Medtronic

InterStim® Therapy

FOR BOWEL CONTROL

Offer a minimally invasive option that can restore function

Do your fecal incontinent patients express frustration that medication, diet modification, and exercise are failing to provide substantial results? Offer your patients a minimally invasive option that can restore function with Medtronic's InterStim® Therapy for Bowel Control.

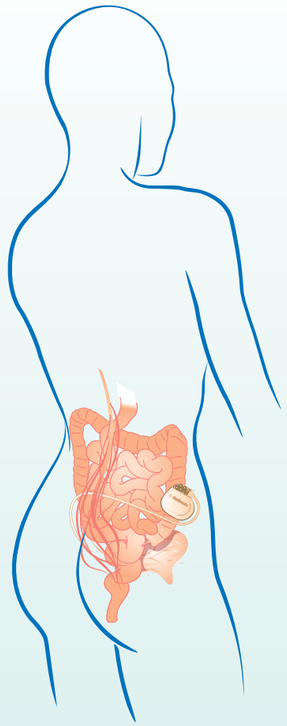
Clinical studies show 83% of patients achieve a ≥50% reduction in fecal incontinent episodes per week,[1,2*] and as many as 47% achieve complete continence at 12 months post implant.[3]

Research is clear. InterStim Therapy for Bowel Control is effective, safe, and may offer your patients improved quality of life.

What Is InterStim Therapy?

The implantable InterStim system uses mild electrical stimulation of the sacral nerves to influence the behavior of the anal sphincters, pelvic floor muscles, and bowel.

Following a test stimulation that identifies patients whose fecal incontinence may be improved by sacral nerve stimulation, the InterStim device is typically implanted in the upper buttock. A wireless programmer is then used to activate and set up the neurostimulator operation. If the implant is not successful or well-tolerated, it can be turned off or surgically removed.



* 83% in per-protocol analysis (n=106) and 73% in intent-to-treat analysis (n=120) for incontinent episodes per week.

Per-protocol analysis (also referred to as completers analysis): Conducted with patients who had complete data at baseline and annual follow-up visits.

Intent-to-treat analysis (also referred to as modified worst case analysis): Assumed no improvement for patients who were missing bowel diaries (tool used to measure symptom improvement from baseline) at follow-up visits, unless a subsequent bowel diary was available.

Research is clear.

InterStim Therapy for Bowel Control is effective, safe, and may offer your patients improved quality of life.

PROOF POSITIVE

Clinical Studies Offer Proof Positive

Clinical studies offer proof positive that InterStim Therapy effectively helps patients gain control of their fecal incontinence symptoms.

Proven Symptom Decline

The InterStim Therapy for Bowel Control Prospective Clinical Study demonstrates a statistically significant decline in patient fecal incontinence 12 months post implant:[1,2]

- 83% of patients achieve ≥50% reduction in incontinent episodes per week.*
- 83% of patients achieve ≥50% reduction in incontinent days per week.*
- 80% of patients achieve ≥50% reduction in urge incontinent episodes per week.**

83%
of patients achieve
≥50% reduction in incontinent episodes per week*

This study uses two statistical analyses. Results are similar, demonstrating a statistically significant and clinically relevant reduction in fecal incontinence severity for subjects implanted with the InterStim system ($p<0.0001$).

More Effective Than Optimal Medical Therapy

A randomized control trial by Tjandra et al. demonstrates that InterStim Therapy at 12 months post implant (n=53) is more effective than supervised optimal medical therapy consisting of bulking agents, pelvic floor exercises, and dietary management. Fecal continence was greatly improved with sacral nerve stimulation immediately after implantation and was sustained during the follow-up period.[3]

InterStim Therapy Results

No InterStim Therapy patients show worsening of fecal incontinence symptoms.

- 47% of patients achieve complete continence.
- 66% of patients achieve 75% – 100% improvement in incontinent days per week.

Optimal Treatment Results

In the supervised optimal medical therapy group, there are no significant improvements in fecal incontinence symptoms, Wexner scores, FIQOL Index, and SF-12 scores.

47%
of patients achieve
complete continence

* 83% in per-protocol analysis (n=106) and 73% for intent-to-treat analysis (n=120) for both incontinent episodes and days per week ($p<0.0001$).

** 80% in per-protocol analysis (n=106) and 71% for intent-to-treat analysis (n=120) for urge incontinent episodes per week ($p<0.0001$).

Benefits for Patients with External Anal Sphincter Defects

A study by Chan et al. assesses the effectiveness of InterStim Therapy for Bowel Control in patients with external anal sphincter defects.[4] All patients—with and without defects—show notable improvements in fecal continence and quality of life following implant and through 12 months:

- Weekly incontinent episodes decrease 64% for patients with a sphincter defect (n=21).
- Weekly incontinent episodes decrease 70% for patients with intact sphincters (n=32).

Improvements in functional outcomes are similar in both groups, with no difference in clinical benefit among patients with some sphincter defects.†

Chan's study finds no septic complications requiring explantation. Adverse events include seroma, which resolved after percutaneous aspiration; mild pain at the implant site, which resolved with analgesics; and excessive tingling in the vaginal region, which subsided after device reprogramming.

Clinical benefit
for patients with some sphincter defects

Safety and Risk Information

InterStim Therapy is proven safe.[1,2] The safety profile for InterStim Therapy for Bowel Control is similar to InterStim Therapy for Urinary Control, which was originally approved by the US Food and Drug Administration in 1997.

The InterStim Therapy for Bowel Control Prospective Clinical Study shows no unanticipated adverse device effects, no patient deaths related to the neurostimulator or therapy, and no surgical injuries during the test or implant procedures.[1,2]

Most adverse events are successfully treated with medication or device reprogramming. The most common adverse events (≥5% of patients, n=120) are implant site pain, paraesthesia, implant site infection, change in sensation of stimulation, urinary incontinence, and diarrhea. The probability of the patient having surgical revision (including device replacement) within the first year is about 10%.[2]

†Safety and effectiveness have not been established in patients with sphincter defects of greater than 60°.

QUALITY OF LIFE

Significant Improvement in Patient Quality of Life

With InterStim Therapy, patients discover new freedom from the embarrassing and socially isolating symptoms of fecal incontinence. Study data demonstrate significant improvement in patient quality of life, including physical and psychological well-being, as determined by a variety of accepted measures.

FIQOL Index–InterStim Prospective Clinical Study

The InterStim Therapy for Bowel Control Prospective Clinical Study shows significant improvement at 12 months in all four scales of the Fecal Incontinence Quality of Life (FIQOL) Index.[2,5†] The results are very similar for the per-protocol analysis and intent-to-treat analysis (see tables below), demonstrating a statistically significant and clinically relevant improvement in FIQOL scores for subjects implanted with the InterStim system (p<0.0001).

Change in FIQOL (Per-Protocol Analysis)[5]

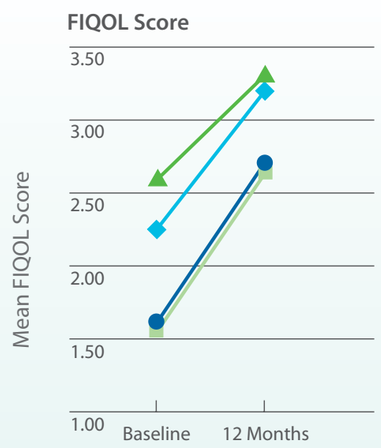
	Baseline n=106	12 Months n=106	Percent Improvement
Depression	2.56	3.54	38%
Lifestyle	2.31	3.35	45%
Embarrassment	1.60	2.80	75%
Coping/behavior	1.48	2.76	86%

(p<0.0001)

Change in FIQOL (Intent-to-Treat Analysis)[2]

	Baseline n=120	12 Months n=120	Percent Improvement
Depression	2.55	3.41	34%
Lifestyle	2.32	3.24	40%
Embarrassment	1.62	2.67	65%
Coping/behavior	1.52	2.64	74%

(p<0.0001)



Change in FIQOL as assessed by the intent-to-treat analysis from baseline (n=120)

† The FIQOL Index is composed of 29 questions that form four scales. Each scale is the average score of all items in the scale and ranges from 1 to 4 (lifestyle, coping/behavior, and embarrassment) or 1 to 5 (depression/self-perception). A lower score indicates a lower functional status or quality of life.

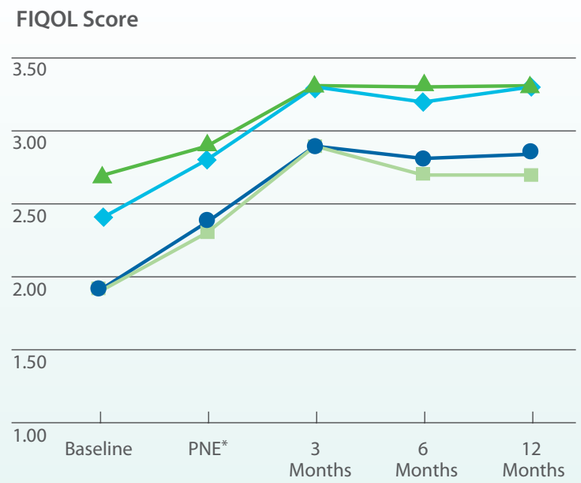
FIQOL Index—Randomized Control Study

InterStim Therapy vs. Optimal Medical Therapy

In the Tjandra study, InterStim Therapy implant patients show immediate and sustained improvement post implant for FIQOL Index scores (n=53, p<0.0001).[3] InterStim Therapy significantly improves all domains of the FIQOL Index (see table below), whereas optimal medical therapy (n=60) shows no effect at 12 months.

Adverse events with InterStim Therapy in this study include implant site pain, especially in slimmer patients; seroma, resolved after percutaneous aspiration; and excessive tingling in the vaginal region.[3]

Change in FIQOL in the Sacral Nerve Stimulation Group



Change in FIQOL from baseline for InterStim Therapy patients in the Tjandra Study (n=53, p<0.0001 except PNE—see below)

Immediate and sustained improvement

post implant for all FIQOL Index scores

*PNE: Peripheral Nerve Evaluation, a temporary test stimulation used to determine the probable effectiveness of the InterStim implant.

QUALITY OF LIFE

Quality Scales

A study by Hetzer et al. demonstrates significant improvement across all QOL scores. InterStim Therapy significantly improves median Wexner scores at 6 months (69%, p<0.001). Patients show a reduction of incontinence symptoms—thus dramatically enhancing QOL, including social lives.[6]

In addition, InterStim Therapy significantly improves generic and incontinence-specific QOL at 6-month follow-up:[6]

SF-36 QOL Questionnaire: Scores improve in all eight categories and significantly improve for physical functioning, social function, mental health, and vitality (p<0.05).

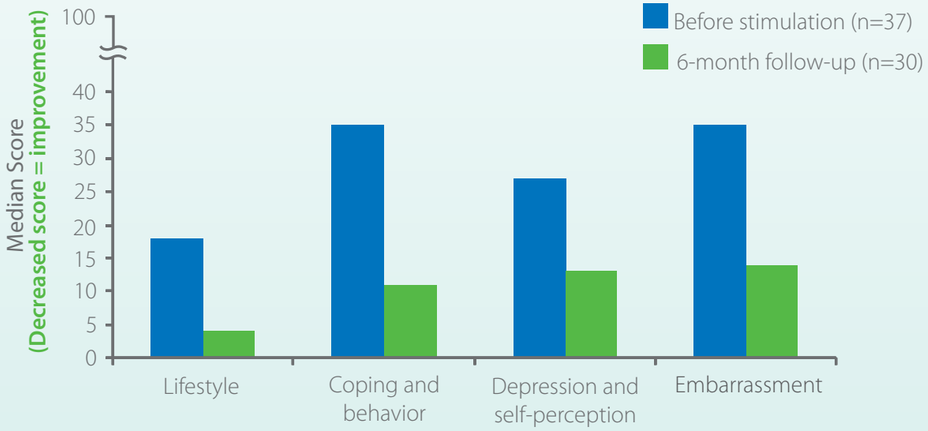
Gastrointestinal QOL Index Score: Median preoperative score improves from a preoperative score of 96 to a postoperative score of 107 (0-144 rated, p=0.02).

Bowel-Specific Royal London Hospital QOL Questionnaire: All median subscores of this bowel-specific questionnaire improve (lifestyle, coping and behavior, depression and self-perception, and embarrassment). See table below.

Adverse events in the Hetzer study include infection, seroma and loss of effect. Eight patients (22% or 8 out of 37 implanted patients) experienced complications that required surgical intervention. (A successful restimulation was possible for 5 of these patients.) Adverse effects of SNS were remedied in 5 patients by reprogramming the stimulator.

Change in QOL, Royal London Hospital Questionnaire

InterStim Therapy improves all subscores of the Bowel-Specific Royal London Hospital QOL Questionnaire at 6-month follow-up (p<0.05).[6] Score range 0-100.



Additional Quality Measures

The InterStim Therapy for Bowel Control Prospective Clinical Study shows patients' average perception of their own bowel health increases 106% from baseline to a more favorable state at 12 months post implant. Where zero indicates the worst imaginable state and 10 indicates the best imaginable state, self-rated bowel health scores improve from 3.53 at baseline to 7.28 at 12-month follow-up (n=106, p<0.0001).[5]

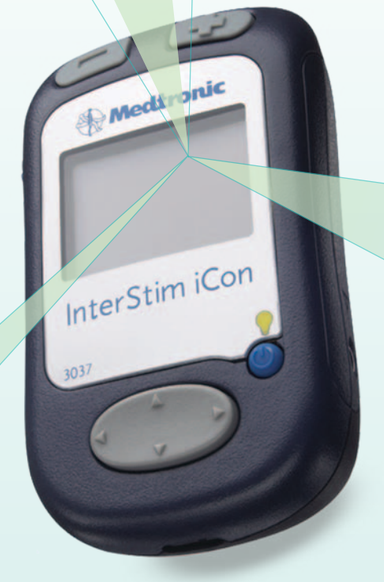
Use of undergarment protection all of the time decreases from 64% of patients at baseline to 37% of patients at 12 months post implant.[1,5] In addition, the percentage of patients reporting no use of undergarment protection improves, going from 3% at baseline to 31% at the 12-month visit.[5]

106%

increase in self-rated bowel health at 12 months

31%

of patients report no use of undergarment protection at the 12-month visit, compared with 3% at baseline



A Confident Choice for Your Indicated Patients

InterStim Therapy is the only bowel control treatment option available that has a test to determine probable success prior to surgery. Following a successful test, the surgical procedure is minimally invasive and does not alter anal/sphincter anatomy. In instances when the implant is not successful or well-tolerated, the device can be turned off or surgically removed.

Test Stimulation for Patient Selection

The test stimulation identifies patients whose fecal incontinence may be improved by sacral nerve stimulation.

In clinical studies,[1-3] up to 90% of patients who participated in test stimulation had a positive response and went on to receive the device implant. The studies defined a positive response as symptom reduction of at least 50%. The most common adverse events during the test stimulation phase (n=132) included implant site pain, lead fracture, hematoma, lead migration/ dislodgement, pain in extremity, and skin irritation.[2]

90%

of test patients
have a positive response

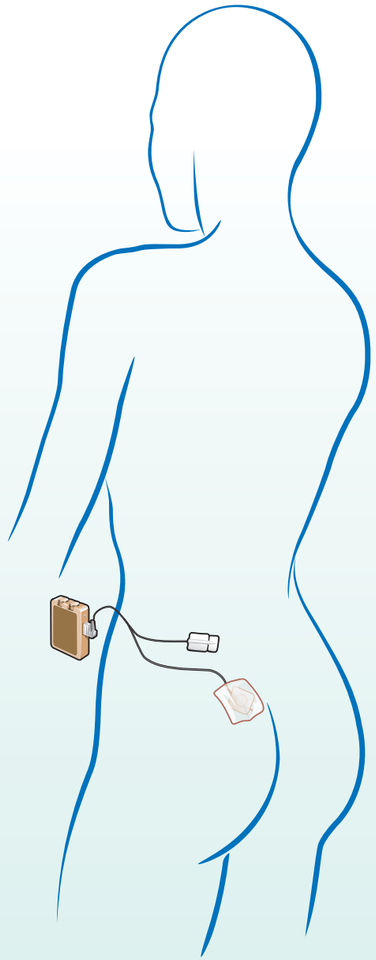


Illustration shows temporary lead test, known as Peripheral Nerve Evaluation.

Test Stimulation Options

Two test stimulation techniques exist for InterStim Therapy. One uses a temporary test stimulation lead, and the other option uses a tined implant lead. In both tests, stimulation is delivered via connection to a portable stimulator that the patient wears for several days during the test period. Patients complete a bowel diary prior to the test period to establish a baseline measure of incontinence and during the test period to measure improvement.

Temporary Lead Test

One test option, sometimes called Peripheral Nerve Evaluation, uses a temporary lead that is removed after the test stimulation. The lead is typically implanted in-office using a local anesthetic. The test stimulation can be conducted up to 7 days. If this test is inconclusive or unsuccessful, then the chronic lead test is recommended.

Chronic Lead Test

This test is also referred to as the staged approach because the components are implanted in two stages. In the first stage, a tined (chronic) lead is implanted and used for the test stimulation. With conclusive test results, the neurostimulator and lead extension are implanted (stage 2). The chronic lead implant is an outpatient procedure using monitored anesthesia care (MAC) or general anesthesia. The test stimulation can be conducted up to 14 days.

Also Effective for Urinary Control

InterStim Therapy is also indicated for the treatment of urinary retention and symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency-frequency alone or in combination. It is indicated for patients who have failed or could not tolerate more conservative treatments.

In a clinical study of InterStim Therapy for Urinary Control, patients demonstrated significant improvements in symptom reduction and quality of life.[7,8]

More than 85,000 patients worldwide

have received InterStim Therapy for Urinary Control and Bowel Control;

FDA approved for urinary control in 1997 and bowel control in 2011

For more information about InterStim Therapy, visit professional.medtronic.com/sns or call 1-800-328-0810.

References

1. Wexner SD, Coller JA, Devroede G, Hull T, McCallum R, Chan M, Ayscue JM, Shobeiri AS, Margolin D, England M, Kaufman H, Snape WJ, Mutlu E, Chua H, Pettit P, Nagle D, Madoff RD, Lerew DR, Mellgren A. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. *Ann Surg*. 2010 Mar; 251(3):441-449.
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8. Siegel SW, Catanzaro F, Dijkema HE, et al. Long-term results of a multicenter study on sacral nerve stimulation for treatment of urinary urge incontinence, urgency-frequency, and retention. *Urology.* 2000;56 (suppl 6A):87-91.

Important Safety Information:

Indications for Use:

InterStim® Therapy for Urinary Control is indicated for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency-frequency alone or in combination, in patients who have failed or could not tolerate more conservative treatments.

The following Warning applies only to InterStim Therapy for Urinary Control:

> **Warning:** This therapy is not intended for patients with mechanical obstruction such as benign prostatic hypertrophy, cancer, or urethral stricture.

InterStim® Therapy for Bowel Control is indicated for the treatment of chronic fecal incontinence in patients who have failed or are not candidates for more conservative treatments.

Contraindications for Urinary Control and for Bowel Control: Diathermy. Patients who have not demonstrated an appropriate response to test stimulation or are unable to operate the neurostimulator.

Precautions/Adverse Events:

For Urinary Control: Safety and effectiveness have not been established for bilateral stimulation; pregnancy, unborn fetus, and delivery; pediatric use under the age of 16; or for patients with neurological disease origins such as multiple sclerosis.

For Bowel Control: Safety and effectiveness have not been established for bilateral stimulation; pregnancy, unborn fetus, and delivery; pediatric use under the age of 18; or for patients with progressive, systemic neurological diseases.

For Urinary Control and for Bowel Control: The system may be affected by or adversely affect cardiac devices, electrocautery, defibrillators, ultrasonic equipment, radiation therapy, MRI, theft detectors/ screening devices. Adverse events include pain at the implant sites, new pain, lead migration, infection, technical or device problems, adverse change in bowel or voiding function, and undesirable stimulation or sensations, including jolting or shock sensations. For full prescribing information, please call Medtronic at 1-800-328-0810 and/or consult Medtronic's website at www.medtronic.com. Product technical manual must be reviewed prior to use for detailed disclosure.

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