal cord tumor<br>1 cervical myelopathy<br>1 transverse myelitis<br>1 Amyotrophic lateral sclerosis<br>Mean age 42 yrs. (16-73) | Medtronic<br>42 months (23-70) | Reported improvements in ADL, transfers, pain, and sleep <u>but in an unspecified number of patients</u>.<br><br>4 females able to resume sexual intercourse.<br>4 ambulatory patients were able to walk more easily.<br>1 wheelchair bound patient became ambulatory.<br>Voice was clearer in 4 patients.<br>2 unemployed patients became employed.<br>The average reduction in bed days was 2.7/patient/yr. (measured in 10 patients). | Mainly subjective outcome measures with failure to give numbers of patients responding |

**APPENDIX B STUDIES INCLUDING PATIENTS WITH SPASTICITY OF CEREBRAL ORIGIN**

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Albright 1993[60] | **I** - Severe spasticity of cerebral origin, failure to respond to oral drugs, response to test dose. | **37 patients**<br><br>33 CP, 3 TBI, 1 post encephalitis<br><br>25 capable of self care (functional group), 22 were ambulatory.<br>12 incapable of self care (non-functional group).<br><br>Mean age 14 (5-27). | Medtronic 8611<br>23 months (3-48) | Self caring patients n=25<br><br>76% modest improvement in ADL<br>76% improved upper limb function<br>40% other benefits such as improved ambulation or speech<br>1 patient became able to walk with a frame<br>2 patients became worse from decreased tone.<br><br>Non-self caring patients with severe disease n=12<br><br>None showed a measurable improvement in activities of daily living<br>7 patient/carers were interviewed<br>6/7 reported improved ease of care<br>4/7 reported improved ease of dressing<br>4/7 reported improved perineal care<br>2/7 transfers became more difficult. | Independence improved in functional group.<br><br>Nursing care improved in non functional group. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Armstrong 1997[89] | **I** - 4-18yrs, severe spasticity involving whole body and interfering with daily care/function, stable underlying condition, response to bolus dose | **12 patients**<br><br>6 CP, 2 TBI, 4 near drowning.<br><br>Mean age 10 (4-19). | 6 Medtronic,<br>6 Infusaid<br><br>1-5 years | **Carer Assessment**<br><br>9/12 carers reported child as greatly improved. 3/12 as somewhat improved. (Areas of improvement included improved ease of care, decreased irritability, tolerance to handling, more participation in daily activities, weight gain). | High doses needed<br><br>Benefits greatest if severe extensor posturing.<br><br>37% failed to respond to bolus or had unwanted effect of bolus. |
| Becker 1997[7] | **I** - Traumatic or Hypoxic Brain Injury. Spasticity interfering with nursing care/physio-therapy. Response to test dose | **18 patients**<br>Traumatic/ Hypoxic Brain injury. Mean age 41(25-70)<br>12 vegetative state<br>5 severely disabled<br>1 mildly disabled<br>12 bedridden | Medtronic 8611H<br>13-54 months | 6 wheelchair bound patients<br>3/6 improved wheelchair mobility.<br><br>12 bedbound patients in a vegetative state.<br>8/12 became able to sit for some of the day.<br><br>Ease of care improved in all patients.<br>11 patients had chronic decubital ulcers - 5 healed, 5 improved. | |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Concalves 1994[61] | **I** - Severe spasticity of supraspinal origin, unresponsive to oral drugs, response to bolus dose. | **11 patients**<br><br>8 TBI<br>3 CP<br>Mean age 29 (13-52) | Medtronic<br>3.2 yrs (1-6) | Of 4 wheelchair-bound patients, 1 developed handicapped walking.<br>Of 2 patients with bladder dysfunction both developed improved control.<br>Of 4 with no speech, 1 developed unintelligible speech and 1 developed dysarthria.<br>Conscious level improved in one patient. | 2/11 pump explanted |
| Gerszten 1997[62] | **I** - Moderate or severe spasticity of cerebral origin. Response to test dose. | **24 patients**<br><br>21 CP.<br>Mean age 18 years (9-30) | Medtronic<br>52 months (12-88) | Of 7 patients who were able to walk only in therapy sessions, 4 became able to walk at home, 2 lost the ability to walk.<br><br>Of 6 patients who were only able to walk at home, 2 became able to walk in the community.<br><br>Of 8 patients who were able to walk in the community, 1 lost the ability to walk in the community.<br><br>Overall 37% showed an improvement in ambulatory category and 12.5% showed a deterioration.<br>Overall Function (subjective assessment of endurance, ease of transfers, and activities of daily living) improved in 20 patients, worsened in 2, and was unchanged in 2 patients.<br>3/19 patients who used ankle orthoses were able to stop using them. | 1 of only a few studies to examine effect on ambulation.<br><br>Moderate benefits to ambulation achieved in some.<br><br>Deterioration in others. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Saltuari 1992[90] | **I** - Severe spasticity of supraspinal origin, unresponsive to oral drugs, and physical therapy, response to bolus dose, informed consent from patients or carers.<br>**E** - Patients with poor prognosis | **9 patients**<br><br>6 TBI<br>1 hypoxic brain injury<br>1 Little's disease<br>1 hereditary spastic paraparesis<br>Mean age 23 (14-46). | Medtronic 8611H<br><br>9 (11 days-28 months) | 1 patient became able to speak.<br>1 patient became able to climb stairs without help.<br>2 patients became continent. | |

**APPENDIX C STUDIES INCLUDING PATIENTS WITH SPASTICITY OF SPINAL ORIGIN AND PATIENTS WITH SPASTICITY OF CEREBRAL ORIGIN**

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Becker 1995[66] | **I** - Severe disabling spasticity not responsive to oral treatment or physical therapy, responsive to test dose. Age 18+yrs<br>**E** - Substance misuse. Psychiatric problems. | **9 patients**<br><br>6 MS, 2 SCI, 1 TBI. Non-ambulatory Mean age 34 (20-56) | **MEDTRONIC** 27 months (13-47) | **NURSING ASSESSMENT**<br>Major improvement in transfers 8/9, pain control 5/9, nursing care 8/9, skin integrity 6/9<br>**Patient satisfaction in 6 MS patients** (1-5 score) – Improvement in score = Transfers 3.5 , Seating 3, Personal hygiene 2.8, sleeping 2.9, mental functioning 1.8, pain 2.7, spasticity 2.3, skin condition 1.3.<br>**Place of residence**. 3 patients who were hospitalised became able to live in the community (1 in a group home). Of 3 patients who lived in a chronic care institution, 2 became able to live in a group home, 1 moved to hospital. All 3 patients who lived at home remained at home.<br>**Hospital days** - average decrease in hospital days 41 days per patient per year. | Multi - disciplinary team approach necessary.<br><br>Careful patient selection necessary. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Broseta 1989[68] | **I** - Severe spasticity caused by brain or spinal cord injury, resistant to oral medication, positive response to bolus dose. | **14 patients**<br><br>5 SCI, 4 MS<br>4 TBI, 1 CP<br><br>7 wheelchair-bound /bed-bound<br>7 ambulatory.<br><br>Mean age 45 (15-62). | Medtronic pump 11 months (3-22) | Overall outcome considered excellent in 5 patients, good in 4, fair in 3, poor in 2.<br><br>5/9 with bladder dysfunction had improved function.<br><br>9/10 with pain became pain free.<br><br>1 bedridden patient became able to walk with canes.<br><br>1/7 ambulatory patients improved walking ability. | |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Lazorthes 1990[69] | **I** - Severe debilitating spasticity. Unresponsive to oral treatment. Respond to test dose. Informed consent. Available for rigorous follow up.<br>**E** - Bedsores or skin lesions which would interfere with pump implantation or aggravate spasticity. Urinary tract infections. | **18 patients**<br><br>6 MS<br>7 spinal trauma<br>1 spinal ischaemia<br>1 transverse myelitis<br>1 cerebral palsy<br>1 brain trauma<br>1 ischemic cerebral lesion<br>Mean age 39 (1-70) | 18 months (4-43)<br><br>1st 6 patients had baclofen delivered through access port. Remainder had Medtronic pump. | Modified Davis and Gray scale for evaluation of motor performance (> 3 = large improvement, 1-3 = moderate improvement, 0 = no improvement).<br>3/18 large improvement in function<br>9/18 moderate improvement<br>6/18 no improvement in function.<br><br>14/16 resolution of painful spasms.<br>Functional improvement was much greater in patients with traumatic lesions than in those with MS although both groups had reduction in spasticity and improvement in ease of nursing care. In bedridden patients the improvement was limited to reduction of spasticity and improved ease of nursing care. | 3/12 Medtronic pumps were discontinued.<br>6/6 access ports were discontinued. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Nance 1995[8] | **I** - Spasticity unremitting for 12 months, satisfactory failed oral treatment. Response to test dose. | **7 patients**<br><br>2 MS, 5 SCI<br><br>Mean age 38.7<br><br>All wheelchair users | 24-41 months<br>4 Medtronic<br>3 Infusaid | No statistically significant change in bladder or respiratory function.<br>All patients reported marked improvement in comfort and ADL: e.g. 1 regained ability to transfer from wheelchair independently; 1 able to go outside having been previously housebound; 2 experienced healing of chronic leg ulcerations.<br>2 patients able to reduce requirement for personal attendant service. | 140 patients referred to unit. Treatment of aggravating factors or optimising oral treatment improved spasticity in 130. |
| Ochs 1996[64] | **I** - Severe, disabling spasticity, resistant to oral treatment, stable or slowly progressive disease or wee diagnosed disease, no contra-indications, response to bolus dose. | **70 patients**<br><br>59 MS, 4 SCI<br>4 Myelopathy<br>3 Brain injury<br>Age 21-71 | 6 month follow-up<br>22 Infusaid<br>48 Medtronic | Of 38 bed-bound patients, 22 became able to use wheelchair.<br>Of 27 wheelchair users who could not walk, 1 became able to walk with crutches.<br>4/29 wheelchair users became able to stand.<br>8/12 patients who required major help in dressing required only a little help in dressing 6 months after CIBI.<br>1/4 patients who required a little help became able to dress without help.<br>2/9 who required help became able to eat alone.<br>20/22 patients rated outcome as good or excellent. | Patients in the late stages of chronic illness (MS) or generalised cerebral deficits (head trauma, intracerebral haemmorhage) had benefit limited to improved ease of care. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Parke 1989[70] | **I** - Failure to respond to oral treatment, response to test doses. | **8 patients**<br><br>4 SCI, 4 MS<br>Mean age 38 (22-61) | 6 months<br>Medtronic 8611H | Patient Evaluation Conference System used to measure level of dependence.<br>4 patients were classified as being dependent on others for bladder function, 2 of these became independent.<br>7 patients were described as being dependent on others for feeding and hygiene, 5 became independent.<br>3 patients had skin integrity problems that resolved following treatment.<br>1 patient became able to drive.<br>1 patient with pain became pain free. | |
| Patterson 1994[52] | **I** - Severe spasticity, failure to respond to oral treatment, response to test dose. | **21 patients**<br><br>15 MS, 3 SCI,<br>1 CP,<br>1 Syringo-myelia,<br>1 Friedrich's Ataxia,<br>1 Transverse myelitis<br>Non-ambulatory<br><br>Mean age 46 (24-67) | 9-79 months<br>Cordis-Secor | No change in Barthel Index in any patients<br><br>16/21 improved ability to sit<br>16/21 improved nursing care<br>2/21 improved social life<br>2/21 became able to drive | Barthel index may not be sensitive to change in this group. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Penn 1987[67] | **I** - Severe spasticity, failure to respond to oral drugs, response to test dose. | **7 patients**<br><br>SCI and MS<br><br>Mean Age 37 (19-54) | 20 months (11-24)<br>Medtronic 8601 | Of 5 non-ambulatory patients, 2 became able to walk with long leg braces and crutches<br>Of 2 patients who were previously ambulatory, 1 became non-ambulatory<br>3/7 patients returned to work<br>4/4 incontinent patients became continent<br>1 patient who was previously unable to self catheterise became able to do this.<br>All reported improved sleep. | |
| Sahuquillo 1991[72] | **I** - Stable neurological condition<br>-Severe spasticity refractory to oral drugs<br>-Normal CSF circulation<br>-Informed consent<br>-Response to test dose | **9 patients**<br><br>6 SCI,<br>1 cervical myelopathy,<br>1 cervical meningioma<br>1 shunt malfunction leading to cerebral damage.<br>Mean age 33 (12-65) | 8 months (5-35)<br><br>Secor resevoir | 8/8 patients with spasm related pain had relief<br>No other functional or quality of life indicators were reported. | Limited outcome data |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Steers 1992[91] | **I** - Severe spasticity, voiding problems, failure to respond to oral drugs, response to test dose. | **10 patients**<br><br>5 SCI, 1 MS<br>1 Syringomyelia<br>3 Hereditary spastic paraplegia<br>Mean age 36 (24-61) | 18 months (12-23)<br>Medtronic | Of 3 patients with indwelling catheters – 2 minimised leakage around catheter, one converted to intermittent self catheterisation.<br>Of 4 patients with voluntary voiding, 4 noted decreased nocturia from an average of 3.1 times per night to 0.8 times per night. | Only urinary functional outcomes measured. |
| Stewart-Wynne 1991[63] | **I** - Failure to respond to oral treatment - response to test dose. | **6 patients**<br><br>2 SCI, 3 MS, 1 Motor Neurone Disease.<br><br>Adult patients – ages not stated | 24 months (6-42)<br>Infusaid pump | No change in dependency levels but all aspects of daily care were said to be performed more easily.<br>ADLs said to improve in all patients but no data provided.<br>All patients became able to sit in a wheelchair and lie comfortably in bed at night. | Mainly subjective outcome measures. |

| Trial, Year, Review Number | Inclusion (I) Exclusion (E) | Description of Patients | Intervention and Duration of Follow Up (Mean-Range) | Results (subjective measures used unless otherwise stated) | Comments |
|---|---|---|---|---|---|
| Zierski 1988[65] | **I** - Severe spasticity not responding to oral drugs. Adequate response to test dose.<br>**E** - Test dose leading to loss of muscle tone sufficient to impair ambulation. | **37 patients**<br><br>SCI, MS, CP, Traumatic/ Hypoxic brain injury<br><br>Age range 2-71 years | 10 months (2-28)<br>Infusaid pump | 14/20 bedridden patients became able to sit in a wheelchair for several hours each day. The nursing care of the remaining 6 bedridden patients became easier.<br>10/12 wheelchair bound patients improved their mobility.<br>3/5 ambulatory patients improved walking ability.<br>13/17 with spasm-related pain became pain-free.<br>On a 1-4 scale (1 very good, 4 poor) carers rated the outcome as 1.37 (mean).<br>Physicians rated the outcome as 1.32 (mean). | Many outcomes were subjective. |

## APPENDIX D REFERRAL CRITERIA FOR CHILDREN WITH SPASTICITY OF CEREBRAL ORIGIN (CP)

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Introduction:
These sub-groups represent the CP children referred to the Neurosurgery Department at Queen's Medical Centre. The following classification is proposed merely for the purposes of considering CIBI treatment. More standardisation of results is required in order to quantify results and determine positive or negative outcomes.

Sub-groups in CP:

1. Spastic tetraplegics: These severely disabled children suffer from increasing nursing problems ranging from positional disability e.g. being unable to sit in a wheelchair, to lying flat in bed, etc.

2. Cognitively disabled mobiles: These children are in special schools, may be able to mobilize with help and are situated on the borderline of the previous group.

3. Cognitively intact mobiles: These children are in mainstream schools and perform normally, but are held back by their physical disability.

The aims of CIBI treatment are different for each group.

Group 1. CIBI aims to improve quality of life and prevent further disability due to orthopaedic deformity.

Group 2. As a borderline of group 1, the aim is to improve quality of life rather than to improve mobility. Nursing can be made easier e.g. by decreasing adductor tone, but marked improvement of gait is unrealistic because of the cognitive disability, which makes compliance with post-procedure physiotherapy difficult.

Group 3. The expectations are very high in this group and a negotiated settlement is necessary with the child and its parents prior to the procedure. This group represents a spectrum of children who may be wheelchair bound, partially mobile or purely gait impaired. The aim of CIBI is to improve mobility and increase social and educational performance due to the net effect of CIBI on the upper limbs.

Referral criteria:

At present Mr Vloeberghs is confronted with an entire spectrum of children in whom spasticity has been treated conservatively. Only the failures of the conservative approach are brought to his attention, but this does give an overview of the need and demand for CIBI. The following criteria are valid for all groups described above.

1. The patient must be over four years old, because of the very limited data on CIBI in patients under four years old and the technical difficulty of inserting a drug delivery system in this age group.
2. Immobile children with CP in which the spasticity is causing increasing deformity or nursing demands, for example in association with positional problems. Conventional means will already have been attempted, e.g. physiotherapy, botulinum toxin, orthopaedic interventions, orthoses. The evidence of benefit of CIBI is best in this type of problem but more evidence is required. Therefore, it is recommended that all children receiving CIBI should be part of a national research study documenting changes with this intervention.
3. Severe gait disturbance in association with spasticity, with or without upper limb involvement in a child with severe learning difficulties. Evidence for the benefit of CIBI in these children is very sparse. All children receiving CIBI must be part of a national multi-centre controlled trial documenting the benefit of this intervention.

**APPENDIX E** **BREAKDOWN OF COSTS RELATED TO CIBI**

| | Cost Element | Low Estimate | High Estimate |
|---|---|---|---|
| **Prescreening** | 1x new out-patient appointment with neurosurgeon | £330.00 | £556.00 |
| Prescreening total | | **£330.00** | **£556.00** |
| **Test dose** | 1x procedure A542 injection of therapeutic substance (minor) | £163.00 | £163.00 |
| | 1x lumbar puncture | £189.00 | £189.00 |
| | 1x lumbar catheter | £20.00 | £30.00 |
| | Ward care/ accommodation (E39) – assuming 2 night in-patient stay. | £490.00 | £1,102.00 |
| | Cost of drug | £60.00 | £70.00 |
| | Physio assessment 1/2 hour | £20.00 | £20.00 |
| Test dose total | | **£942.00** | **£1,574.00** |
| **Pump implantation** | Cost of pump | £6,768.00 | £6,768.00 |
| | Cost of catheter | £229.13 | £229.13 |
| | 1x procedure - implant pump (code) - major procedure A3300 | £509.00 | £509.00 |
| | Ward care/accommodation (E39) – assuming 5 night in-patient stay. | £1,225.00 | £2,755.00 |
| Pump implantation total | | **£8,731.13** | **£10,261.13** |
| **Other costs** | Laptop | Free - on loan | Free - on loan |
| | Transport costs | £50.00 | £100.00 |
| | Education requirement | not known | not known |
| **Tests, pathology, radiology, microbiology (all)** | | £500.00 | £500.00 |
| **Other costs total** | | **£550.00** | **£600.00** |
| **Aftercare (post-op)** | Refill kit | £22.00 | £22.00 |
| | Drug costs 2000 mcmgs baclofen | £59.00 | £72.00 |
| | Follow-up out-patient appointment / PIU | £50.00 | £50.00 |
| | Physio assistant 1/2 hour per day | £10.00 | £10.00 |
| Aftercare (post-op) total | | **£141.00** | **£154.00** |
| **Pump replacement procedure** | 1x procedure | £509.00 | £509.00 |
| | Ward care/accomodation (E39) - range of nights stay | £1,225.00 | £2,755.00 |
| | Pump (latest cost from Medtronic) | £6,768.00 | £6,768.00 |
| | Catheter | £229.13 | £229.13 |
| | Drugs | £59.00 | £72.00 |
| **Pump replacement procedure total** | | **£8,790.13** | **£10,333.13** |
| | | | |
| **Total costs for CIBI implantation - prescreening, test dose, pump implantation, other costs and tests** | | **£10,553.13** | **£12,991.13** |
| | | | |
| **Mid point estimate** | | **£11,772.13** | |

**APPENDIX F SUMMARY OF COST PAPERS RELATING TO CIBI**

| Study | Patient Characteristics | Method | Results | Savings and Comments |
|---|---|---|---|---|
| Nance et al. (1995)[8] | 6 patients in costing study.<br><br>SCI or MS | Hospital admissions where spasticity was causally related to spasticity 2 years prior to treatment, 2 years post treatment. | Prior 2 years: 376 in-patient hospital days (range: 0-186, average 63 days). Post 2 years: 136 in-patient days (range: 11-36, average 23 days), none of which was due to spasticity. All admissions post CIBI were related to screening, implantation, treatment of problems related to the intrathecal drug delivery devices and problems related to marked reduction in muscle tone. | The authors report average net savings of CDN $25,250 per patient, taking account of the cost of pump and hospital days (average cost per in-patient day $813). The authors consider the treatment to be cost-effective.<br><br>Using UK costs of £211 per in-patient day, there would be savings of £8,440 over 2 years in reductions of hospital days. This would balance the cost of the pump.<br><br>The number of days used within the post CIBI years may be over-estimated due to use of placebo days in the screening phase.<br><br>2 patients reported ability to decrease personal attendant services and one patient obtained employment following CIBI. 2 patients had skin ulcers which healed following CIBI.<br><br>Only 6 patients were included within the costing exercise. |
| Becker et al. (1995)[66] | 9 patients<br><br>6 MS, 2 cervical SCI and 1 head injury. | Hospital acute care hospitalisation costs 1 year prior and one year post implantation. | Prior to implantation: 755 acute hospital days (range: 0-319, average 84 days).<br>Year of implantation: 259 days (range: 10-48, average 29 days). | Based on cost of hospital stay of $570 per day, reductions in hospital days give average saving of $31,000 per patient (this does not include pump and implant).<br><br>Using UK costs of £211 per in-patient day, there would be savings of £11,660 within the first year in reductions of hospital days. This would balance the cost of the pump.<br><br>At time of implantation, 6 of the 9 patients were institutionalised in either chronic or acute care hospitals due to problems managing their spasticity. Following |

| Study | Patient Characteristics | Method | Results | Savings and Comments |
|---|---|---|---|---|
| | | | | CIBI 3 patients were discharged after prolonged hospitalisation, 2 back home and 1 to a group home.<br><br>Savings are likely to be under-estimated as 2 patients were in chronic care institutions prior to implantation and, thus, would not have required acute care.<br>Authors conclude CIBI to be beneficial in terms of nursing assessment, patient satisfaction and cost-effectiveness. |
| Ordia et al. (1996)[55] | 10 patients<br><br>Spasticity of spinal cord origin, MS or SCI<br><br>59 patients in total had pump implant, but only first 10 were included in cost study. | Number of bed days used for 1 year prior and 1 year following implantation. Hospitalisations were all cause and not specifically related to spasticity. | Prior to implantation: 95 bed days.<br>Post implantation: 68 bed days.<br>i.e. 2.7 days per patient saved for general hospitalisations in 1 year.<br><br>Also 58 days used for screening and implantation, i.e. 5.8 days used per patient for the screening and implantation. | This study does not report the proportion of days that are related to spasticity and, thus, may include admissions for unrelated causes. Similarly, there is no information as to the number of post implant bed days that are due to complications from the procedure.<br>The number of bed days reported is low as patients who received acute rehabilitation less than 1 year prior to surgery were excluded from cost study.<br><br>Authors concluded CIBI to be a cost-effective method for treatment of severe intractable spinal spasticity. However, this was based upon a average cost of $2,500 per day. |
| Postma et al. (1999)[81] | Case control study –<br>18 patients undergoing CIBI, (11 MS, 7 SCI)<br>15 match patients of similar age, sex and diagnosis (9 MS, 6 SCI). | Comparison of the number of days in hospital between groups 1 year prior to implantation and 1 year following implantation. | Average number of hospital days in year of implant in treated group was 31.5 days; 9.9 in the test phase, 12.3 for the implantation phase and 8.4 days resulting from complications.<br>This was in comparison to 18.7 days for the matched patients.<br>In the year following implantation no significant difference was found. | A calculation of the average direct costs that would be likely to occur in a non-experimental situation was made in this study. For this analysis only 2 days were allocated to the test phase, 10.3 for the implantation phase and again, 8.4 days for complications. If this had been the case, the average number of days for the treated group would have been 20.7, that is only 2 additional days in comparison to the matched group.<br><br>For the non-experimental situation, the total average cost of selection, testing, implantation and medical follow up amounted to US$28,473 per patient for the first year. Full break down given in paper. |

## APPENDIX G INDEX OF HEALTH RELATED QUALITY OF LIFE

The IHQL provides a broad and sensitive measure of social, psychological and physical functioning and is designed to be applicable across all diagnostic groups. Using this instrument, it is possible to derive an assessment of health status on a single unidimensional scale.

The IHQL is derived from the original two-dimensional Rosser Index based on the dimensions of disability and distress. In this scale, distress is separated into physical and emotional components, to give three dimensions (disability, physical distress and emotional distress).

Valuations for the 175 composite health states were obtained using standard gamble for states of 1 year duration. No assessment has yet been made of the test-retest reliability of the scaling method, the stability of ratings over time, or the consensus of the values obtained from different sample groups.

**3-Dimensional Classification**

**Disability**

| | |
|---|---|
| D1: | No physical disability; perfectly mobile and physically active; able to perform all self-care and role functions. |
| D2: | Slight social disability, e.g. having a slight cold. No limitations with physical ability, self-care or mobility, but some role functions slightly impaired by social disability. |
| D3: | Slight physical disability. Able to get round house and community, but unable to perform heavy physical tasks. Role functions slightly limited by physical disability. Able to perform all self-care activities. |
| D4: | Able to get round house and do lighter physical work. Some difficulty in getting community due to weakness or other physical limitations. Can perform all self-care activities. Ability to perform role functions limited. |
| D5: | Difficulty in getting around house, can only go out with assistance. Major physical limitations, e.g. can only do light work. Can perform most self-care activities, but need help getting in and out of the bath. Limited ability to perform role functions. |
| D6: | Confined to a chair, therefore, can only get out with assistance. Can only do the lightest of tasks, e.g. switch on the TV. Can feed self, but needs help with all other health care activities. Very limited ability to perform role functions. |
| D7: | Confined to bed. Needs help with all self-care activities. Minimal ability to perform role functions. |
| D8: | Unconscious. |

**Discomfort (Physical)**

P1: No pain.

P2: Slight pain: (a) occasionally, (b) frequently, (c) almost all the time.

P3: Moderate pain: (a) occasionally, (b) frequently, (c) almost all the time.

P4: Severe pain: (a) occasionally, (b) frequently, (c) almost all the time.

P5: Agonising pain: (a) occasionally, (b) frequently, (c) almost all the time.

**Distress (Emotional)**

E1: No distress: very happy and relaxed almost all of the time.

E2: Slight distress : happy and relaxed most of the time, but anxious and depressed some of the time.

E3: Moderate distress: anxious and depressed most of the time, but happy and relaxed some of the time.

E4: Severe distress: very anxious and depressed almost all of the time.

E5: Extremely depressed: actively suicidal.

**Composite state valuations (0-1 scale of values)**

| | | E1 | E2 | E3 | E4 | E5 |
|---|---|---|---|---|---|---|
| P1 | D1 | 1.000 | 0.970 | 0.894 | 0.791 | 0.643 |
| | D2 | 0.990 | 0.960 | 0.884 | 0.781 | 0.632 |
| | D3 | 0.971 | 0.940 | 0.864 | 0.762 | 0.614 |
| | D4 | 0.946 | 0.917 | 0.840 | 0.738 | 0.590 |
| | D5 | 0.917 | 0.887 | 0.811 | 0.710 | 0.561 |
| | D6 | 0.885 | 0.855 | 0.780 | 0.678 | 0.530 |
| | D7 | 0.838 | 0.804 | 0.729 | 0.628 | 0.481 |
| P2 | D1 | 0.944 | 0.915 | 0.838 | 0.736 | 0.588 |
| | D2 | 0.934 | 0.904 | 0.828 | 0.726 | 0.578 |
| | D3 | 0.915 | 0.885 | 0.810 | 0.708 | 0.559 |
| | D4 | 0.891 | 0.861 | 0.785 | 0.684 | 0.537 |
| | D5 | 0.861 | 0.831 | 0.756 | 0.654 | 0.508 |
| | D6 | 0.829 | 0.799 | 0.724 | 0.623 | 0.477 |
| | D7 | 0.779 | 0.750 | 0.675 | 0.574 | 0.427 |
| P3 | D1 | 0.867 | 0.837 | 0.761 | 0.660 | 0.513 |
| | D2 | 0.857 | 0.827 | 0.751 | 0.650 | 0.503 |
| | D3 | 0.837 | 0.808 | 0.732 | 0.631 | 0.485 |
| | D4 | 0.814 | 0.784 | 0.709 | 0.608 | 0.461 |
| | D5 | 0.785 | 0.755 | 0.680 | 0.579 | 0.433 |
| | D6 | 0.753 | 0.723 | 0.648 | 0.548 | 0.402 |
| | D7 | 0.702 | 0.674 | 0.598 | 0.498 | 0.353 |
| P4 | D1 | 0.714 | 0.685 | 0.610 | 0.510 | 0.365 |
| | D2 | 0.703 | 0.675 | 0.599 | 0.499 | 0.354 |
| | D3 | 0.685 | 0.656 | 0.581 | 0.481 | 0.337 |
| | D4 | 0.661 | 0.632 | 0.557 | 0.458 | 0.313 |
| | D5 | 0.632 | 0.604 | 0.528 | 0.429 | 0.285 |
| | D6 | 0.601 | 0.572 | 0.497 | 0.399 | 0.254 |
| | D7 | 0.551 | 0.522 | 0.449 | 0.350 | 0.207 |
| P5 | D1 | 0.468 | 0.439 | 0.365 | 0.267 | 0.125 |
| | D2 | 0.457 | 0.428 | 0.355 | 0.257 | 0.114 |
| | D3 | 0.439 | 0.410 | 0.337 | 0.239 | 0.097 |
| | D4 | 0.416 | 0.387 | 0.314 | 0.216 | 0.074 |
| | D5 | 0.387 | 0.358 | 0.285 | 0.188 | 0.047 |
| | D6 | 0.356 | 0.327 | 0.255 | 0.159 | 0.017 |
| | D7 | 0.308 | 0.279 | 0.207 | 0.111 | -0.030 |

## REFERENCES


1 Lance J. Symposium synopsis. Feldman RG, Young RR, Koella WP, eds. *Spasticity: Disordered Motor Control*. Chicago, IL: Year book Medical Publishers, 1980; 485-494.

2 Abel NA, Smith RA. Intrathecal baclofen for treatment of intractable spinal spasticity. *Arch Phys Med Rehabil* 1994; 75: 54-58.

3 Taricco M, Telaro E, Adone R, et al. Pharmacological interventions for spasticity following spinal cord injury. *The Cochrane Library, Issue 1* 1998;

4 Shakespeare DT, Toung CA, Boggild M. Anti-spasticity agents for multiple sclerosis. *The Cochrane Library, Issue 1* 1998;

5 McLean BN. Intrathecal baclofen in severe spasticity. *Br J Hosp Med* 1993; 49: 262-267.

6 Porter B. A review of intrathecal baclofen in the management of spasticity. *Br J Nurs* 1997; 6: 253-260.

7 Becker R, Alberti O, Bauer BL. Continuous intrathecal baclofen infusion in severe spasticity after traumatic or hypoxic brain injury. *J Neurol* 1997; 244: 160-166.

8 Nance P, Schryvers O, Schmidt B, et al. Intrathecal baclofen therapy for adults with spinal spasticity: therapeutic efficacy and effect on hospital admissions. *Can J Neurol Sci* 1995; 22: 22-29.

9 Penn RD, Kroin JS. Intrathecal baclofen alleviates spinal cord spasticity. *Lancet* 1984; 1: 1078

10 Albright AL. Address at meeting of Royal Society of Medicine, London. 1997.

11 Gage RJ, Fabian D, Hicks R, et al. Pre and post operative gait analysis in patients with spastic diplegia. *J Pediatr Orthop* 1984; 4: 715-725.

12 Confavreux C. Course and prognosis of MS assessed by the computerised data processing of 349 patients. *Brain* 1980; 103: 281-300.

13 McAlpine, Compston. Some aspects of the natural history of MS. *QJM* 1952; 21: 135-167.

14 Raine C, McFarland H, Tourtellotte. MS clinical and pathogenic basis. Chapman and Hall Medical, 1997.

15 Panelius M. Studies on epidemiological clinical and etiological aspects of MS. *Acta Neurol Scand* 1996; 45: 1-82.

16 Richards RG, Sampson FC. The Epidemiology and Natural History of Multiple Sclerosis. A report for the National Institute of Clinical Excellence. 2000.

17 Barnes M. The modern management of spasticity using a combined approach. *Prog Neurol Psych* 1999; 26-30.

18 Wagstaff A, Bryson H. Tizanidine. *Drugs* 1997; 53: 435-452.

19 Maynard FM, Karunas RS, Waring WP. Epidemiology of spasticity following traumatic spinal cord injury. *Arch Phys Med Rehabil* 1990; 71: 566-569.

20 Soni BM. Management of spasticity - Southport experience. Pedotti A, Ferrarin M, Quintern J, Reiner R, eds. *Neuroprosthetics; from basic research to clinical applications - biomedical and health research program (BIOMED) of the European Union. Concerteed action: restoration of muscle activity through FES and associated technolgy - RAFT.* Springer-Verlag, 1996; 469-479.

21 McClelland MR. Conversation on the incidence of SCI.(1999).

22 Harvey C, Rothschild BB, Asmann AJ, et al. New estimates of traumatic SCI prevalence: a survey-based approach. *Paraplegia* 1990; 28: 537-544.

23 Morton R. Conversation on the incidence, prevalence and estimates of need in CP.(1999)

24 Woodard C. Conversation on the annual number of pumps implanted for Intrathecal Baclofen - data from Medtronic Ltd.(1999)

25 Lewis KS, Mueller WM. Intrathecal baclofen for severe spasticity secondary to spinal cord injury. *Ann Pharmacother* 1993; 27: 767-774.

26 Shaw BJ, Tsui JK, Bhatt MH, et al. Treatment of spasticity with botulinum toxin: a double-blind study. *Ann Neurol* 1990; 28: 512-515.

27 Bata BB, Cozen JA, Bamford JM, et al. Use if botulinum toxin in the stroke patient with severe upper limb spasticity. *J Neurol Neurosurg and Psychiatry* 1996; 61: 30-35.

28 Cosgrove AP, Corry IS, Graham HK. Botulinum toxin and the management of the lower limb in cerebral palsy. *Dev Med Child Neurol* 1994; 36: 386-396.

29 Hambleton P, Cohen HE, Palmer BJ, et al. Antitoxins and botulinum treatment. *BMJ* 199; 304: 959-960.

30 Tsui JK, Wong NL, Wong E, et al. Production of circulating antibodies to botulinum A in patients receiving repeated injections for dystonia. *Am Neurolog Assoc* 1998; 24: 181-219.

31 Peter JC, Hoffinan EB, Aren LJ. Spondylosis and spondylysthesis after five-level lumbosacral laminectomy for selective posterior rhizotomy in cerebral palsy. *Childs Nerv Syst* 1993; 9: 285-288.

32 Meyerson BA, Cui JG, Yakhnitsa V, et al. Modulation of spinal pain mechanisms by spinal cord stimulation and the potential role of adjuvant pharmacotherapy. *Stereotact Funct Neurosurg* 1997; 68: 129-140.

33 Vaughan CL, Berman B, Peacock WJ. Cerebral palsy and rhizotomy; a three year follow up evaluation with gait analysis. *J Neurosurg* 1991; 74: 178-184.

34 Boscarino LF, Ounpuu MS, Davis RB, et al. Effects of selective dorsal rhizotomy on gait in children with cerebral palsy. *J Pediatr Orthop* 1993; 13: 174-179.

35 Marty GM, Dias LS, Gaebler-Spira D. *J Bone Joint Surg* 1995; 77: 713-718.

36 Abbott R, Johann-Murphy M, Shiminski-Maher T, et al. Selective dorsal rhizotomy; outcome and complications in treating spastic cerebral palsy. *Neurosurgery* 1993; 33: 1-857.

37 Russell DJ, Gowland C, Hardy S, et al. Gross motor functional measure manual. 1993; 2nd Edition. Neurodevelopmental Clinical Research Unit, McMasterUniversity; Hamilton, Ontario.

38 Steinbok P, Reiner AM, Beauchamp R, et al. A randomised clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic cerebral palsy. *Dev Med Child Neurol* 1997; 39: 8-184.

39 Wright VW, Sheil EMH, Drake JM, et al. Evaluation of selective dorsal rhizotomy for the reduction of spasticity in cerebral palsy; a randomised controlled trial. *Dev Med Child Neurol* 1998; 39: 8-184.

40 McLaughlin JF, Bjomson KE, Astley SJ, et al. Selective dorsal rhizotomy; efficacy and safety in an investigator masked randomised clinical trial. *Dev Med Child Neurol* 1998; 40: 220-232.

41 Steinbok P, Daneshvar H, Evans D, et al. Cost analysis of continuous intrathecal baclofen versus selective functional posterior rhizotomy in the treatment of spastic quadriplegia associated with cerebral palsy. *Pediatr Neurosurg* 1995; 22: 255-64; discussion 265.

42 Ko CK, Ward AB. Management of spasticity. *Br J Hosp Med* 1997; 58: 400-405.

43 Parziale JR, Akelman E, Herz DA. Spasticity: pathophysiology and management. *Orthopedics (Thorofare, NJ)* 1993; 16: 801-811.

44 Ashworth B. Preliminary trial of carisoporodol in Multiple Sclerosis. *Practitioner* 1964; 192: 540-542.

45 Bohannon RW, Smith MB. Inter rater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther* 1987; 67: 206-207.

46 Haas BM, Bergstrom E, Jamous A, et al. The inter rater reliability of the original and modified Ashworth scale for the assessment of spasticity in patients with spinal cord injury. *Spinal Cord* 1996; 34: 560-564.

47 Kui-Chung L, Carson L, Kinnin E, et al. The Ashworth Scale; A reliable and reproducible method of measuring spasticity. *J Neuro Rehab* 1989; 3: 205-209.

48 Bergner M, Bobbitt RA, Carter WB, et al. The sickness impact profile: development and final revision of a health status measure. *Med Care* 1981; 19: 787-805.

49 Gianino JM, York MM, Paice JA, et al. Quality of life: effect of reduced spasticity from intrathecal baclofen. *J Neurosci Nurs* 1998; 30: 47-54.

50 Middel B, Kuipers-Upmeijer H, Bouma J, et al. Effect of intrathecal baclofen delivered by an implanted programmable pump on health related quality of life in patients with severe spasticity. *J Neurol Neurosurg Psychiatry* 1997; 63: 204-209.

51 Granger CV, Hamilton BB. The Uniform Data System for medical rehabilitation report of first admissions for 1990. *Am J Phys Med Rehabil* 1992; 71: 108-113.

52 Patterson V, Watt M, Byrnes D, et al. Management of severe spasticity with intrathecal baclofen delivered by a manually operated pump. *J Neurol Neurosurg Psychiatry* 1994; 57: 582-585.

53 Mertens P, Parise M, Garcia-Larrea L, et al. Long-term clinical, electrophysiological and urodynamic effects of chronic intrathecal baclofen infusion for treatment of spinal spasticity. *Acta Neurochir* 1995; 64: 17-25.

54 Creedon SD, Dijkers MPJM, Hinderer SR. Intrathecal baclofen for severe spasticity: A meta-analysis. *Int J Rehabil Health* 1997; 3: 171-185.

55 Ordia JI, Fischer E, Adamski E, et al. Chronic intrathecal delivery of baclofen by a programmable pump for the treatment of severe spasticity. *J Neurosurg* 1996; 85: 452-457.

56 Azouvi P, Mane M, Thiebaut JB, et al. Intrathecal baclofen administration for control of severe spinal spasticity: functional improvement and long-term follow-up. *Arch Phys Med Rehabil* 1996; 77: 35-39.

57 Loubser PG, Akman MN. Effects of intrathecal baclofen on chronic spinal cord injury pain. *J Pain Symptom Manage* 1996; 12: 241-247.

58 Nanninga JB, Frost F, Penn R. Effect of intrathecal baclofen on bladder and sphincter function. *J Urol* 1989; 142: 101-105.

59 Frost F, Nanninga J, Penn R, et al. Intrathecal baclofen infusion. Effect on bladder management programs in patients with myelopathy. *Am J Phys Med Rehabil* 1989; 68: 112-115.

60 Albright AL, Barron WB, Fasick P, et al. Continuous intrathecal baclofen infusion for spasticity of cerebral origin. *JAMA* 1993; 270: 2475-2477.

61 Concalves J, Garcia-March G, Sanchez-Ledesma MJ, et al. Management of intractable spasticity of supraspinal origin by chronic cervical intrathecal infusion of baclofen. *Stereotact Funct Neurosurg* 1994; 62: 108-112.

62 Gerszten PC, Albright AL, Barry MJ. Effect on ambulation of continuous intrathecal baclofen infusion. *Pediatr Neurosurg* 1997; 27: 40-44.

63 Stewart-Wynne EG, Silbert PL, Buffery S, et al. Intrathecal baclofen for severe spasticity: five years experience. *Clin Exp Neurol* 1991; 28: 244-255.

64 Ochs GA, Tonn JC. Functional outcome and clinical significance of long-term intrathecal baclofen therapy for severe spasticity. *J Neurolog Rehabil* 1996; 10: 159-66.

65 Zierski J, Muller H, Dralle D, et al. Implanted pump systems for treatment of spasticity. *Acta Neurochir - Suppl* 1988; 43: 94-99.

66 Becker WJ, Harris CJ, Long ML, et al. Long-term intrathecal baclofen therapy in patients with intractable spasticity. *Can J Neurol Sci* 1995; 22: 208-217.

67 Penn RD, Kroin JS. Long-term intrathecal baclofen infusion for treatment of spasticity. *J Neurosurg* 1987; 66: 181-185.

68 Broseta J, Morales F, Garcia-March G, et al. Use of intrathecal baclofen administered by programmable infusion pumps in resistent spasticity. *Acta Neurochir - Suppl* 1989; 46: 39-45.

69 Lazorthes Y, Sallerin-Caute B, Verdie JC, et al. Chronic intrathecal baclofen administration for control of severe spasticity. *J Neurosurg* 1990; 72: 393-402.

70 Parke B, Penn RD, Savoy SM, et al. Functional outcome after delivery of intrathecal baclofen. *Arch Phys Med Rehabil* 1989; 70: 30-32.

71 Wall SA, Chait LA, Temlett JA, et al. Botulinum A chemodenervation: a new modality in cerebral palsied hands. *Br J Plast Surg* 1993; 46: 703-706.

72 Sahuquillo J, Muxi T, Noguer M, et al. Intraspinal baclofen in the treatment of severe spasticity and spasms. *Acta Neurochir* 1991; 110: 166-173.

73 Penn RD, Kroin JS. Continuous intrathecal baclofen for severe spasticity. *Lancet* 1985; 2: 125-127.

74 Loubser PG, Narayan RK, Sandin KJ, et al. Continuous infusion of intrathecal baclofen: long-term effects on spasticity in spinal cord injury. *Paraplegia* 1991; 29: 48-64.

75 Gerszten PC, Albright AL, Johnson GF. Intrathecal baclofen infusion and subsequent orthopedic surgery in patients with spastic cerebral palsy. *J Neurosurg* 1998; 88: 1009-1013.

76 Rawlins P. Patient management of cerebral origin spasticity with intrathecal baclofen. *J Neurosci Nurs* 1998; 30: 32-35.

77 McClelland MR. Conversation on the typical length of stay in acute care after an uncomplicated implant of a baclofen pump for spinal cord injury patients.1999.

78 Vloeberghs M. CIBI for Cerebral Palsy. (Personal Communication, 1999).

79 Morton R. Percentage of children tested for response to intrathecal baclofen, undergoing implant. (Personal Communication, 1999).

80 Albright AL. Baclofen in the treatment of cerebral palsy. *J Child Neurol* 1996; 11: 77-83.

81 Postma TJBM, Oenema D, Terpstra S, et al. Cost analysis of the treatment of severe spasticity with a continuous intrathecal Baclofen infusion system. *Pharmacoeconomics* 1999; 15: 395-404.

82 Netten A, Dennet J. Unit costs of health and social care 1998. Canterbury: PSSRU, University of Kent, 1998.

83 Bandolier. Pressure sores: five reviews and an RCT. 1997.

84 Frantz RA, Bergquist S, Specht J. The cost of treating pressure ulcers following the implementation of a research-based skin care protocol in a long term care facility. *Adv Wound Care* 1995; 8: 36-45.

85 McClelland MR. Conversation on the cost of treating pressure sores. 1999.

86 Morton R. CIBI in Cerebral Palsy. (Personal Communication, 1999)

87 Campbell SK, Almeida GL, Penn RD, et al. The effects of intrathecally administered baclofen on function in patients with spasticity. *Phys Ther* 1995; 75: 352-362.

88 Mertens P, Parise M, Garcia-Larrea L, et al. Long-term clinical, electrophysiological and urodynamic effects of chronic intrathecal baclofen infusion for treatment of spinal spasticity. *Acta Neurochir - Suppl* 1995; 64: 17-25.

89 Armstrong RW, Steinbok P, Cochrane DD, et al. Intrathecally administered baclofen for treatment of children with spasticity of cerebral origin. *J Neurosurg* 1997; 87: 409-414.

90 Saltuari L, Kronenberg M, Marosi MJ, et al. Long-term intrathecal baclofen treatment in supraspinal spasticity. *Acta Neurol* 1992; 14: 195-207.

91 Steers WD, Meythaler JM, Haworth C, et al. Effects of acute bolus and chronic continuous intrathecal baclofen on genitourinary dysfunction due to spinal cord pathology. *J Urol* 1992; 148: 1849-1855.

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