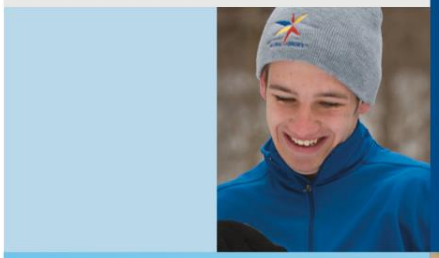
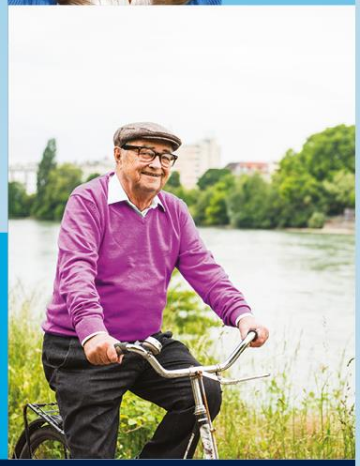
INTRATHECAL BACLOFEN (ITB) THERAPY VALUE SUMMARY

For treatment of severe, generalised spasticity





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SPASTICITY IS A DISORDERED SENSORI-MOTOR CONTROL, RESULTING FROM AN UPPER MOTOR NEURON LESION, PRESENTING AS INTERMITTENT OR SUSTAINED INVOLUNTARY ACTIVATION OF MUSCLES[1]

THE ORIGIN OF SPASTICITY

RECOGNIZING THE SIGNS OF SPASTICITY

Spasticity is often described as tight, stiff muscles or spasms that may make movement, posture and balance difficult.

When spasticity is perceived by the individual or caregiver as hindering body function, activities and/or participation, it is referred to as **disabling spasticity**[2].

Disabling spasticity is also refered to as severe spasticity by some clinicians/authors.

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THE ORIGIN OF SPASTICITY

CEREBRAL ORIGIN

- STROKE
- CEREBRAL PALSY (CP)
- BRAIN INJURY

OR

SPINAL ORIGIN

- SPINAL CORD INJURY (SCI)
- MULTIPLE SCLEROSIS (MS)*

* Multiple sclerosis is routinely considered of spinal origin due to the location of the lesions in the spinal cord, although patients may also present with brain lesions[3].

RECOGNIZING THE SIGNS OF SPASTICITY

SEVERAL SCALES HAVE BEEN **DEVELOPED AND VALIDATED TO ASSESS SPASTICITY**

While some scales are indication-specific, others are commonly used across indications. The most commonly used scales include:

- (Modified) Ashworth Scale (AS/MAS)
- Functional Independence Measure (FIM)
- Electrophysiological Measures
- Gait and Movement Analysis
- Walking Tests (e.g., 10 metres, 6 minutes)

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EPIDEMIOLOGY

THE PREVALENCE OF SEVERE SPASTICITY VARIES WITH THE UNDERLYING CONDITION

SPASTICITY AFFECTS AN ESTIMATED 12 MILLION PEOPLE WORLDWIDE[1]

SPINAL ORIGIN

MULTIPLE SCLEROSIS

550,000 persons in Europe have multiple sclerosis[2].

Up to **30%** are living with severe spasticity[3-7].

SPINAL CORD INJURY

200,000 persons in Europe are living with spinal cord injury[8].

Over **30%** are living with severe spasticity[9-14].

CEREBRAL ORIGIN

STROKE

1.1 million persons suffer a stroke in Europe each year[15].

Up to **13%** are living with a more severe degree of spasticity[16-21].

CEREBRAL PALSY

Close to 1 million persons in Europe have cerebral palsy[22].

Over **40%** are living with severe spasticity[23-27].

BRAIN INJURY

Prevalence is not well characterized.

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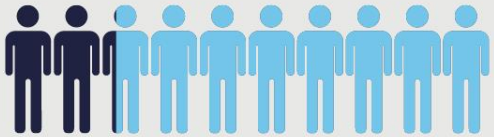
MULTIPLE SCLEROSIS (MS)

SPASTICITY IS A COMMON COMPLICATION IN MULTIPLE SCLEROSIS AND OFTEN AFFECTS THE LEGS

Several patient survey-based studies have found that **65-84%** of patients with MS experience spasticity[3-6].



17-29% of patients in these studies report severe spasticity[3-7].

MICHELLE
ITB Therapy Patient

SPINAL CORD INJURY (SCI)

INCIDENCE AND PREVELANCE OF SCI DIFFER BETWEEN DEVELOPING AND DEVELOPED COUNTRIES[9]

Across studies, spasticity is reported to develop in **40-68%** of patients with SCI[10-13].

Patients with cervical injuries are more likely to experience spasticity than patients with thoracic or lumbosacral level injuries[10-11].

Nearly **30%** of patients with SCI may experience disabling spasticity[10-12,14].

STROKE

SPASTICITY IS A WELL-KNOWN DISABLING CONSEQUENCE OF STROKE

Several studies have observed that **17-43%** of post-stroke patients develop spasticity[16-21].

One study reports that **13%** of post-stroke patients develop severe disabling spasticity[20-21].

PATSY
ITB Therapy Patient

CEREBRAL PALSY (CP)

CEREBRAL PALSY IS THE MOST COMMON CAUSE OF SPASTICITY IN CHILDREN AND YOUNG ADULTS[23-24]

A comparison of 28 CP registry studies from 8 geographic regions, reports that **90%** of patients with CP have a spastic motor type[25].

One study on functional status (using the definition for motor function suggested by the Surveillance of cerebral palsy in Europe, which may be a proxy for severe spasticity) reports that **42.3%** of patients have severe disability caused by the underlying disease[26-27].

MATT
ITB Therapy Patient

BRAIN INJURY

An estimated 5% of all traumatic brain injuries are classified as severe, with contractures due to spasticity occurring in up to **85%** of patients with severe traumatic brain injuries[28].

EPIDEMIOLOGICAL EVIDENCE FOR SPASTICITY DEVELOPMENT AFTER BRAIN INJURY IS NOT WELL-CHARACTERIZED. INCIDENCE ESTIMATES VARY FROM 13-63%[29-30]

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SIGNIFICANT HUMAN IMPACT

SPASTICITY IS A BURDENSOME CONDITION AND **HAS BEEN SHOWN TO IMPACT ON ALL ASPECTS OF PATIENTS' HEALTH-RELATED QUALITY OF LIFE, ACROSS DISEASE INDICATIONS.**

MULTIPLE SCLEROSIS

SPINAL CORD INJURY

STROKE

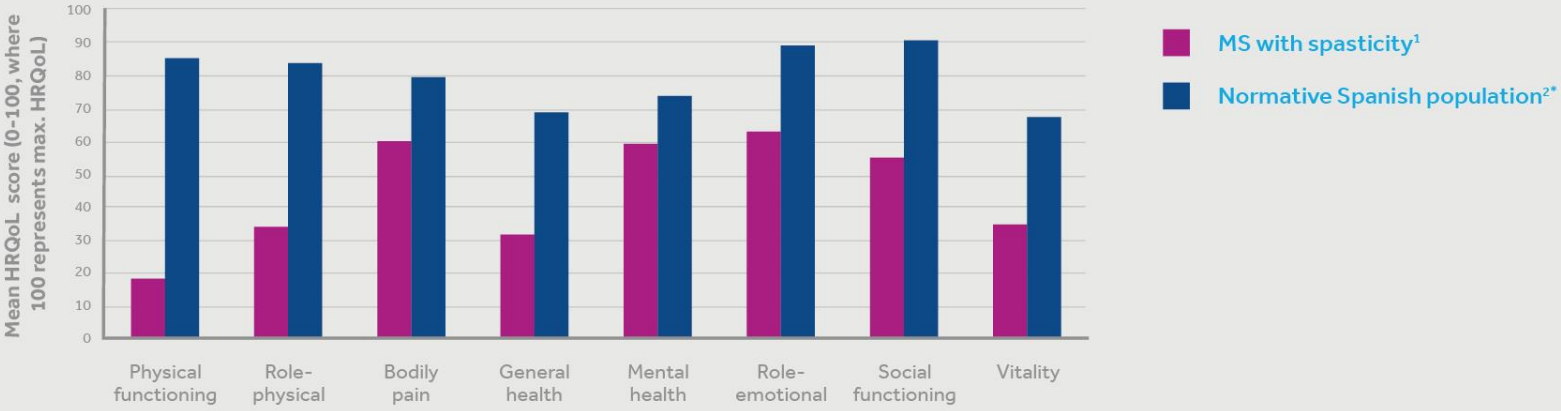
IMPACT OF SPASTICITY SEVERITY

MULTIPLE SCLEROSIS (MS)

OTHER IMPACTS OF SPASTICITY

In a 2013 Spanish study, scores on the Short Form-12 (SF-12®) quality of life survey indicated that **MS-related spasticity** had a **more pronounced effect on patients' general health and on the physical**, rather than mental, aspects of well-being [1].

MS patients with spasticity also demonstrate a quality of life decrement compared to a general population [1,2].



HRQoL: HEALTH-RELATED QUALITY OF LIFE

* In the absence of normative SF-12 data, normative SF-36 data from a Spanish population is used here as an approximate comparison[3]

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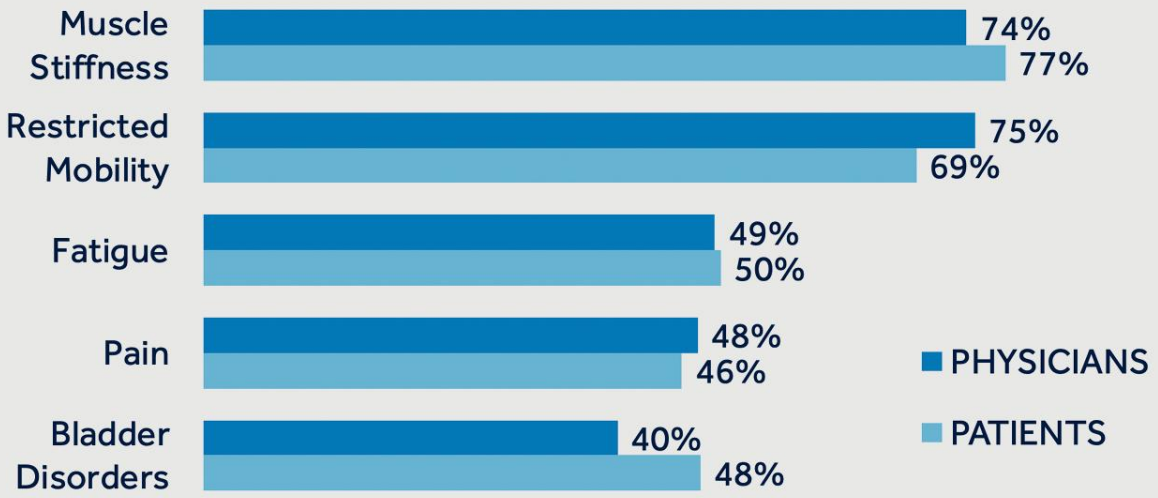
OTHER IMPACTS OF SPASTICITY

A 2014 cross-sectional study from Germany, which focused on patients who had experienced multiple sclerosis-related spasticity for at least 12 months, reported general agreement in the **most disturbing symptoms associated with spasticity** according to both physicians (N=411) and patients (N=398), being **stiffness** and **mobility restriction**[4].



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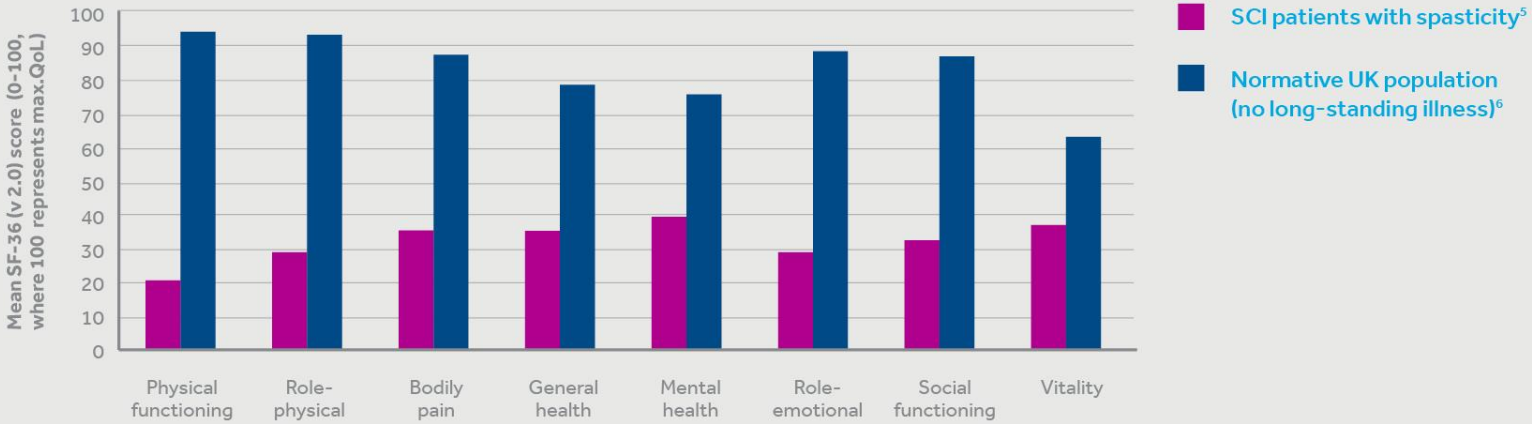
SPINAL CORD INJURY (SCI)

OTHER IMPACTS OF SPASTICITY

From a 2014 UK survey of 162 persons with SCI who experienced spasticity, significant **decreases in health-related quality of life,** as measured by the SF-36 survey (version 2.0), were observed **in all health domains, when compared to a general population[5,6].**



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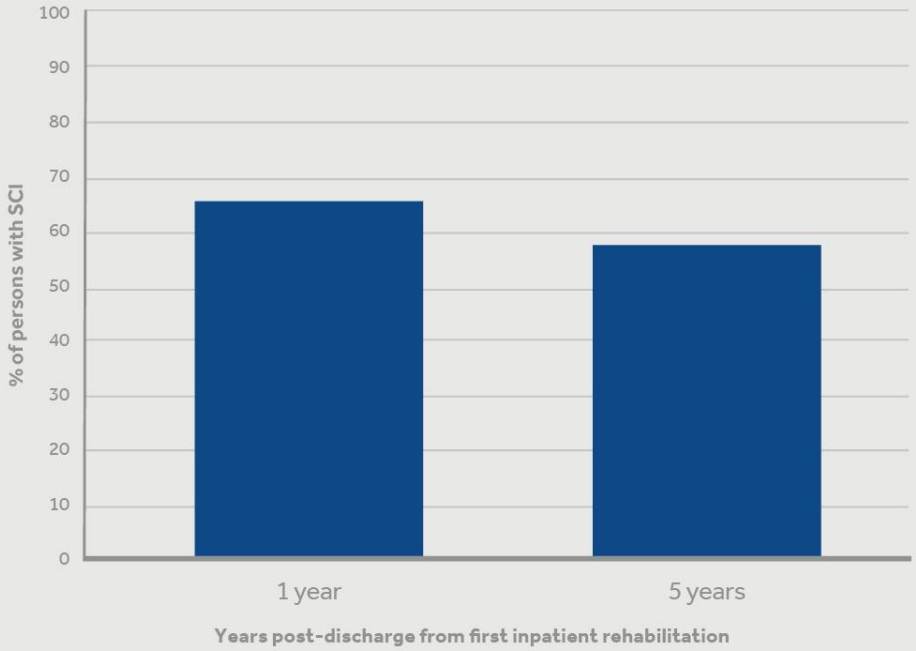
OTHER IMPACTS OF SPASTICITY

A 2017 multi-centre study from the Netherlands examining community-dwelling SCI patients who used a wheelchair for everyday mobility (N=110), found that **more than half** of participants **experienced restrictions on functioning due to spasticity, persisting at 5 years post-discharge** from their first inpatient rehabiltation.[7]

Functional restrictions due to spasticity[7]



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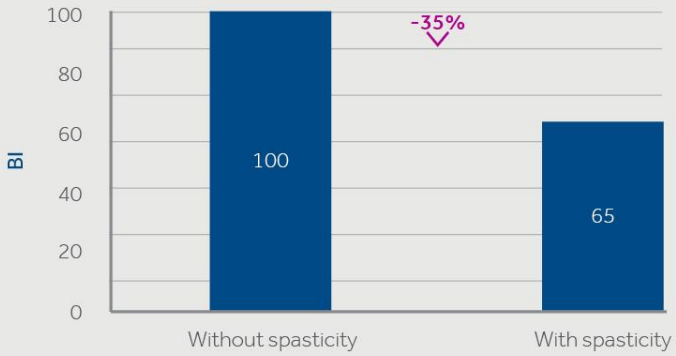
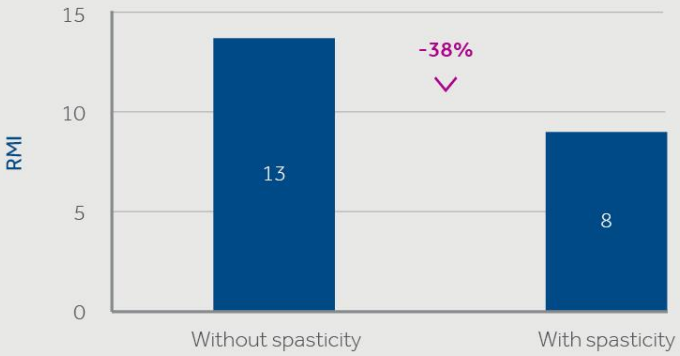
STROKE

IMPACT OF POST-STROKE SPASTICITY ON HRQOL

IMPACT OF POST-STROKE SPASTICITY ON CAREGIVERS

Post-stroke patients with spasticity suffer from a **reduction in function of 35–38%** compared to those without spasticity ($p \leq 0.001$)[8].





BI: BARTHEL INDEX
RMI: RIVERMEAD MOBILITY INDEX

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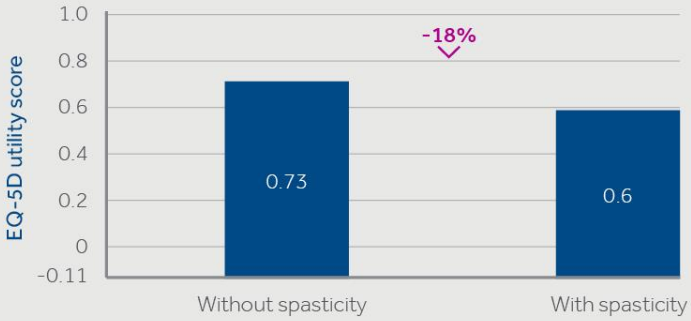
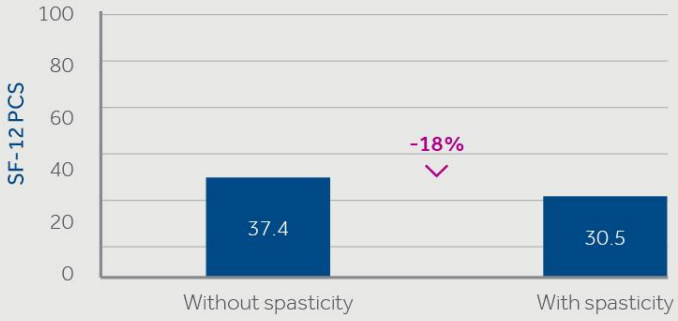
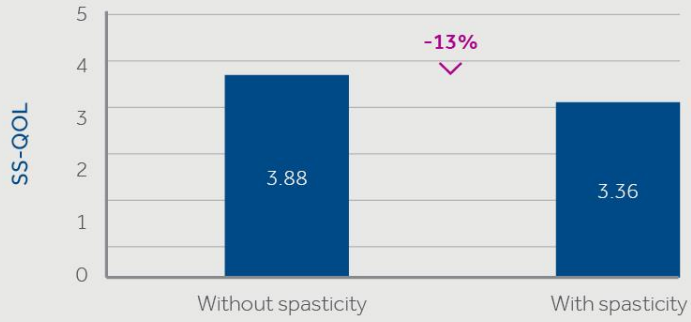
STROKE

Spasticity **negatively impacts** the health-related quality of life (HRQoL) of stroke survivors compared to those without spasticity ($p \leq 0.001$)[9].







EQ-5D: EUROQOL-5D
SF-12 PCS: SHORT FORM-12 PHYSICAL COMPONENT SUMMARY
SS-QOL: STROKE-SPECIFIC QUALITY OF LIFE

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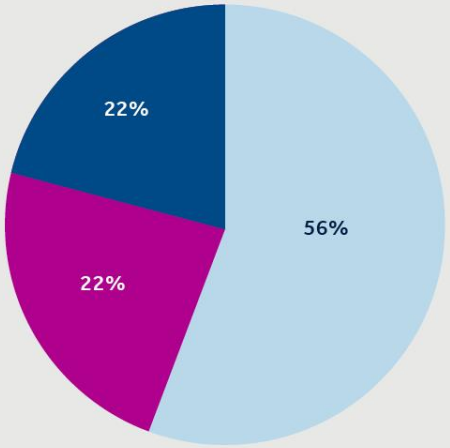
STROKE

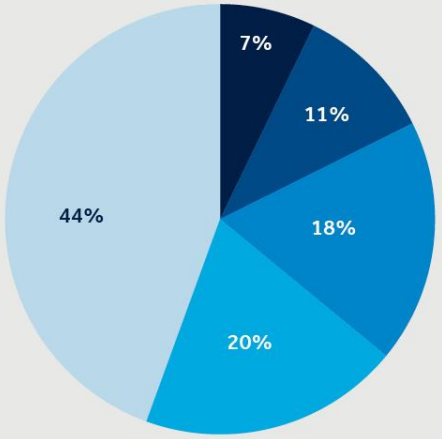
Caregivers of stroke survivors with spasticity suffer from **increased anxiety or depression**[10].

Physician diagnosis



- None (86 caregivers)
- Depression (34 caregivers)
- Anxiety (33 caregivers)

Patient Health Questionnaire-9 (PHQ-9) categories of depression



- None (68 caregivers)
- Mild depression (30 caregivers)
- Moderate depression (28 caregivers)
- Moderate severe depression (16 caregivers)
- Severe depression (11 caregivers)

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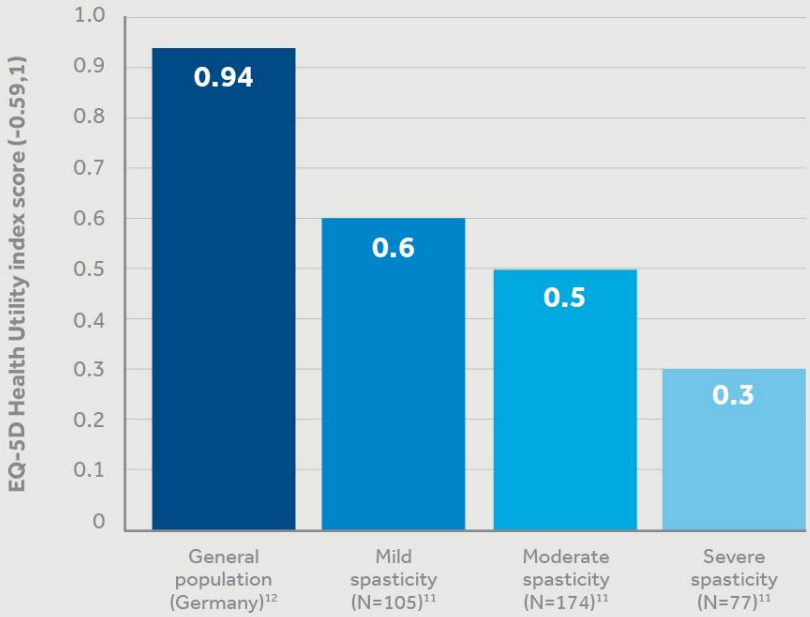
QUALITY OF LIFE WORSENS WITH INCREASING SEVERITY OF SPASTICITY

Data from a German cross-sectional, burden-of-disease study on patients who had experienced multiple sclerosis-related spasticity for at least 12 months reported **increasing impact on health-related quality of life with increasing spasticity severity** (N=389)[11].



EQ-5D: EUROQOL-5D

HEALTH-RELATED QUALITY OF LIFE **DECREASE BECOMES MORE PROMINENT WITH AN INCREASING SEVERITY OF SPASTICITY**[11]

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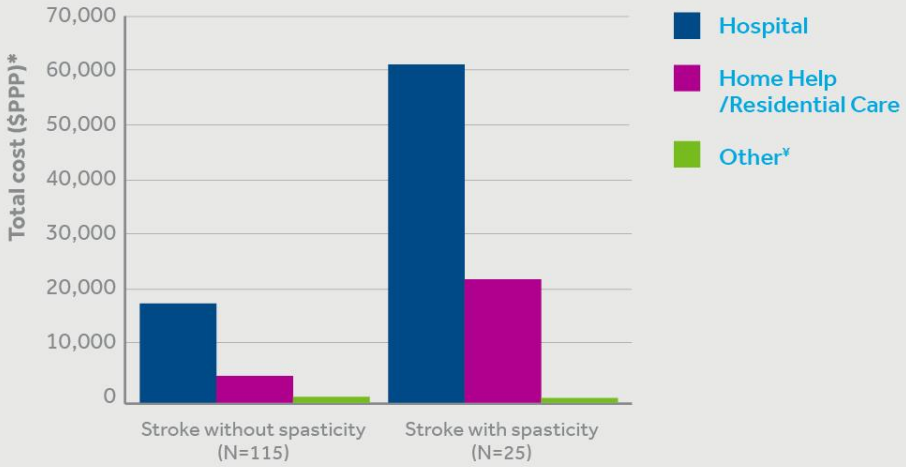
HIGHER HEALTHCARE COSTS ASSOCIATED WITH PATIENTS WHO DEVELOP SPASTICITY

INCREASING SEVERITY, INCREASES COSTS

A Swedish study has shown that in the 12-months **post-stroke**, direct healthcare costs for patients who experience spasticity are **4 times higher** than for those who do not develop spasticity[1].

Mean Direct Healthcare Costs of patients with post-stroke spasticity was PPP $84,195 vs. PPP $21,842 for non-spastic stroke patients[1].



HOSPITALISATIONS, HOME HELP AND RESIDENTIAL CARE WERE THE MAIN **COST DRIVERS IN THE POST-STROKE POPULATION, WITH HIGHER COSTS OBSERVED FOR SPASTIC PATIENTS** COMPARED TO NON-SPASTIC PATIENTS[1]

*For this study, Swedish currency (SEK) was converted into Purchasing Power Parities, which are rates of currency conversion that eliminate the difference in price levels between countries[2]. US dollar (PPP$) at the exchange rate of 9.34 SEK for 1 PPP$ (2003 value)[3].

¥ Other direct costs include primary care and medication.

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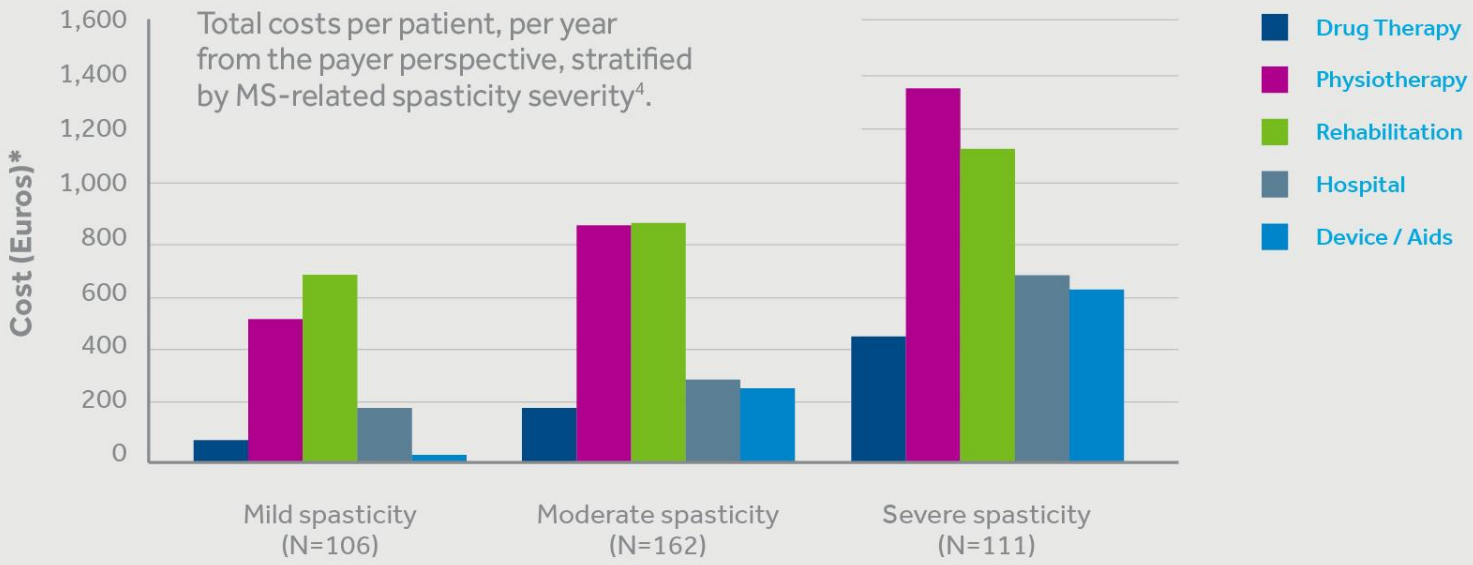
HIGHER HEALTHCARE COSTS ARE ASSOCIATED WITH AN INCREASING DEGREE OF SPASTICITY

Data from a German burden-of-disease study on patients with multiple sclerosis (MS)-related spasticity demonstrates **increasing healthcare costs accompany increasing spasticity severity** (N=379)[4].



*2011 costs from Germany

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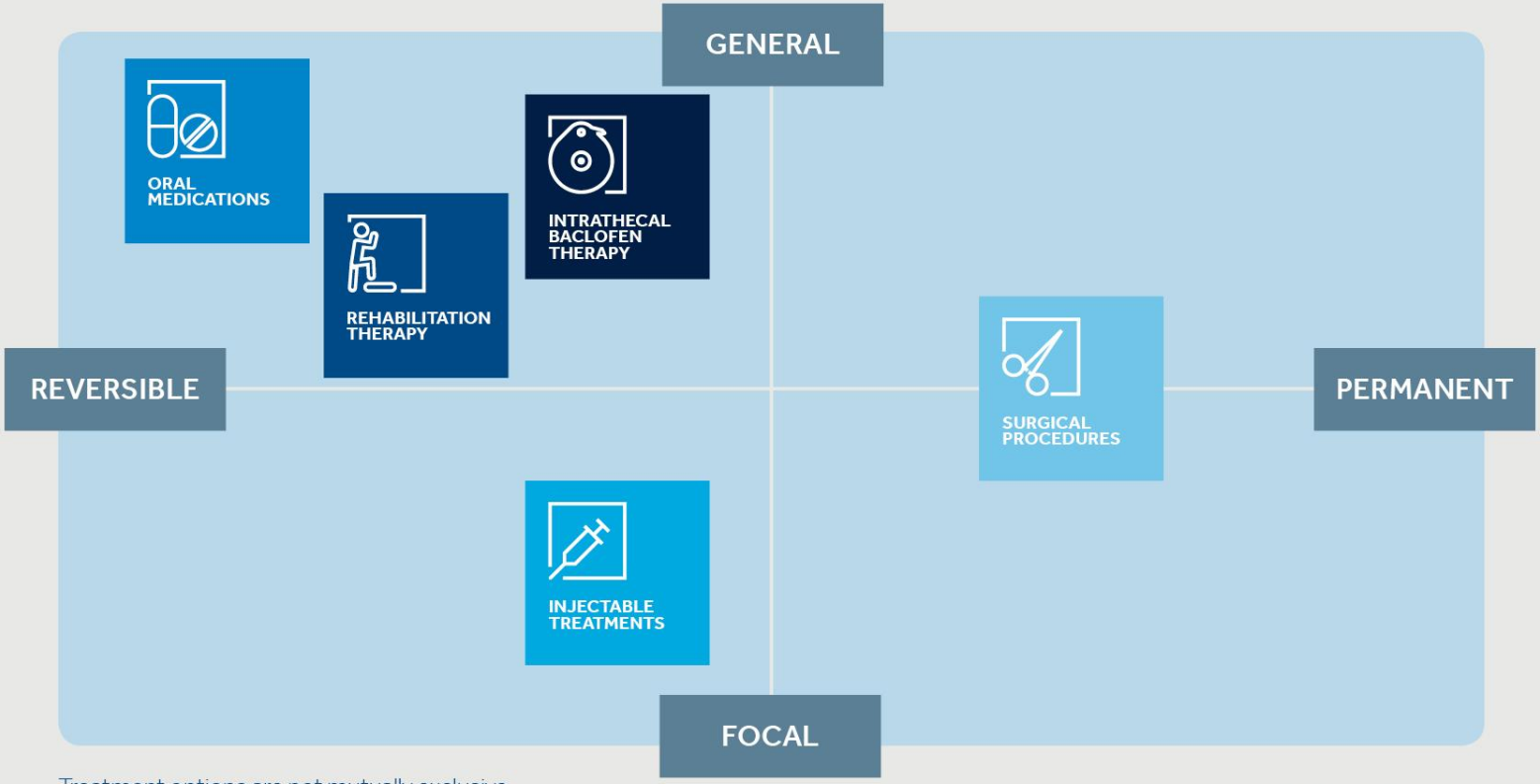
TREATMENT OPTIONS

DISABLING SPASTICITY IS CHALLENGING TO CONTROL EFFECTIVELY AND TYPICALLY REQUIRES A COMBINATION OF TREATMENTS

CLICK ON THE ICONS FOR MORE INFORMATION ON EACH TREATMENT OPTION



Treatment options are not mutually exclusive.
They may be used in conjunction with each other.

References
Glossary

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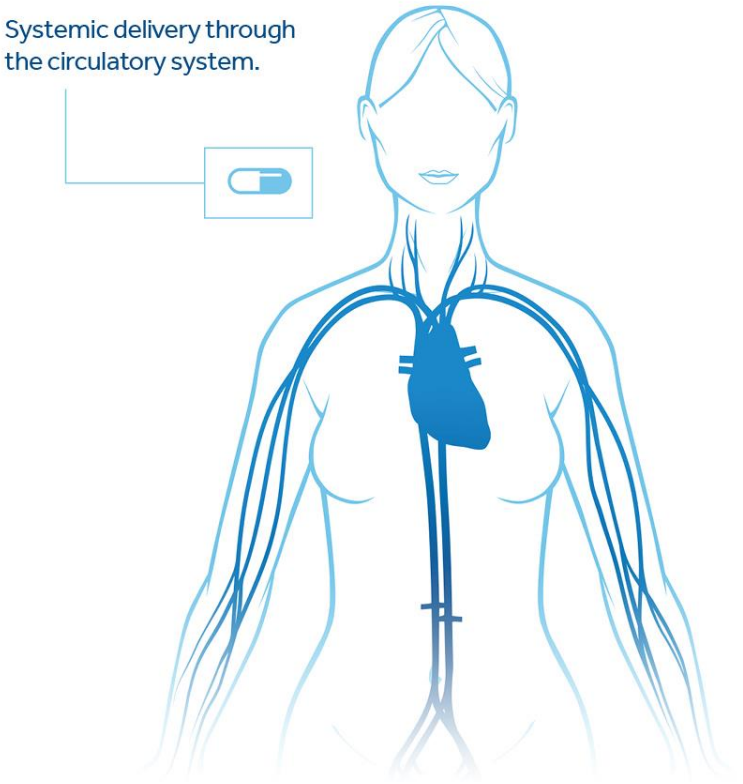
ORAL MEDICATIONS

ORAL BACLOFEN IS ONE OF THE MOST COMMONLY USED ANTISPASMODIC DRUGS IN THE TREATMENT OF SPASTICITY

For some patients, the amount of drug that penetrates the blood-brain barrier may not provide adequate relief for their disabling spasticity.

Increasing the dose may often result in unacceptable central nervous system (CNS) side effects such as sedation, dizziness, and muscle weakness[1-4].



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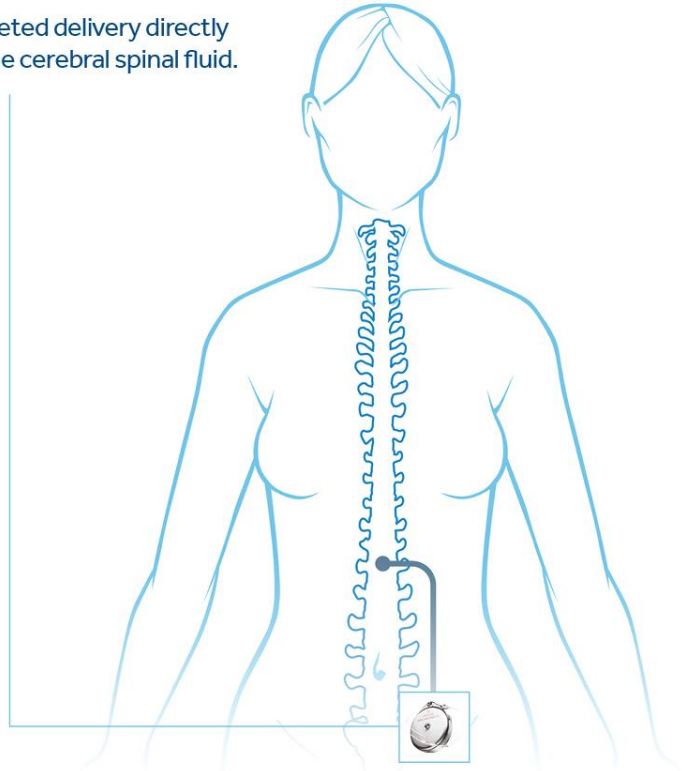
INTRATHECAL BACLOFEN (ITB) THERAPY

AN ALTERNATIVE ROUTE OF DELIVERY

ITB THERAPY DELIVERS THE DRUG DIRECTLY TO THE INTRATHECAL SPACE SURROUNDING THE SPINAL CORD

This allows effective drug concentrations to reach the cerebrospinal fluid, while the plasma remains relatively unaffected, compared with oral administration[5].

Targeted delivery directly to the cerebral spinal fluid.



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REHABILITATION THERAPY

PHYSICAL THERAPY to maximize motor skills, train muscles, improve mobility and promote flexibility.

OCCUPATIONAL THERAPY for upper limb function and fine motor skills to improve self-care and comfort.

SPEECH THERAPY to improve speech or use of alternative means of communication.

INJECTABLE TREATMENTS

PHENOL AND ALCOHOL are neurolytic agents which induce chemodenervation.

BOTULINUM TOXIN (BoNT) agents, administered by intramuscular injection, are available for the treatment of focal spasticity.

Injections must be repeated regularly as their effectiveness wears off over time.

SURGICAL PROCEDURES

General or focal, non-reversible procedures targeting:

NERVES (e.g., selected dorsal rhizotomy, neurotomy).

MUSCLES AND TENDONS (e.g., lengthening transfer).

BONES (eg. osteotomies, fusions).

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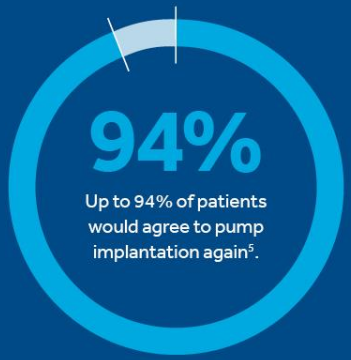
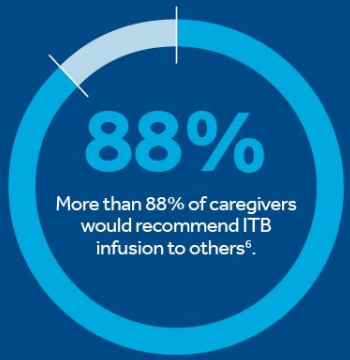
INTRATHECAL BACLOFEN (ITB) THERAPY





ITB is a viable option in patients who experience intolerable side effects or who fail to respond to the maximum recommended dose of oral baclofen[1].

Delivers a liquid form of medicine directly to fluid around spinal cord

Requires **100 to 1000x** smaller doses than oral baclofen[2]

Expected to produce fewer or more tolerable side effects when compared to oral baclofen[3-4]

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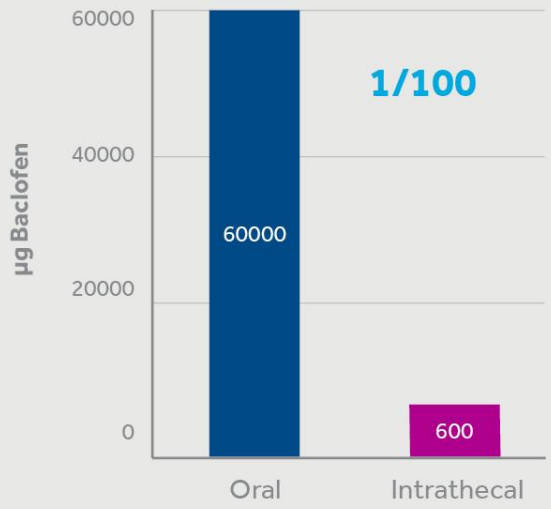
PHARMACOLOGY

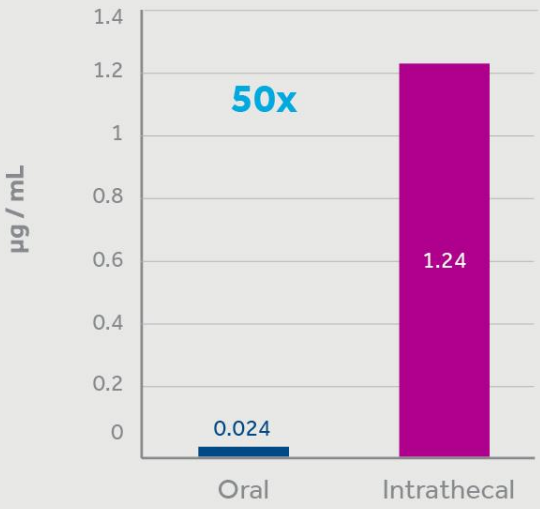
ITB ONLY REQUIRES 1/100 OF THE ORAL DAILY DOSAGE AND RESULTS IN A 50X HIGHER SPINAL CONCENTRATION[1-4]

Compared to oral baclofen, much lower (1/100) doses of ITB are required to achieve a relatively high (50x) concentration in the cerebrospinal fluid (CSF), thus minimizing side effects.

Daily administered dosage



Resulting CSF concentration



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BENEFITTING PATIENTS AND CLINICIANS FOR MORE THAN 30 YEARS

Medtronic's global reach enables our intrathecal drug delivery therapy to be available in many countries across the world.

Wireless Communicator | SynchroMed™ II Pump | Clinician Programmer

1988
SynchroMed™ pump (first used for pain management)

1992
SynchroMed™ pump for severe spasticity of spinal origin

1996
SynchroMed™ pump for severe spasticity of cerebral origin

1999
SynchroMed™ EL pump

2003
SynchroMed™ II pump

2008
myPTM™ Personal Therapy Manager

2016
SynchroMed™ II pump with durable design*

MyPTM™ Personal Therapy Manager

2017
New clinician programmer

2018
New MyPTM™ Personal Therapy Manager for patient

New MyPTM™ Personal Therapy Manager

2019

* Design changes to improve performance and reliability; data on file at Medtronic.

Note: This timeline only shows extracts of the Medtronic TDD product portfolio

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PERFORMANCE AND RELIABILITY

94.2%
Pump survival after 6.5 years[1]

Confidence year after year

±0.3%
Repeatability[2]

Consistency day after day

The SynchroMed™ II Programmable Infusion System:

- is available with a 20ml and 40ml reservoir size
- precisely moves medication through a peristaltic action
- has constant and flexible infusion modes with bolus dosing
- allows patient to self administer a therapeutic bolus
- makes safe 1.5T and 3.0 full body MRI possible*
- is designed to resume therapy immediately after MRI scan

19.5mm thickness (20ml pump)
26mm thickness (40ml pump)

* Under specific conditions for 1.5T and 3.0T MRI scans. Requires interrogation to confirm pump status.

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PERFORMANCE ASCENDA™

This is why Medtronic designed the Ascenda™ catheter[3]:

Real data shows only **28%** of therapy complications are **system related.**

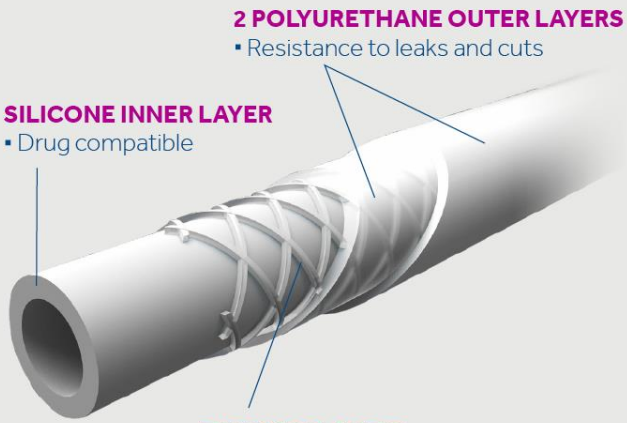
Of the 28%, **75.7%** are **catheter related.**

Of the 75.7%, **82%** are due to:

- **Dislodgement/ Migration**
- **Fracture/ Break**
- **Kink/ Occlusion**

DESIGN ENHANCEMENTS[4]

4 layers vs. 1 (silicone catheters)



Designed to reduce catheter dislodgement through more secure anchoring & better stabilization during placement.

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PERFORMANCE ASCENDA™

CLINICAL DATA DEMONSTRATES FAVOURABLE RESULTS FOR ASCENDA™ COMPARED TO OTHER CATHETERS[5,6]

RESULTS (Motta et al 2016)		OTHER CATHETERS	ASCENDA™
Number of ITB Patients	# of Patients	416	92
Catheter related complications	# of Patients (%)	**75 (18%)**	**0 (0%)**

RESULTS (Pucks-Faes et al 2018)		OTHER CATHETERS	ASCENDA™
Number of ITB Patients	# of Patients	73	36
Catheter related complications	# of Patients (%)	**19 (26%)**	**3 (8%)**

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AVAILABLE IN MULTIPLE REGIONS ACROSS THE GLOBE

PLEASE CONTACT A MEDTRONIC REPRESENTATIVE TO FIND OUT MORE ABOUT IMPLANT AND REFILL CENTRES WORLDWIDE

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A STAGED APPROACH TO SUCCESSFUL THERAPY

Patient assessment is an essential step in selecting ITB Therapy candidates.

A thorough assessment should ensure that all facets of the patient's condition are considered.

The goals of treatment vary for each patient and must be realistic given their current level of function and disability.

Patients, caregivers and physicians should work together to develop and agree upon all objectives that may be possible with ITB Therapy.

THERAPY ALWAYS STARTS WITH A SCREENING TEST (TEST DOSE)

A screening test determines if ITB may work for the patient. It involves the administration by lumbar puncture of an ITB bolus injection. The patient's response is monitored for an 8 hour period following the procedure.

If the medical team, together with the patient, decide ITB is the right treatment option, a Programmable Infusion System (pump and catheter) will be implanted in the patient's lower abdomen for long-term management of their spasticity.

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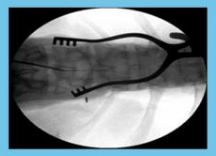
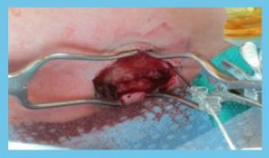
A 5-STEPS IMPLANTATION TECHNIQUE

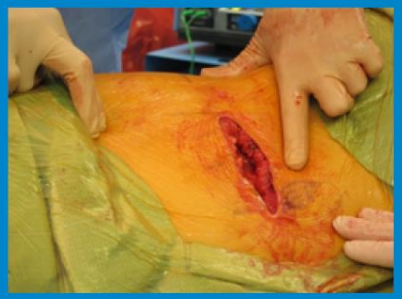
1. POSITION PATIENT

2. PLACE CATHETER

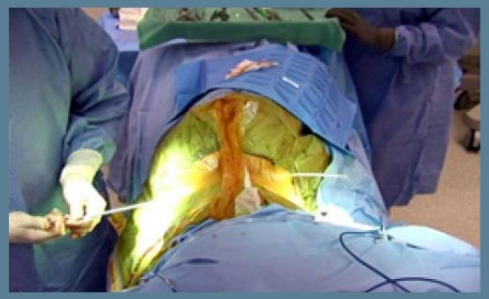




3. PREPARE PUMP POCKET



4. TUNNEL CATHETER



5. CONNECT PUMP AND CATHETER

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INTERDISCIPLINARY THERAPY MANAGEMENT IS ESSENTIAL TO ENSURE OPTIMAL TREATMENT BENEFITS

TITRATION

Schedules are individually set to benefit the patient, depending on activities and needs.

REPLACEMENT

Every 6-7 years[1], an alarm is activated 90 days before battery life ends.

REFILLS

Every 6 weeks-6 months depending on dosing requirements and reservoir size.

TROUBLE SHOOTING

Patients should be monitored for the occurrence of complications.

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REFERENCE

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ITB IS SUPPORTED BY CLINICAL EVIDENCE ACROSS INDICATIONS

ITB can help manage spasticity, decrease spasms and pain, as well as improve function and quality of life.

	SPASTICITY OF CEREBRAL ORIGIN			SPASTICITY OF SPINAL ORIGIN	
	CEREBRAL PALSY	**BRAIN INJURY**	**STROKE**	**SPINAL CORD INJURY**	**MULTIPLE SCLEROSIS**
NO. OF RANDOMISED PATIENTS	Up to 54	Up to 18	Up to 74	Up to 33	Up to 106
LENGTH OF FOLLOW-UP	Up to 9 years	Up to 9 years	Up to 12 months	Up to 12 years	Up to 21 years
MUSCLE TONE	7 Studies[1- 3,5- 9*]	4 Studies[9-12]	5 Studies[13-16,18]	5 Studies[8,19-22]	8 Studies[8,20,21,23-27]
SPASMS	2 Studies[7,8]	3 Studies[10-12]		5 Studies[8,19-22]	8 Studies[8,20,21,23-27]
PAIN	2 Studies[2, 4-6*]		1 Study[17]		4 Studies[23,25-27]
FUNCTION	4 Studies[2,3,5,6, 8*]	1 Study[10]	3 Studies[13-15]	2 Studies[8,19]	2 Studies[8, 25]
QUALITY OF LIFE	1 Study[4-6*]		3 Studies[13,14, 17]		3 Studies[21,23,25]

Clinical studies including at least 10 patients and showing a significant improvement of the outcome measures.

*Publications 4,5 and 6 refer to the same clinical trial.

CEREBRAL PALSY: 1 retrospective analysis[3], 4 prospective studies[1,2,8,9], 1 randomized controlled study[6] followed by 2 prospective studies on the same patient group[4,5] and 1 prospective controlled study[7]. In the 2 controlled studies, the outcomes have been compared to the conventional medical management.

BRAIN INJURY: 4 prospective studies[9,10,11,12].

STROKE: 3 prospective studies[13,14,18], 1 case series[15] and 1 randomized controlled study[16,17].

SPINAL CORD INJURY: 4 prospective studies[8, 19-21] and 1 retrospective analysis[22].

MULTIPLE SCLEROSIS:
2 retrospective study[24,26],
5 prospective studies[8,20,21,25,27] and 1 randomized control study for the first 13 weeks and prospective study for the follow-up at 26 and 52 weeks[23].

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ITB HAS A DEMONSTRATED SAFETY PROFILE ACROSS INDICATIONS

Adverse effects of different origins may occur with ITB[1-8].

DRUG

The most common side effects of ITB are related to the drug itself.

E.g., drowsiness, somnolence, nausea, vomiting, muscle weakness, urinary retention.

DEVICE/ PROCEDURE

E.g., infection, catheter migration or disconnection, pump dysfunction, cerebrospinal fluid leak, spinal headache.

Almost half of complications related to ITB occur within the first year post surgical implantation, with 25% occurring within the first month.[9]

Most system-related complications are linked to the catheter[11]. Use of the **Ascenda™ catheter** is associated with a more than 3-fold decrease in the risk of catheter complication[9,10].

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PATIENT BENEFIT

7 ITB STUDIES SHOW A SIGNIFICANT IMPROVEMENT IN QUALITY OF LIFE FOR PATIENTS OR CAREGIVERS

CLICK ON EACH AUTHOR NAME FOR MORE INFORMATION ON THE STUDY

	INDICATION	AUTHOR	OUTCOME MEASURE	DOMAINS
CEREBRAL	Stroke	Creamer 2018	EQ-5D	Utility score
	CP	Vles 2013	CHQ-PF50	Pain/discomfort, mental health, parental impact emotional, parental impact time, physical summary
	Stroke	Schiess 2011	SS-QOL	Family role, mobility, social roles, thinking, upper extremity, function work productivity, personality, self-care
	Stroke	Ivanhoe 2006	SIP	Physical dimension, psychological dimension, home management, recreation/pastimes
SPINAL	MS	Natale 2016	SDS	Overall score
	MS and SCI	Delhaas 2008	EQ-5D	Visual analog scale
	MS and SCI	Middel 1997	SIP	Overall score, sleep and rest, recreation and pastimes, mobility, body care and movement, physical dimension
			HSC	Overall score, physical health

CHQ-PF50: Child Health Questionnaire Parent Form 50
CP: Cerebral Palsy
EQ-5D: EuroQol-5D
HSC: Hopkins Symptoms Checklist
MS: Multiple Sclerosis
SCI: Spinal Cord Injury
SDS: Self Rating Depression Scale
SIP: Sickness Impact profile
SS-QOL: Stroke Specific Quality of Life

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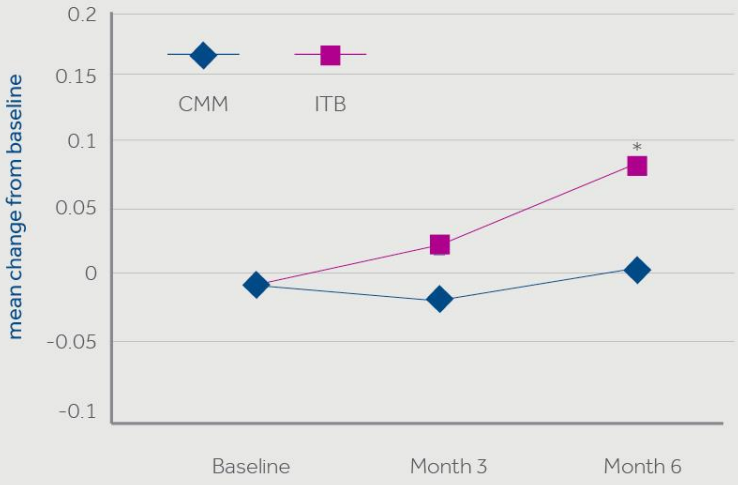
Further, Together

CREAMER 2018

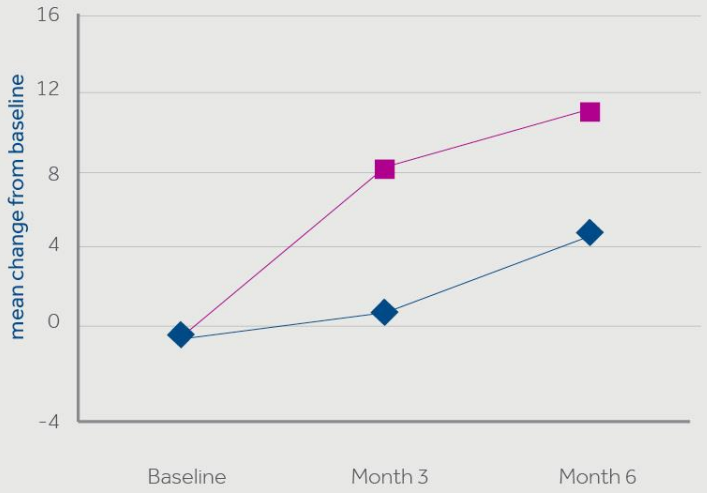
PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In stroke patients, after 6 months of ITB treatment a significant improvement of the EQ-5D utility score was observed when compared to patients treated with conventional medical management (oral medication)[17].

EQ-5D UTILITY SCORE



EQ-5D VISUAL ANALOGUE SCORE



CMM= conventional medical management
Change from baseline, between group difference*p<.05

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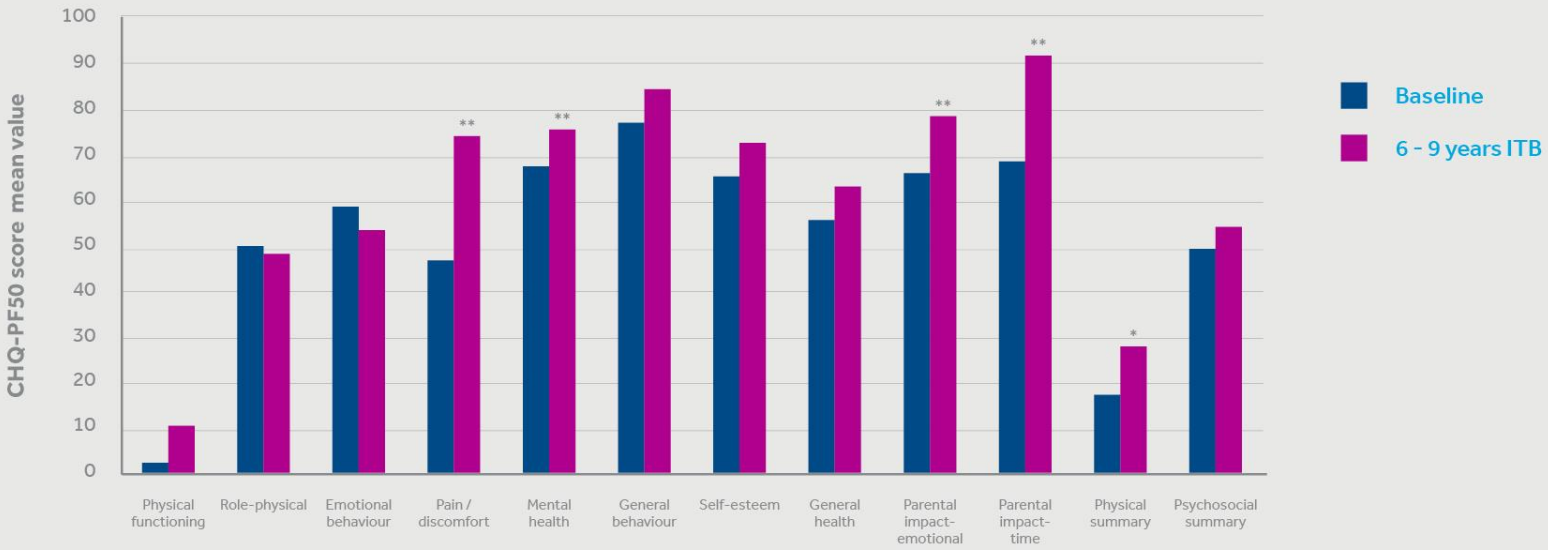
VLES 2013

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

Assessment of the CHQ-PF50 score showed an improvement in pain, mental health, parental impact emotional, parental impact time and physical summary after long-term follow up of ITB treatment (6-9 years) in children with intractable spastic cerebral palsy[4].



Changes from baseline: * p<.05; ** p≤.01

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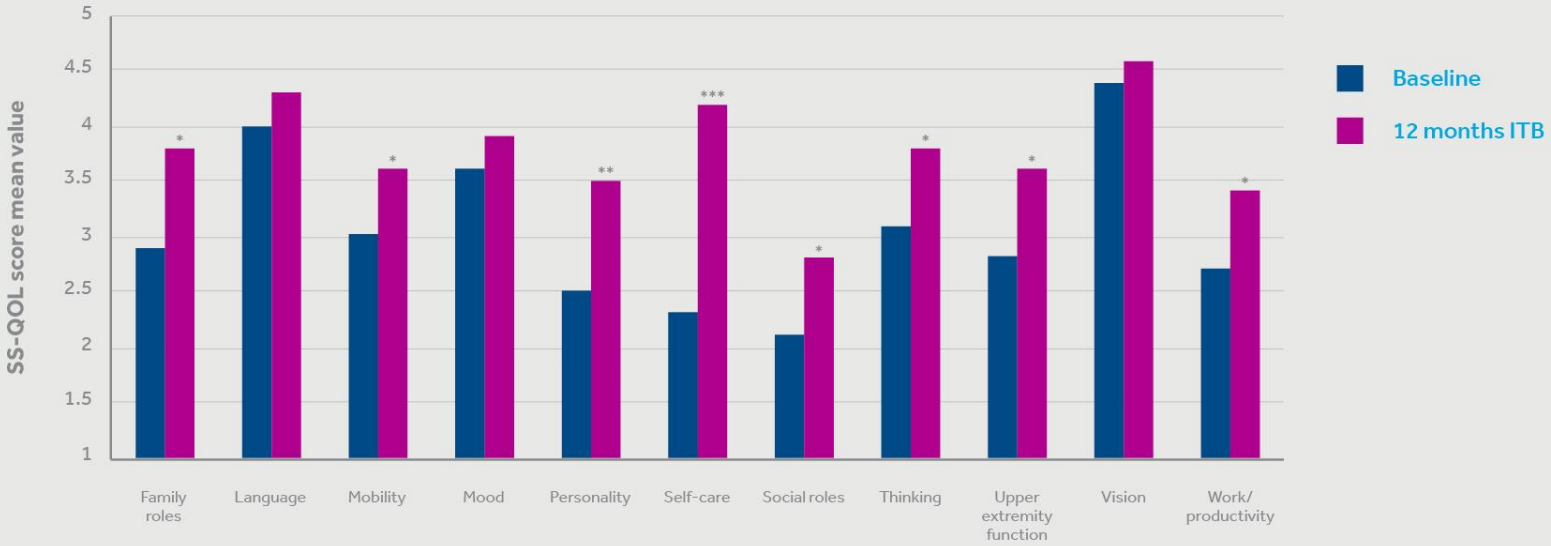
Further, Together

SCHIESS 2011

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In stroke patients, the SS-QOL showed significant improvement at 12 months of ITB treatment, specifically in the domains of family roles, mobility, personality, self-care, social roles, thinking, upper extremity function, and work/productivity[13].



Change from baseline: *p≤.05; ** p<.01; *** p≤.001

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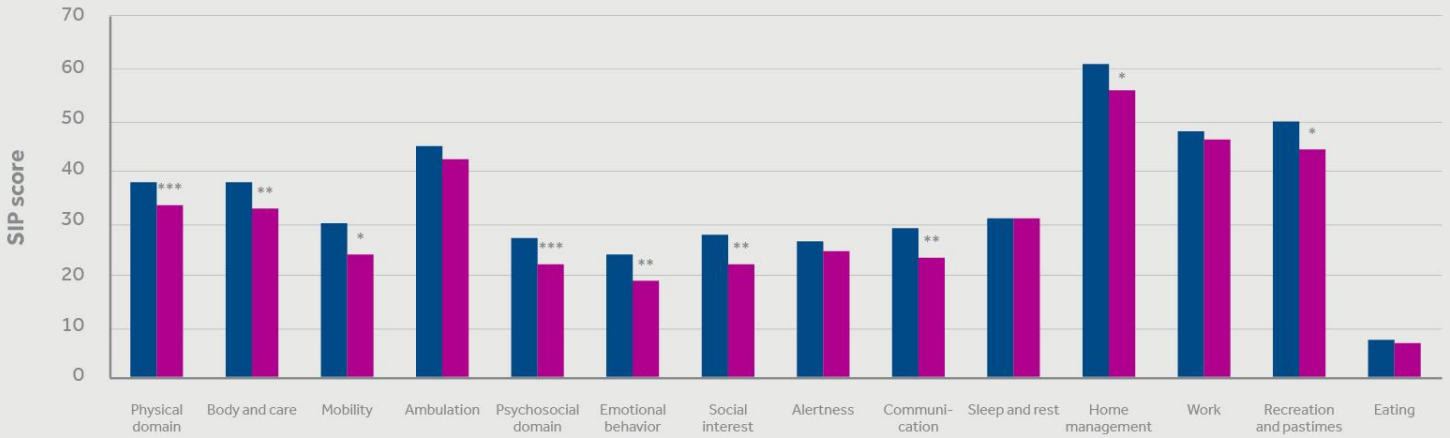
Further, Together

IVANHOE 2006

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In stroke patients, after 12 months of ITB treatment, SIP scores improved significantly overall in both the physical domain (that includes body and care movement, mobility and ambulation) and the psychosocial domains (that includes emotional behaviour, social interest, alertness behaviour and communication), as well as in other categories such as home management or recreation and pastimes[14].



Changes from baseline:* p<.05; ** p<.01; *** p<.001

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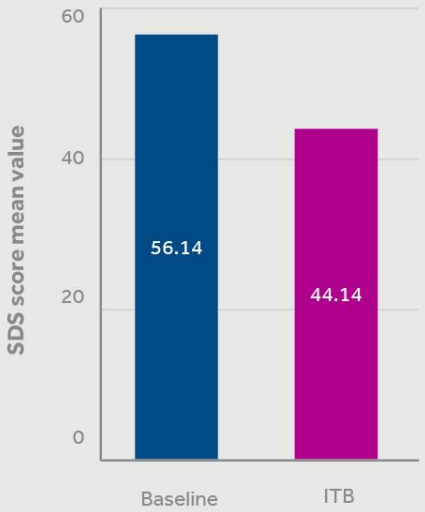
Further, Together

NATALE 2016

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In multiple sclerosis patients, the SDS score varied significantly from pump implantation (baseline value) to last follow-up (74 months in average)[25].



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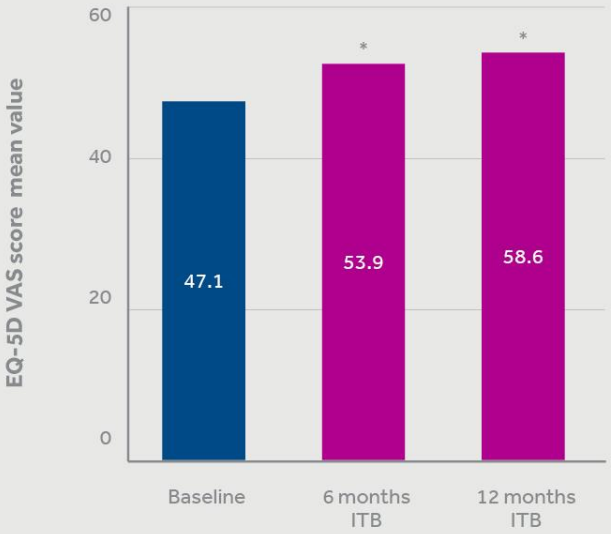
DELHAAS 2008

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In a group of spasticity patients (71% of which, were multiple sclerosis and spinal cord injured patients), the average EQ-5D visual analog scale was significantly higher after 6 and 12 months of ITB treatment[21].



Change from baseline: *p≤.05

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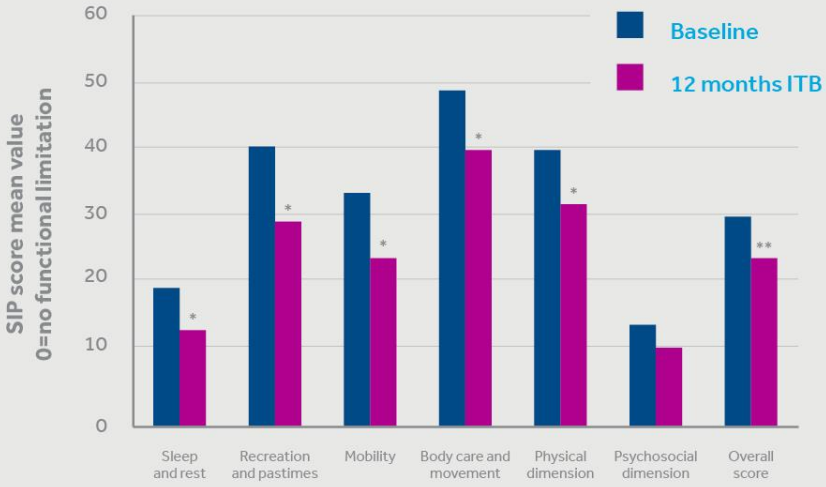
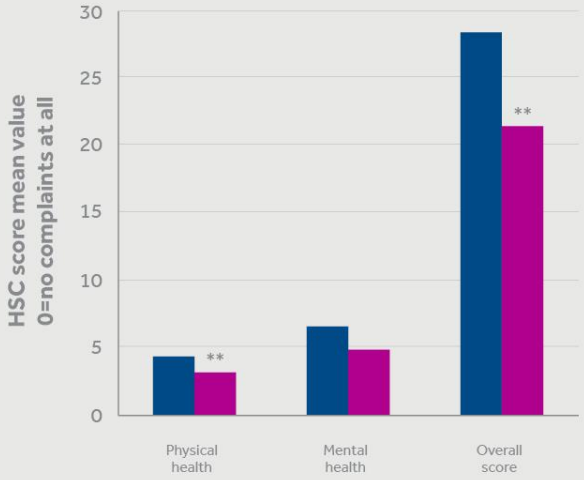
MIDDEL 1997

PATIENT BENEFIT IMPROVING QUALITY OF LIFE

In multiple sclerosis and spinal cord injured patients, SIP scale and HSC score improved overall after 12 months of ITB treatment. In particular, sleep and rest, recreation and pastimes, mobility, body care and movement, physical dimensions and physical health showed a significant decrease[23].





Change from baseline: *p≤.05; ** p≤.001
SIP overall score has been calculated without the ambulation subscores as not applicable in this population group.

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Further, Together

PATIENT BENEFIT

11 ITB STUDIES SHOW A SIGNIFICANT IMPROVEMENT IN PATIENT FUNCTION

CLICK ON EACH AUTHOR NAME FOR MORE INFORMATION ON THE STUDY

	INDICATIONS	AUTHOR	OUTCOME MEASURE	DOMAINS
CEREBRAL	CP	Motta 2011	GMFM	Overall score
	Stroke	Schiess 2011	FIM	Transfer, grooming, eating, bathing, toileting, ambulation, dressing-upper body and gait distance
			UEMAL	Gross and fine activities and amount of scale, quality of movement
			Walking Speed	
	CP	Ramstad 2010	PEDI	Self-care, mobility, social function
			GMFM	Overall score
	CP	Hoving 2009	GMFM	Sitting dimension, goal dimension
	Stroke	Ivanhoe 2006	FIM	Overall score, motor , transfer, self-care subscores
	CP	Guillaume 2005	FIM, WeeFIM	Overall score
	Stroke	Francisco 2003	Modified FIM	Locomotion-walking, stair, sit to stand, stand to sit
			Walking Speed	
	CP and TBI	Rawicki 1999	FIM, Snow Hygiene Scale	Transfer score, hygiene (ability to clean and self-catheterize)
SPINAL	MS	Natale 2016	BI	Overall score
	MS and SCI	Guillaume 2005	FIM, WeeFIM	Overall score
	MS and SCI	Azouvi 1996	FIM	Overall score

BI: Barthel Index
CP: Cerebral Palsy
FIM: Functional Independence Measure
GMFM: Gross Motor Function Mobility
MS: Multiple Sclerosis
PEDI: Pediatric Evaluation of Disability Inventory
SCI: Spinal Cord Injury
TBI: Trauma Brain Injury
UEMAL: Upper Extremity Manual Activity Log
WeeFIM: Functional Independence Measure for children

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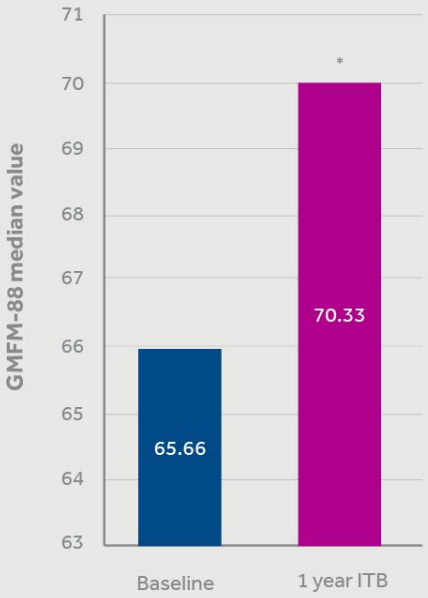
Further, Together

MOTTA 2011

IMPROVEMENT IN PATIENT FUNCTION

ITB increased the total median GMFM score in children with cerebral palsy after 1 year of treatment[3].



Change from baseline: * p<.001

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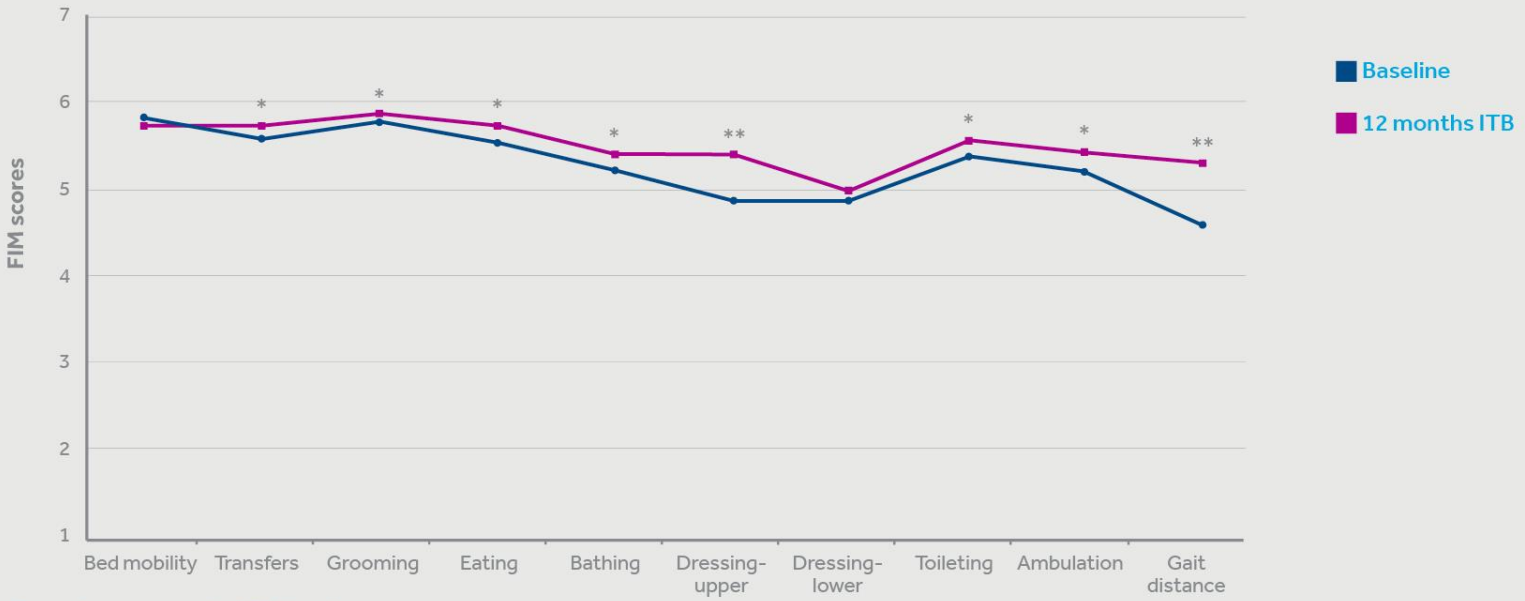
Further, Together

SCHIESS 2011

IMPROVEMENT IN PATIENT FUNCTION

After 12 months of ITB treatment, stroke patients demonstrated improvement in all FIM scores (except bed mobility and lower body dressing), in walking velocity speed and in amount of use (AOU) and quality of movement (QOM) of the spastic upper extremities measured with the UEMAL[13].



Change from baseline: * p<.05; ** p<.01

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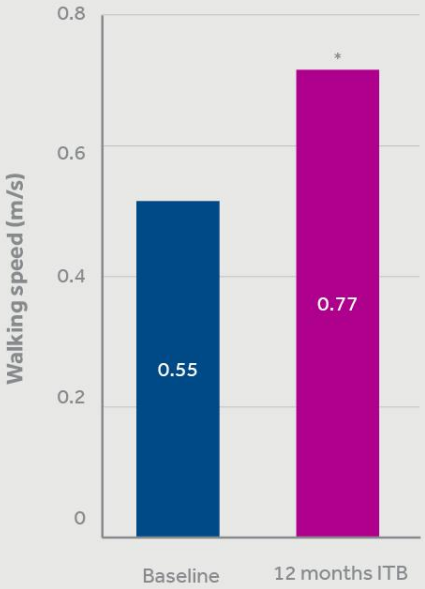
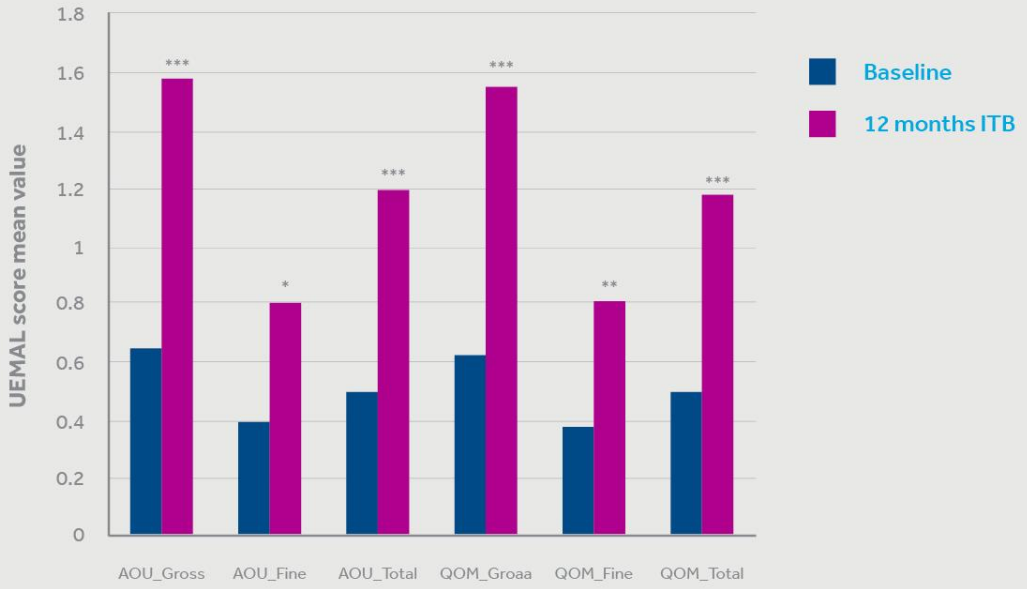
SCHIESS 2011

IMPROVEMENT IN PATIENT FUNCTION





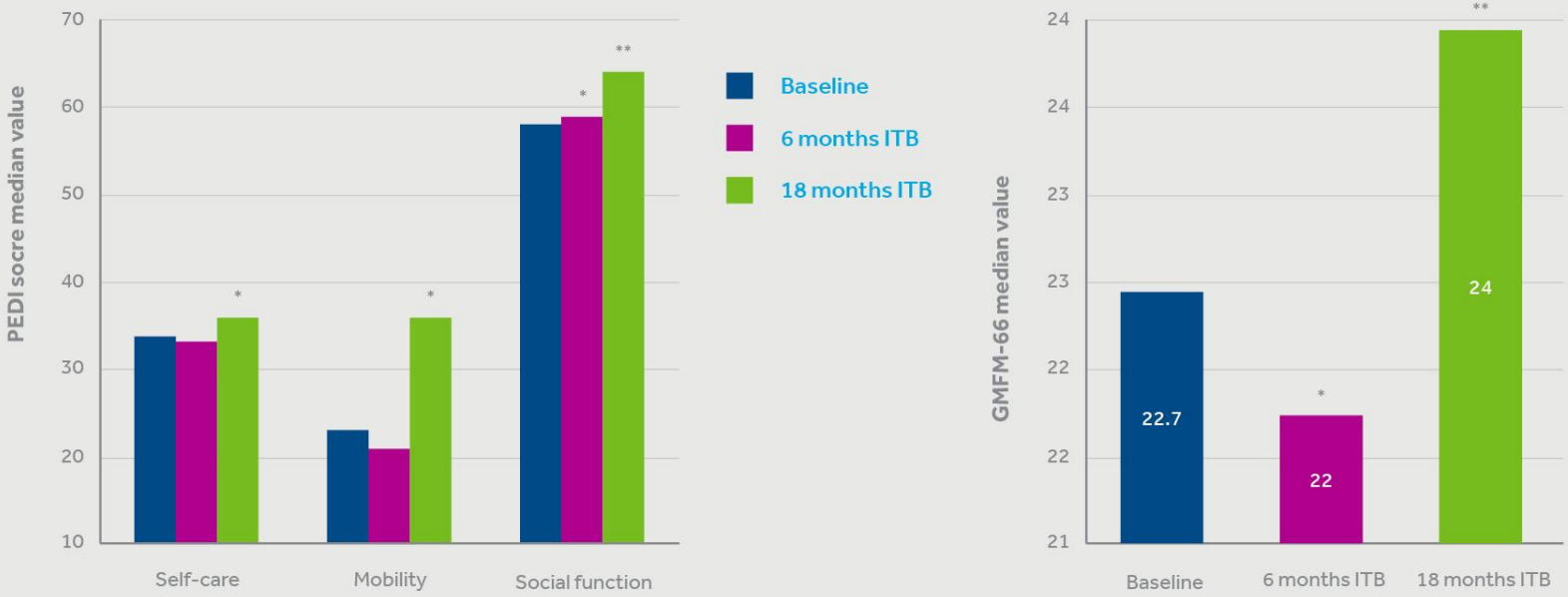
Change from baseline: * p<.05; ** p<.01; *** p<.001

Medtronic
Further, Together

RAMSTAD 2010

IMPROVEMENT IN PATIENT FUNCTION

In children with cerebral palsy, ITB treatment improved functional skills as demonstrated by the PEDI individual scores and GMFM-66 total score after 6 and 18 months[2].



Change from baseline: * p<.05; ** p<.01

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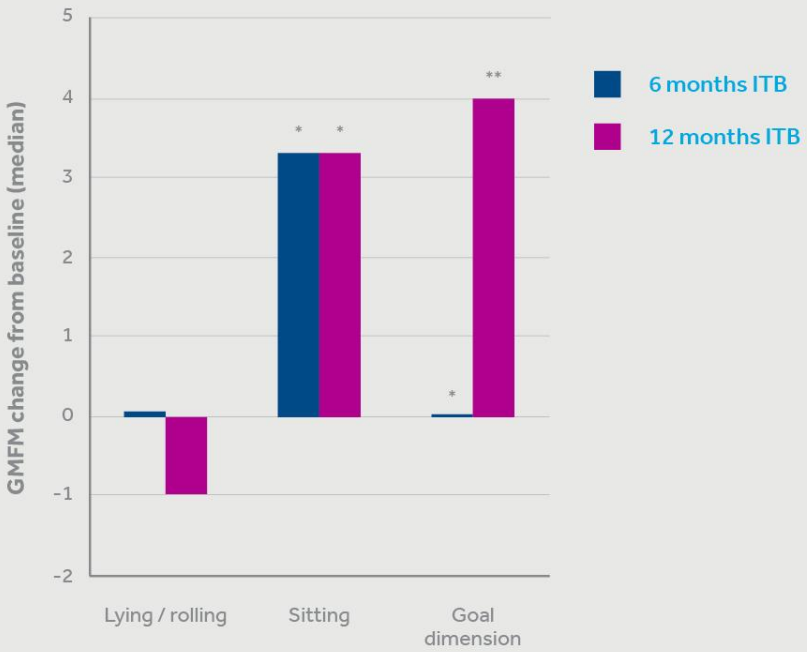
Further, Together

HOVING 2009

IMPROVEMENT IN PATIENT FUNCTION

After 12 months of ITB treatment, children with cerebral palsy significantly improved GMFM sitting and goal dimension scores with 3.3 and 4.0 points, respectively[5].



Change from baseline: * p<.05; ** p<.01

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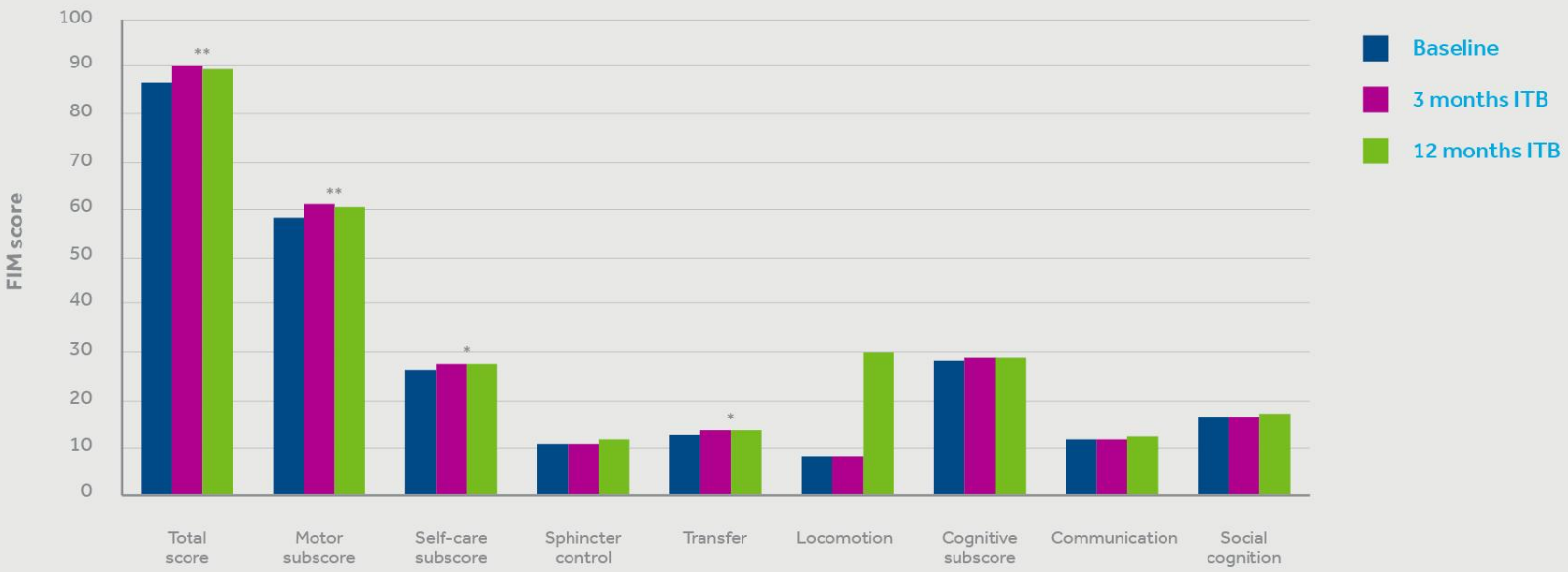
Further, Together

IVANHOE 2006

IMPROVEMENT IN PATIENT FUNCTION

In stroke patients, after 3 and 12 months of ITB treatment, FIM scores improved significantly overall and particularly in motor, transfer, self-care subscores[14].



Change from baseline, overall (3 and 12 months) p value: * p≤.05; ** p<.01

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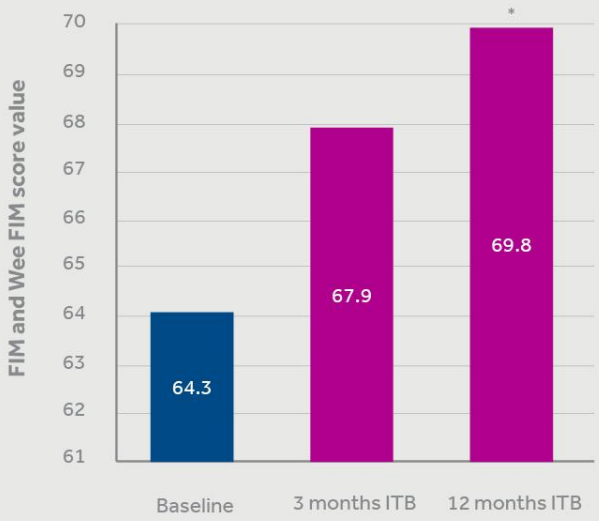
Further, Together

GUILLAUME 2005

IMPROVEMENT IN PATIENT FUNCTION

In patients with intractable spasticity of cerebral and spinal origin, the WeeFIM (used for patients ≤ 7 years of age) and the FIM (for patients over 7 years of age) overall score increased significantly after 12 months of ITB treatment[8].



Change from baseline: * p<.001

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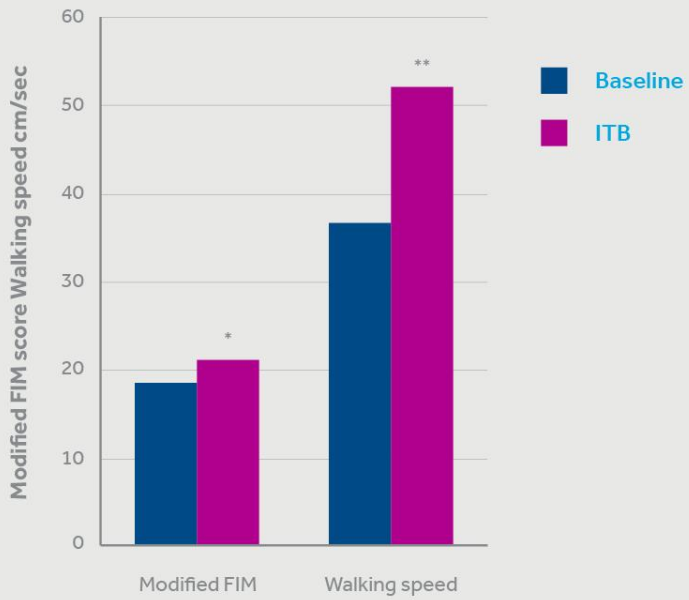
Further, Together

FRANCISCO 2003

IMPROVEMENT IN PATIENT FUNCTION

In stroke patients, ITB significantly improved walking speed and functional mobility rating, measured with a modified FIM score, at an average follow-up time of 8.9 months[15].



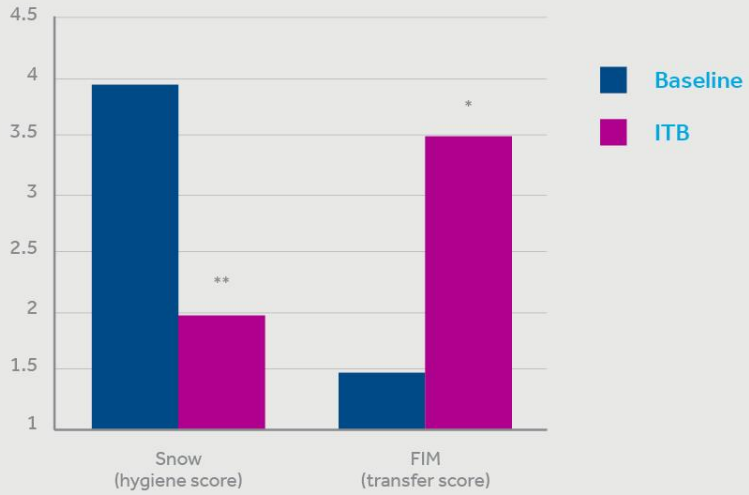
Change from baseline: * p<.05; ** p<.01

Medtronic
Further, Together

RAWICKI 1999

IMPROVEMENT IN PATIENT FUNCTION

In patients suffering from spasticity of cerebral origin (cerebral palsy, cerebrovascular disease, trauma brain injury) ITB improved hygiene score (Snow) and transfer score (FIM) after long-term treatment (from 12 months to 9 years)[10].



Change from baseline: * p<.05; ** p<.001

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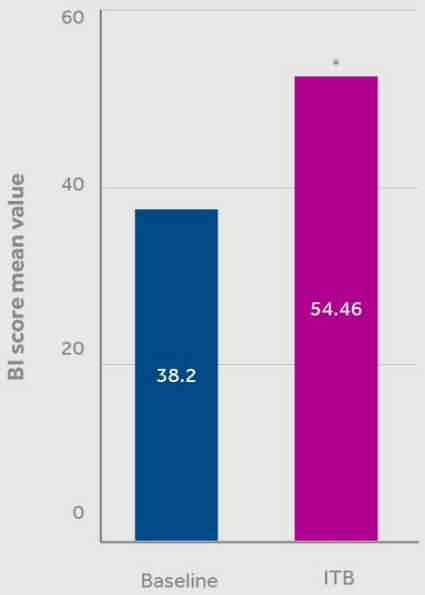
Further, Together

NATALE 2016

IMPROVEMENT IN PATIENT FUNCTION

In multiple sclerosis patients, the BI score varied significantly from pump implantation (baseline value) to last follow-up (74 months on average)[25].



Change from baseline: * p<.005

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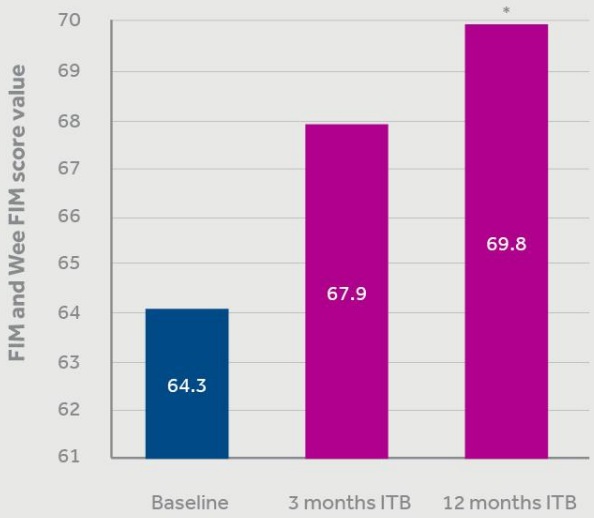
GUILLAUME 2005

IMPROVEMENT IN PATIENT FUNCTION

In patients with intractable spasticity of cerebral and spinal origin, the WeeFIM (used for patients ≤ 7 years of age) and the FIM (used for patients over 7 years of age) overall score increased significantly after 12 months of ITB treatment[8].



Change from baseline: * p<.001

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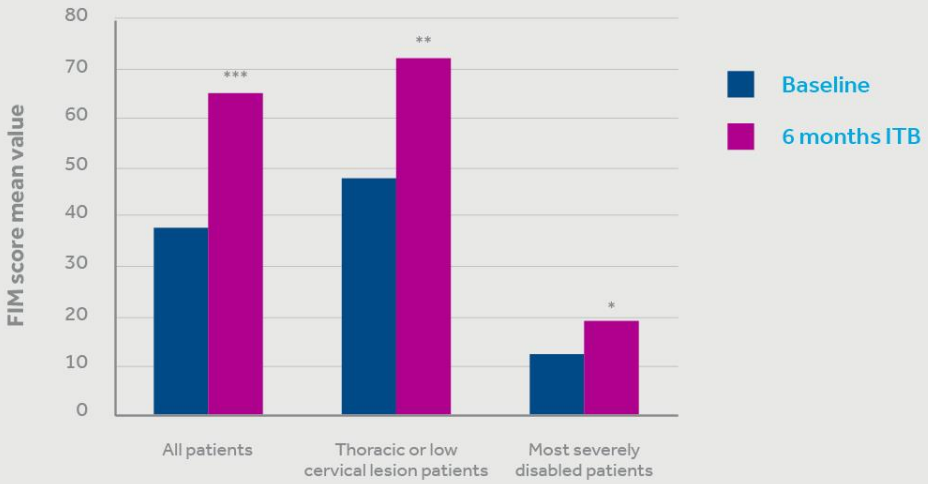
Further, Together

AZOUVI 1996

IMPROVEMENT IN PATIENT FUNCTION

In patients with severe and disabling spinal spasticity, ITB treatment improved FIM overall score after 6 months. Most dramatic improvements were observed in patients exhibiting a thoracic or low cervical lesion. Functional improvement for the most severely disabled patients, who were nearly totally dependent, was still significant[19].



Change from before ITB: * p <.05; ** p<.01; *** p<.001

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Further, Together

PATIENT BENEFIT

7 ITB STUDIES SHOW A SIGNIFICANT IMPROVEMENT IN PAIN

CLICK ON EACH AUTHOR NAME FOR MORE INFORMATION ON THE STUDY

	INDICATION	AUTHOR	OUTCOME MEASURE
CEREBRAL	Stroke	Creamer 2018	NPRS (0-10 scale, actual, least, worst pain)
	CP	Vles 2013	VAS (satisfaction for decrease in pain)
	CP	Ramstad 2010	Pain frequency during last 4 weeks, pain severity (0-4 scale)
SPINAL	MS	Lee 2018	NPRS (0-10 scale)
	MS	Sammaraiee 2018	VAS (0-10 scale)
	MS	Natale 2016	VAS (0-10 scale)
	MS	Middel 1997	VAS (0-10 scale)

CP: Cerebral Palsy
MS: Multiple Sclerosis
NPRS: Numerical Pain Rating Scale
VAS: Visual Analogue Scale

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Further, Together

CREAMER 2018

PATIENT BENEFIT REDUCING PAIN

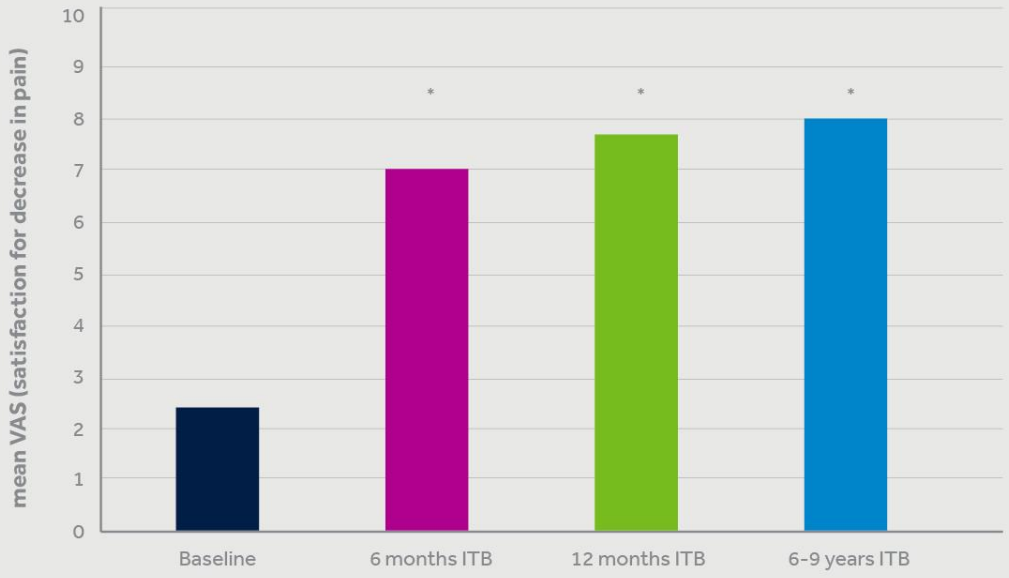
In stroke patients, after 6 months of ITB treatment, a significant improvement in NPRS for actual and least pain was observed compared to patients treated with conventional medical management (oral medication)[17].

Medtronic
Further, Together

VLES 2013

PATIENT BENEFIT REDUCING PAIN

Satisfaction for improvement in pain significantly increased after 6 months of ITB treatment and was stable over time in children with spastic cerebral palsy. Higher VAS score represents less pain[4].



Change from baseline *p<.01

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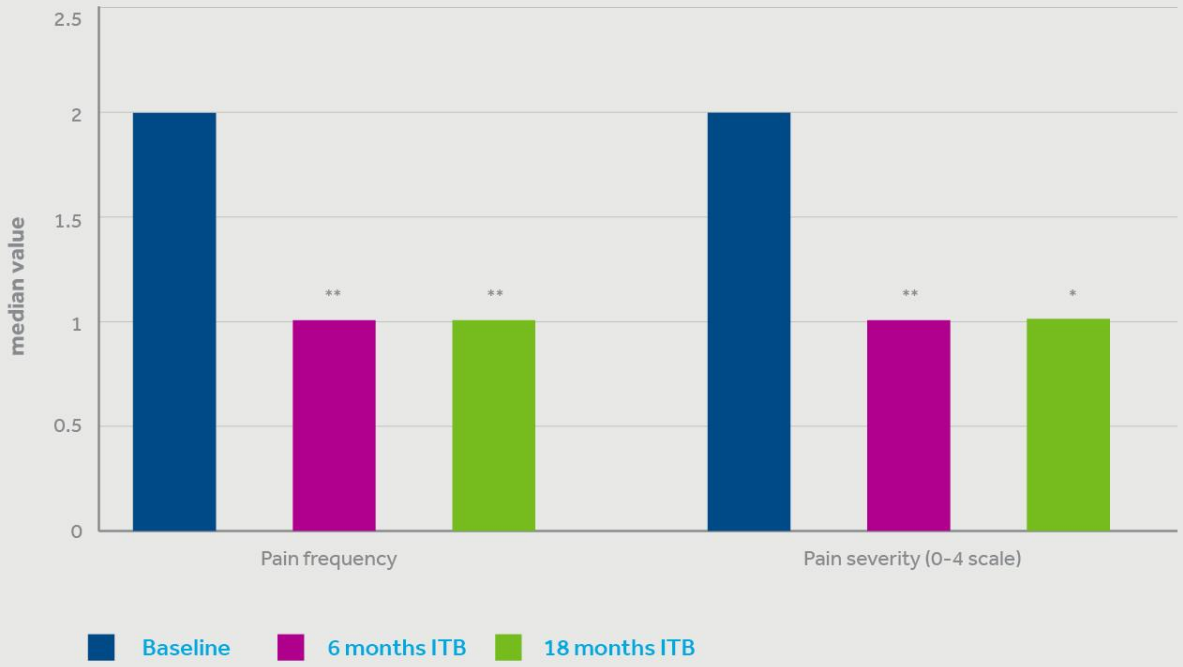
RAMSTAD 2010

PATIENT BENEFIT REDUCING PAIN

Pain frequency (during the last 4 weeks) and pain severity were statistically reduced after 6 and 18 months of ITB treatment in a pediatric population with cerebral palsy[2].



Change from baseline *p≤.05; **p≤.01

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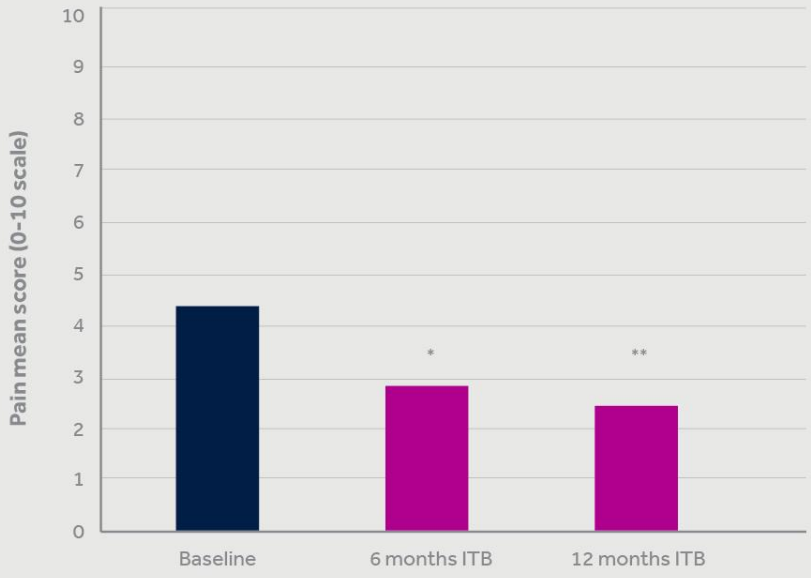
LEE 2018

PATIENT BENEFIT REDUCING PAIN

In ambulatory multiple sclerosis patients, pain score decreased significantly after 6 and 12 months of ITB treatment[26].



Change from baseline *p<.05, *p<.005

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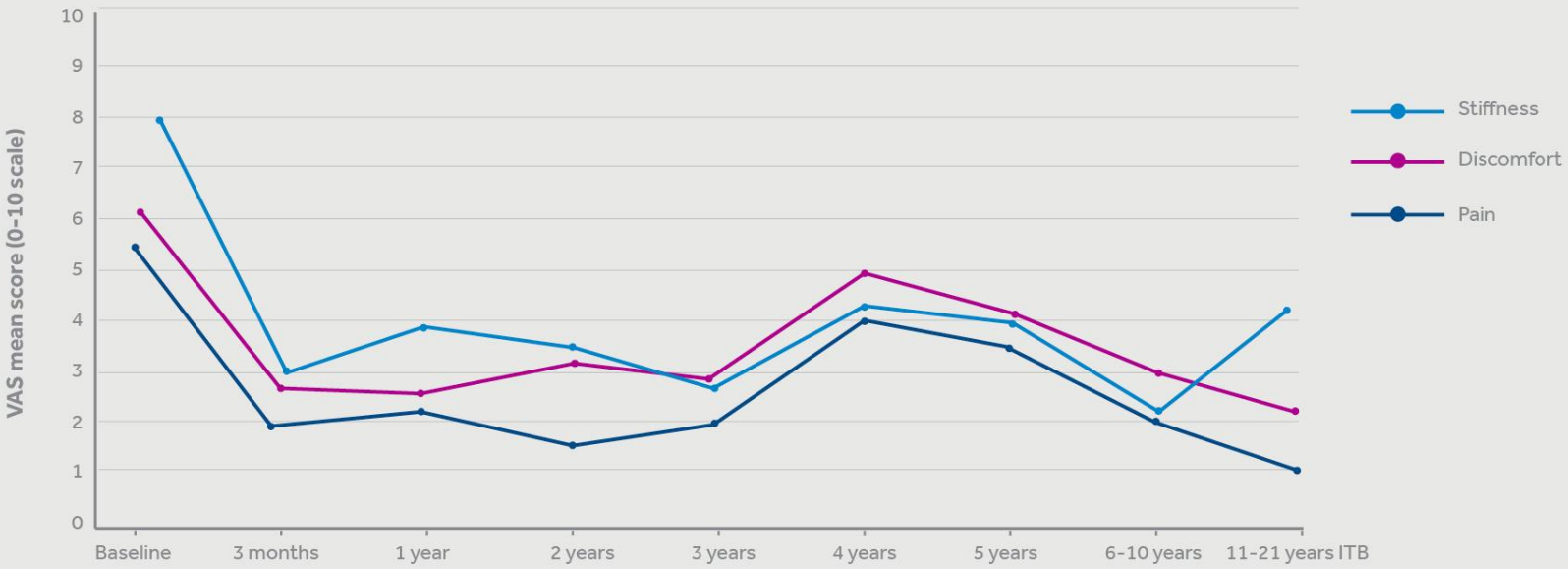
SAMMARAIEE 2018

PATIENT BENEFIT REDUCING PAIN

In multiple sclerosis patients, the VAS score for pain, stiffness and discomfort decreased significantly after ITB implant and efficacy was sustained over time[27].



Change from baseline were significant over time. Pain p<.005, Stiffness p<.0001, Discomfort p<.05

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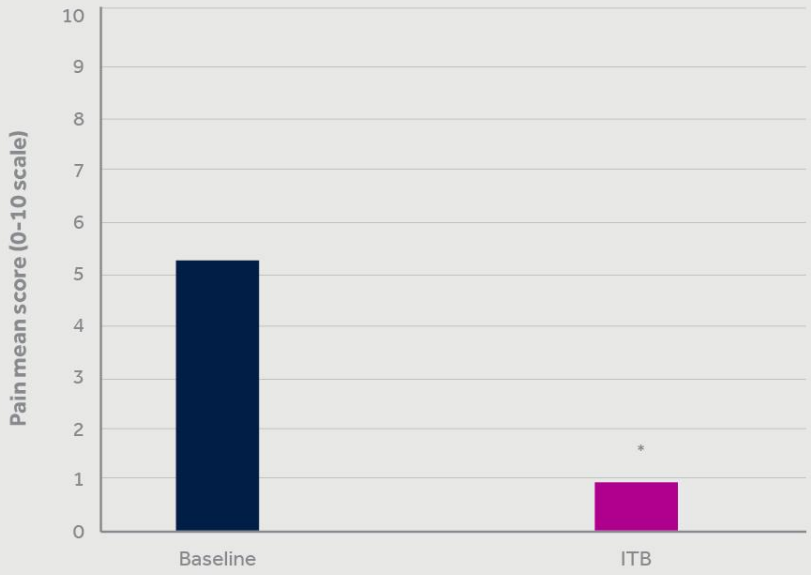
Further, Together

NATALE 2016

PATIENT BENEFIT REDUCING PAIN

In multiple sclerosis patients, the pain score significantly decreased from pump implantation (baseline value) to last follow-up (74 months on average)[25].



Change from baseline *p<0.005

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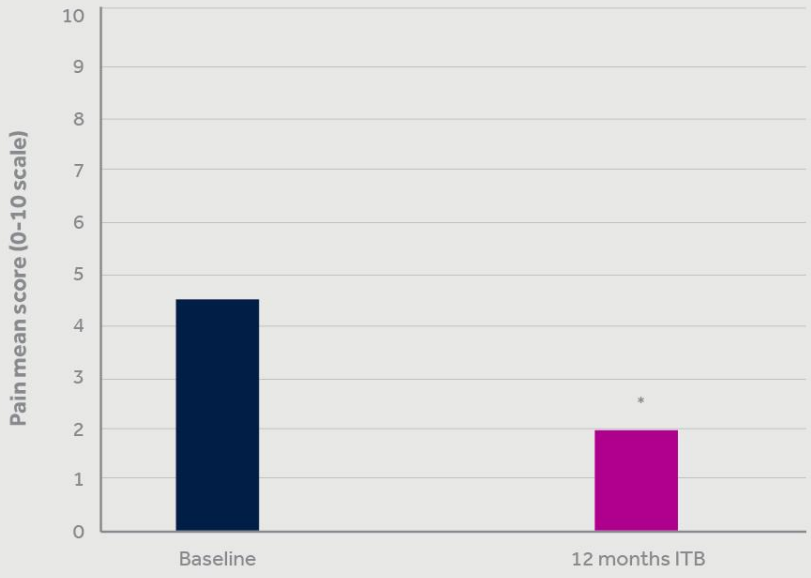
Further, Together

MIDDEL 1997

PATIENT BENEFIT REDUCING PAIN

In multiple sclerosis and spinal cord injured patients, pain score significantly improved after 12 months of ITB treatment[23].



Change from baseline *p<.01

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ECONOMIC VALUE

COST-EFFECTIVENESS OF ITB

INTRODUCTION OF ITB DEMONSTRATES COST-SAVINGS OVER TIME, POST IMPLANTATION

A few studies have shown reduction in hospitalization length of stay vs. conventional medical management (CMM)[1-3].

Lifetime analysis cost modeling indicates that ITB could afford cost savings of up to $8,009 USD/patient/year, compared with conventional therapy[4].

Cost savings from this analysis were derived primarily from reduced hospital admissions and physician visits[4].

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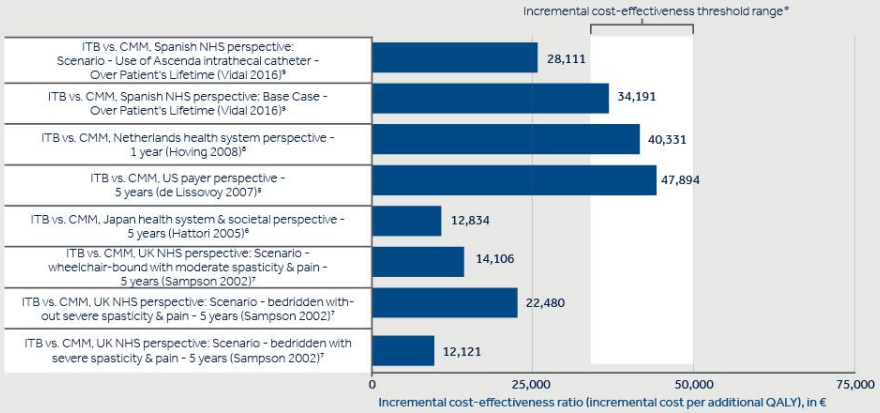
COST-EFFECTIVENESS

ITB IMPROVES PATIENT OUTCOMES WHILE MAINTAINING REASONABLE HEALTHCARE COSTS, IN THE LONG TERM.

To date, there are **5 published cost-effectiveness studies** from Europe, Japan and the U.S. which provide cost-effectiveness ratios (ICERs) for ITB vs. comparative treatments that, in most cases, are below, or close to, the willingness-to-pay (WTP) thresholds across different country systems[5-9].

These studies demonstrate that ITB provides incremental health benefits at an acceptable incremental cost vs. comparative treatments, when used to treat disabling spasticity in appropriately-selected patients, across time horizons of 1-5 years and patient's lifetime[5-9].



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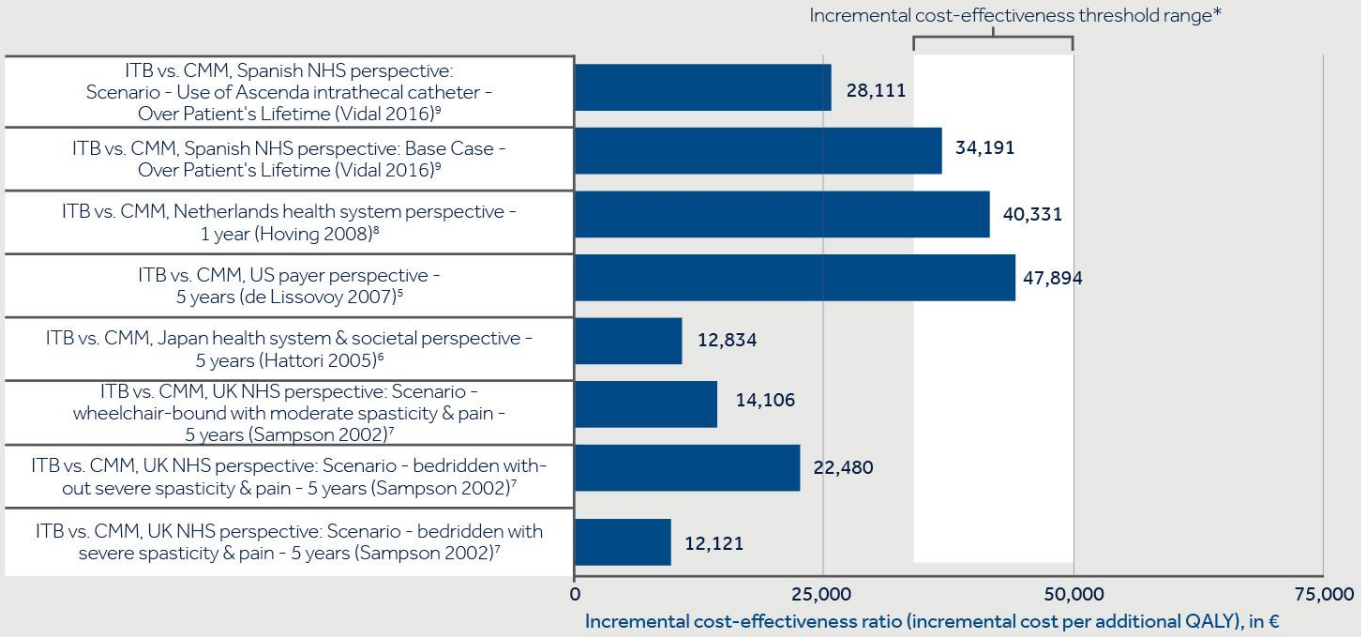
COST-EFFECTIVENESS OF ITB

Incremental cost-effectiveness ratios for ITB from cost-effective analyses with CMM as comparator

(Original values inflated to 2017 then currency converted to 2017 Euros)



*Range of incremental cost-effectiveness thresholds generally accepted in Europe. Only the UK provides published explicit ICER thresholds.[10]

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HEALTH TECHNOLOGY ASSESSMENT AND POLICY GUIDANCE

CANADA

HTA/GOVERNMENT BODY

Ontario Ministry of Health and Long-Term Care (Medical Advisory Secretariat) HTA, 2005: Intrathecal baclofen pump for spasticity[1].

RECOMMENDATIONS

Level 2 evidence supports effectiveness of ITB infusion for short-term reduction of severe spasticity in patients who are unresponsive/cannot tolerate oral baclofen.

Level 3 evidence supports effectiveness of ITB for long-term reduction of severe spasticity in patients who are unresponsive/cannot tolerate oral baclofen.

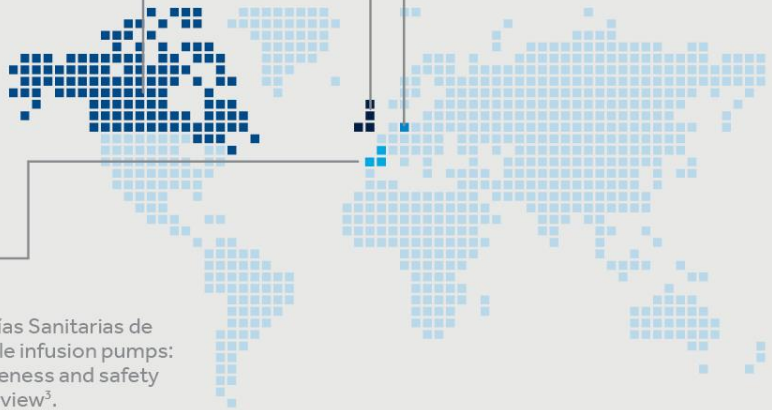
SPAIN

HTA/GOVERNMENT BODY

Agencia de Evaluación de Tecnologías Sanitarias de Andalucía (AESTA) (2000): Implantable infusion pumps: clinical uses and evidence of effectiveness and safety in pain and spasticity – systematic review[3].

RECOMMENDATIONS

ITB can be indicated for selected cases of severe spasticity of spinal origin.



UK

HTA/GOVERNMENT BODY

NHS Clinical Commissioning
Policy: Intrathecal baclofen (ITB)[2], April 2013

RECOMMENDATIONS

ITB for adults or paediatrics with chronic, severe, diffuse spasticity and/or dystonia of spinal or cerebral origin which renders them a full-time wheelchair user or bed-bound.

The policy supports the use of ITB for the groups for which it is the most cost-effective, where other options are exhausted, and where patient and carer evidence shows a real likelihood of success.

POLAND

HTA/GOVERNMENT BODY

Agency for Health Technology Assessment for provision of healthcare (2011)[4].

RECOMMENDATIONS

ITB for the treatment of spasticity refractory to pharmacological treatment.

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CLINICAL GUIDELINES FOR INTRATHECAL BACLOFEN

INDEPENDENT EUROPEAN GUIDELINES RECOMMEND ITB FOR DISABLING NON-FOCAL SPASTICITY

CLINICAL GUIDELINE & COUNTRY	SYMPTOMS/POPULATION	RECOMMENDATIONS FOR ITB
National Institute for Health & Care Excellence (NICE), United Kingdom. Cerebral palsy in adults. NICE Guideline 119 (2019)[5] Link: https://www.nice.org.uk/guidance/NG119	Cerebral palsy in adults	Consider referral to a tone/spasticity management service offering continuous pump-administered ITB if they still have difficulties with spasticity, despite enteral muscle relaxant drug treatment or botulinum toxin type A treatment.
Federatie Medisch Specialisten: Netherlands Society of Rehabilitation Medicine (NSRM), The Netherlands. Guideline for the treatment of cerebral and/or spinal spasticity in adults (2017)[6] Link: https://revalidatiegeneeskunde.nl/article/richtlijn-behandeling-van-cerebrale-enof-spinale-spasticiteit-bij-volwassenen-gepubliceerd	Spasticity in adults	ITB is efficient in decreasing spasticity compared to placebo in patients with cerebral and/or spinal spasticity with both observable impact on upper and lower extremities. Evidence Grade: High

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CLINICAL GUIDELINES FOR INTRATHECAL BACLOFEN

INDEPENDENT EUROPEAN GUIDELINES RECOMMEND ITB FOR DISABLING NON-FOCAL SPASTICITY

CLINICAL GUIDELINE & COUNTRY	SYMPTOMS/POPULATION	RECOMMENDATIONS FOR ITB
The Finnish Medical Society Duodecim, Finland national guidelines for stroke (2016)[7] Link: http://www.kaypahoito.fi/web/kh/suositukset/suositus;jsessionid=6958396585ECA8BA65BE630C1293EF0C?id=nix00624	Spasticity related to cerebrovascular disease; stroke	ITB is efficient in decreasing spasticity compared to placebo in patients with cerebral and/or spinal spasticity with both observable impact on upper and lower extremities. Evidence Grade: High
German Neurology Society (Deutsche Gesellschaft für Neurologie) S1 Guideline: Therapy of spastic syndromes (2012)[8] (currently under review) Link: https://www.dgn.org/leitlinien/2431-ll-89-2012-therapie-des-spastischen-syndroms	Spastic syndromes	In patients with severe, generalized spasticity, spastic tetra- or paraplegia that cannot be adequately treated with physiotherapy, oral antispastic medication, botulinum toxin type A, or ITB should be considered.
National Institute for Health & Care Excellence (NICE), United Kingdom. Spasticity in under 19s: management. Clinical Guideline 145 (2012)[9] (Last updated November 2016) Link: https://www.nice.org.uk/guidance/cg145	Spasticity in people aged 0-19 years old	Consider treatment with continuous pump-administered ITB if, despite the use of non-invasive treatments, spasticity is causing difficulties with pain, muscle spasms, posture, function or self-care (or ease of care by parents or carers).

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CLINICAL GUIDELINES FOR INTRATHECAL BACLOFEN

INDEPENDENT EUROPEAN GUIDELINES RECOMMEND ITB FOR DISABLING NON-FOCAL SPASTICITY

CLINICAL GUIDELINE & COUNTRY	SYMPTOMS/POPULATION	RECOMMENDATIONS FOR ITB
Socialstyrelsen, Sweden National guidelines for the treatment of multiple sclerosis (MS) and parkinson's disease: support for governance and management (2016)[10] Link: http://www.socialstyrelsen.se/nationellariktlinjermsochparkinsonssjukdom	Multiple sclerosis in adults	ITB pump therapy should be offered for the treatment of severe spasticity associated with MS in the upper or lower limbs (Priority 4*). *Scale of Priority 1-10, where Priority 1 should receive the greatest share of resource allocation, and Priority 10 the least.
British Pain Society, United Kingdom. Intrathecal drug delivery for the management of pain and spasticity in adults; recommendations for best clinical practice (2015)[11] Link: https://www.britishpainsociety.org/static/uploads/resources/files/itdd_2015_pro_v3.pdf	Pain and spasticity in adults	The working group believes* that ITB is well-established in the management of both cerebral and spinal spasticity and is a cost-effective method of baclofen delivery for spasticity. *These recommendations are primarily evidence-based but where necessary comprise the consensus opinion of the working groups.

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GLOSSARY

Acquired Brain Injury (ABI) or Brain Injury (BI): Brain injury is an inclusive term for damage to the brain that occurs after birth and is not related to a hereditary, congenital, or degenerative disease. Traumatic brain injury, hypoxic and anoxic brain injury, and stroke are forms of acquired brain injuries.

Ashworth Scale / Modified Ashworth Scale: The Ashworth Scale tests resistance to passive movement around a joint with varying degrees of velocity. Scores range from 0-4, with 0 indicating no resistance and 4 indicating rigidity. The Modified Ashworth Scale is similar, but adds a +1 score used to indicate resistance throughout less than half of the range of movement.

Baclofen: Drug that inhibits the release of excitatory neurotransmitters, inhibiting spastic response to stretch reflex.

Barthel Index (BI): The Barthel Index is an ordinal scale used to measure the ability of an individual with a neuromuscular or musculoskeletal disorder to care for him/herself and perform activities of daily living. It assesses 10 activities of daily living and mobility activities rated by the amount of assistance required to complete: feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, chair transfer, ambulation, and stair climbing.
See also: Functional Independence Measure.

Bolus: Discrete amount of medication, drug or other compound in order to raise its concentration in blood to an effective level.

Case series: Coherent and consecutive set of cases of a disease (or similar problem) which derive from the practice of one or more health care professionals or health care setting. The cases were defined by similar diagnoses/disease state or having undergone the same intervention/procedure.

Central nervous system (CNS): The central nervous system is the part of the nervous system consisting of the brain and spinal cord.

Cerebral palsy (CP): Cerebral palsy is a non-progressive neurological disorder due to brain injury or malformation early in life. It is a group of permanent early childhood movement disorders. Motor symptoms may include spasticity.

Cerebrospinal fluid (CSF): The cerebrospinal fluid is a clear, colorless body fluid found in the brain and spine. It occupies the subarachnoid space (between the arachnoid mater and the pia mater) and the ventricular system around and inside the brain and spinal cord.

Child Health Questionnaire ™ Parent Form (CHQ-PF50): The CHQ-PF50 is a standardized quality of life questionnaire designed for children of 5-18 years of age. It measures 14 individual health concepts and can be aggregated into 2 summary component scores for physical functioning and psychosocial health on a 0-100 scale.

Controlled study: A study with 2 or more groups, with different intervention/exposure, and outcomes were measured in all groups and compared between groups.

Conventional Medical Management (CMM): A nonsurgical spasticity treatment protocol that may include physical and occupational therapy, orthotics, mobility aids, oral medications, and chemodenervation. CMM does not include ITB therapy, neurosurgery, or orthopedic surgery.

Cost-effectiveness Analysis (CEA): A form of economic analysis used to support decision making about a treatment choice versus an alternative. CEA compares the relative costs and outcomes (effects) of two courses of action, and its results are expressed as a ratio (ICER).

EuroQol-5D (EQ-5D): The EQ-5D is a non-disease-specific patient self-assessment questionnaire that measures health-related quality of life.

Functional Independence Measure (FIM): The FIM is an 18-item tool used in an inpatient rehabilitation setting to measure the severity of disability and need for assistance in carrying out activities of daily living. Tasks are rated on a 7-point ordinal scale from total assistance/complete dependence to complete independence. A higher score indicates higher level of function. The FIM's 18 items are categorized into 6 motor and cognitive subscales.

Gross Motor Function Measure (GMFM): The GMFM is a standardized clinical tool that evaluates change over time in five dimensions of motor function ability in children aged 5 months to 16 years with CP: lying and rolling, sitting, crawling and kneeling, standing and walking, and running and jumping. It uses a 4-point score for each item, summed to calculate raw and percent scores for each dimension and overall score.

Hopckins Symptoms Checklist (HSCL): The HSCL is a self-report symptom inventory which measures symptoms of anxiety and depression. It is comprised of 58 items which are representative of the symptom configurations commonly observed among outpatients. It is scored on five underlying symptom dimensions—sommatization, obsessive-compulsive, interpersonal sensitivity, anxiety and depression—which have been identified in repeated factor analyses.

Incremental cost-effectiveness ratio (ICER): The key result of a CEA, expressed as the additional cost per QALY gained. The incremental cost per QALY is interpreted as the additional cost for 1 additional year of life in full health.

Intrathecal (subarachnoid) space: The space containing cerebrospinal fluid (CSF) between the arachnoid mater and pia mater of the spinal cord.

Intrathecal baclofen (ITB): Delivery of baclofen directly into the intrathecal space by lumbar puncture or an indwelling intrathecal catheter connected to a drug delivery pump.

Lumbar Puncture: Procedure in which a needle is inserted into the spinal canal.

Multiple sclerosis (MS): Multiple sclerosis is an immune-mediated progressive disease that destroys the myelin membrane of nerves in the brain and spinal cord. Demyelination impedes neuronal communication, which may result in motor symptoms including spasticity.

Patient Health Questionnaire (PHQ-9): The PHQ-9 is a multipurpose instrument for screening, diagnosing, monitoring and measuring the severity of depression.

Pediatric Evaluation of Disability Inventory (PEDI): The PEDI is an assessment tool for children that measures capability and performance of functional activities in 3 content areas: self-care, mobility, and social function. Scores range from 0-100, with higher scores indicating lesser disability.

Peristaltic Pump: Mechanical pump in which pressure is provided by the movement of a constriction along a tube, similar to biological peristalsis.

GLOSSARY

Pharmacology: Branch of medicine concerned with the uses, effects, and modes of action of drugs.

Prevalence: Percentage of a population that is affected with a particular disease at a given time.

Prospective study: The subjects were enrolled in the study after the study had been designed and approved, and the subjects were followed for some period of time.

Quality Adjusted Life Year (QALY): A QALY is a generic measure of effectiveness that encompasses both quality and quantity of life (i.e., survival), providing a consistent and common measure that healthcare funders can use to inform funding decisions.

Randomized Controlled Trial (RCT): An experimental comparative study in which participants are randomly assigned to intervention or control and followed over time to measure differences in outcomes. Concealment of the allocation of the randomized assignment is important. Known and unknown prognostic factors (confounders) should be evenly distributed between the groups.

Retrospective study: The study started after the data/information had been collected.

Rivermead Mobility Index (RMI): 15 items questionnaire for quantifying functional abilities such as gait, balance, and transfers after stroke.

Self Rating Depression Scale (SDS): The Self-Rating Depression Scale is a 20-item self-report questionnaire that is widely used as a screening tool, covering affective, psychological and somatic symptoms associated with depression. Each item is scored on a Likert scale ranging from 1 to 4. A total score is derived by summing the individual item scores, and ranges from 20 to 80. Most people with depression score between 50 and 69, while a score of 70 and above indicates severe depression.

Short Form Survey (SF-36 and SF-12): 36 or 12-question measure of health perception in eight dimensions: physical functioning, role limitation because of physical health, social functioning, vitality or energy, bodily pain, mental health, role limitation because of emotional problems, and general health. Provides Physical Component Scores (PCS) and Mental Component Scores (MCS-36) ranging from 0-100, with higher scores representing better self-reported health.

Sickness Impact Profile (SIP): The SIP is a yes/no patient self-assessment that measures psychosocial and physical quality of life in 12 categories (sleep and rest, eating, work, home management, recreation and pastimes, social interaction, alertness behavior, emotional behavior, communication, ambulation, mobility, and body care and movement). A lower score indicates improvement. It is designed to objectively assess outcomes from health care services. There are 2 versions of the SIP; one with 136 items and one with 68 items.

Snow Hygiene Score: A measurement of ability to clean and self-catheterize first described by Snow et al (1990) within a case series of 9 MS patients receiving botulinum toxin for spasticity. This score was used by Rawicki (1999) to measure hygiene in 18 patients with cerebral origin spasticity receiving ITB therapy.

Spasm: Sudden involuntary muscular contraction or convulsive movement.

Spasticity: Spasticity is an abnormal increase in muscle tone caused by injury of upper motor neuron pathways regulating muscles. Spasticity may be a result of multiple sclerosis, cerebral palsy, stroke, brain injury, or spinal cord injury.

Spinal Cord Injury (SCI): Injury to the spinal cord resulting in a change, either temporary or permanent, in the cord's normal motor, sensory, or autonomic function. SCI symptoms vary widely, and can include pain, paralysis, or spastic hypertonia.

Stretch Reflex: Muscle contraction in response to stretching within the muscle. It is a monosynaptic reflex which provides automatic regulation of skeletal muscle length.

Stroke: Also known as cerebrovascular accident (CVA), or cerebrovascular insult (CVI). Types of stroke include ischemic, resulting from impeded blood flow to a region of the brain, and hemorrhagic, due to bleeding in the brain. Symptoms of stroke may include an inability to move or feel on one side of the body, difficulty understanding or speaking, and spastic hypertonia in the long term.

Stroke-Specific Quality of Life scale (SS-QOL): Patient-centered outcome measure assesses health-related quality of life (HRQOL), specific to patients with stroke.

Traumatic Brain Injury (TBI): Traumatic brain injury, a form of acquired brain injury (ABI), is damage to the brain caused by an external mechanical force, such as a motor vehicle accident, explosive blast injury, or penetrating injury.

Upper Extremity Manual Activity Log (UEMAL): Structured interview intended to examine how much and how well the subject use of their affected arms. Participants are asked standardized questions about the amount of use of their more-affected arm and the quality of their movemen during the functional activities indicated uses their more-affected arm.

Upper Motor Neuron Lesion: An upper motor neuron lesion (also known as pyramidal insufficiency) is a lesion of the neural pathway above the anterior horn cell of the spinal cord or motor nuclei of the cranial nerves. This is in contrast to a lower motor neuron lesion, which affects nerve fibers traveling from the anterior horn of the spinal cord or the cranial motor nuclei to the relevant muscle(s).

Upper Motor Neuron Syndrome (UMNS): Upper motor neuron syndrome (UMNS) is the motor control changes that can occur in skeletal muscle after an upper motor neuron lesion.

WeeFIM: The WeeFIM or Pediatric Functional Independence Measure is a validated pediatric outcomes tool that measures disability in children with developmental disorders. It measures how much assistance a child needs to perform activities of daily living. It can be used to track functional improvement and goal attainment.

Willingness-To-Pay Threshold: Willingness-to-pay threshold is a threshold above which treatments are no longer considered cost-effective. An ICER is meaningful with respect to this threshold, which is approximately £20,000-£30,000 in the United Kingdom (Shiroiwa 2010, Health Economics 19(4):422-37). The probability of payers not paying for a therapy increases significantly with increases in the ICER. (Shiroiwa T, Sung YK, Fukuda T et al. International survey on willingness-to-pay (WTP) for one additional QALY gained: What is the threshold of cost effectiveness? Health Econ. 2010;19(4):422-437).

Brief Statement

See the device manual for detailed information regarding the instructions for use, the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events. For further information please contact your local Medtronic representative and/or consult the Medtronic website at www.medtronic.com.

www.medtronic.com/manuals

Consult instructions for use on this website. Manuals can be viewed using a current version of major internet browser. For best results, use Adobe Acrobat® Reader in the browser.

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