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Efficacy of sacral nerve modulation evaluated with *International Consultation on Incontinence Questionnaire-Bowels*

A prospective case series assessing efficacy one month after implantation of a sacral nerve modulator

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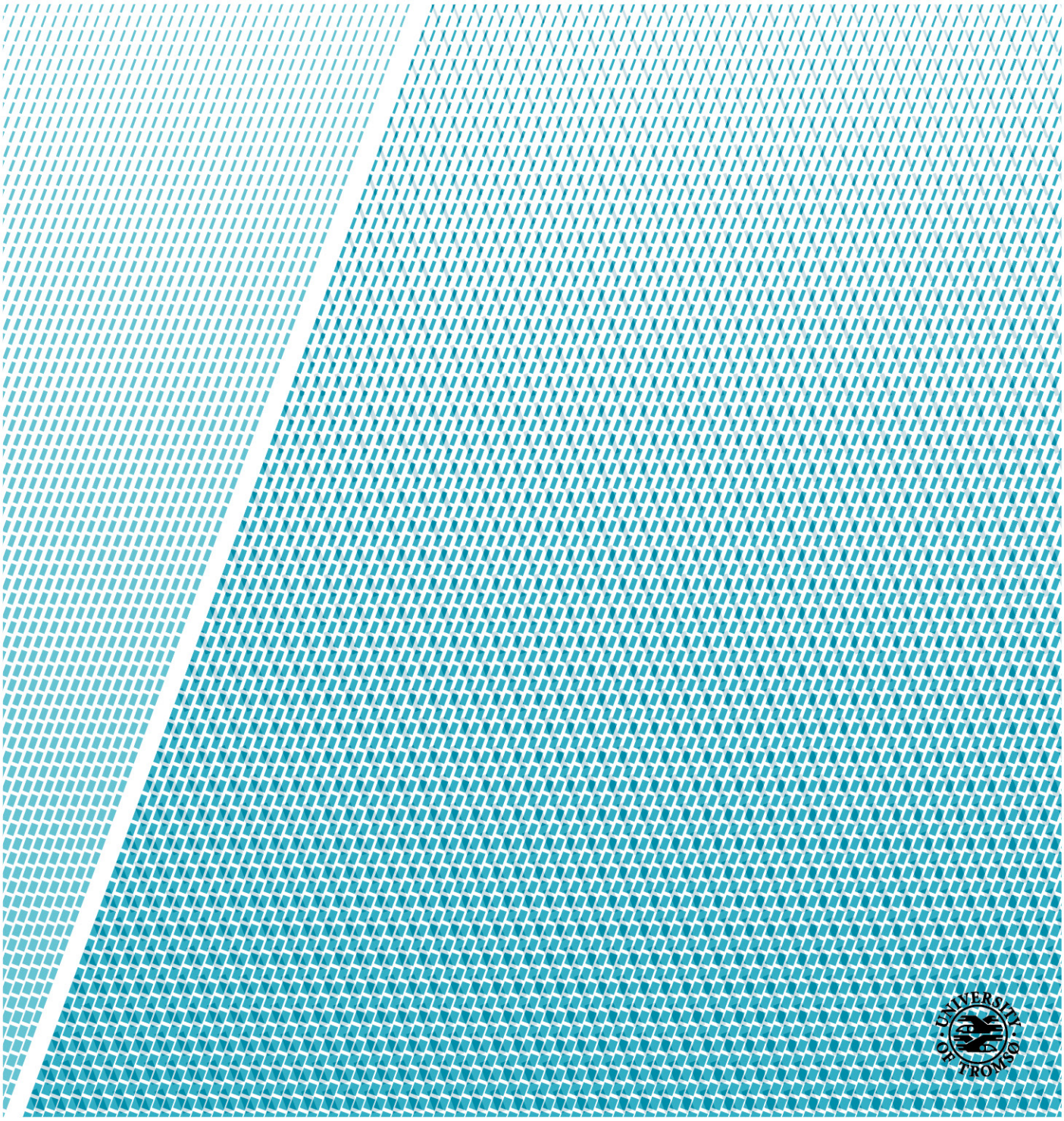
Master's thesis MED 3950, June 2019



Preface

This thesis is based on my interest in women's health and the many invasive and neglected concerns that are not frequently spoken of. Prior and throughout my medical studies I have had the privilege of working at a gastrointestinal surgery unit, and my interest in this field has since the beginning been expanding by the day. This study is a step further from a project I worked on during my second year in medical school that involved obstetric anal sphincter injuries. I got an insight on how much this birth trauma can affect a young woman's life when it comes to incontinence, psychological and social problems. Sacral nerve modulation is a method for treating incontinence, where the majority of patients have an obstetric aetiology.

My extraordinary supervisor and senior surgeon at the Department of Gastroenterological Surgery at the University Hospital of Northern Norway (UNN Tromsø), dr. Mona Rydningen, has gone beyond every means to help me succeed in this project. She has been available throughout the whole process with guidance, encouragement and ideas. She evolved the idea of the project, directed me on the structure of the paper and statistical analysis. Collection of data, analysis and writing of the manuscript was done by the author.

Senior surgeon at the Department of Gastroenterological Surgery at UNN Tromsø, Prof. Stig Norderval, created the foundation of the pelvic floor centre and supervises the development and research within this field. His input on this project was greatly appreciated.

This project would not happen without the help of the great nurses Wenche Jenssen and Elin Johansen that made sure patients were thoroughly followed-up and questionnaires were completed.

Tromsø, 03.06.2019

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Abstract

Objective Sacral nerve modulation (SNM) is an established method for treating faecal incontinence (FI) if conservative measures fail. The *International Consultation on Incontinence Questionnaire-Bowels* (ICIQ-B) is a patient-completed symptom and quality of life assessment tool created by clinical experts with patient input. The purpose of this study was to use the ICIQ-B to evaluate the short-term efficacy of SNM in patients with FI.

Method This was a prospective case series involving all patients with FI eligible for SNM at the University Hospital of Northern Norway (UNN). Patients were scored with ICIQ-B and St. Mark's score at baseline and one month after SNM. Primary endpoint was efficacy defined as a change in ICIQ-B score from baseline to one month after SNM. Secondary outcomes were change in St. Mark's score and the assessment of non-responders, defined as no change in score or higher score at one month, comparing the ICIQ-B to the St. Mark's score.

Results All 17 patients that were treated with SNM between February 2018 and October 2018 were included in this study. All domains in the ICIQ-B showed a significant change in score from baseline to one month after SNM, except the domain concerning sexual impact. The bowel pattern score (0-21) had a mean change of 2.7 (95% CI: 1.2 - 4.2, $p = 0.002$), whereas the bowel control score (0-28) had a change of 6.8 (95% CI: 5.9 - 8.6, $P < 0.001$). A mean change of 1.7 (95% CI: 0.84 - 2.57, $p = 0.001$) was seen in the other bowel symptoms score (0-15). The quality of life score (0-26) showed a mean difference of 8.1 (95% CI: 4.5 - 11.7, $p < 0.001$), and the overall quality of life score (0-10) presented a change of 2.7 (95% CI: 1.3 - 4.1, $p = 0.001$). The St. Mark's score (0-24) had a mean change in score of 4.5 (95% CI: 3.0 - 5.9, $p < 0.001$). Seven patients (41%) were non-responders with the ICIQ-B compared to one (6%) in the St. Mark's group.

Conclusion A significant reduction in score one month after treatment with SNM was seen in 5/6 domains of the ICIQ-B and with the St. Mark's score. The ICIQ-B selected more non-responders compared to St. Mark's score, but the complexity of the ICIQ-B makes clinical applicability in the evaluation of efficacy after intervention uncertain.

Abbreviations and definitions

AI	Anal incontinence - the impaired ability to control passage of gas or stool
Bowel-habit diary	A diary registering frequency of bowel movements, stool consistency, use of antidiarrheal medication, incontinence episodes and more. Used prior to implantation of SNM and at follow-up
Conservative treatment	Pelvic floor training, assisted defecation regimes and regulation of stool consistency
DI	Double incontinence - concomitant urinary and anal incontinence
Female sexual dysfunction	Problems related to sexual response, pain, orgasm and desire
FI	Faecal incontinence - inability to control passage of stool
ICIQ-B	The International Consultation on Incontinence Questionnaire-Bowels
ICIQ-UI	The International Consultation on Incontinence Questionnaire-Urinary Incontinence
OneStage-study	Multicentre study in Norway and Denmark where SNM is performed in one step without PNE
PNE	Peripheral nerve evaluation
SNM	Sacral nerve modulation
St. Mark's score	Validated questionnaire grading anal incontinence
UNN	University Hospital of Northern Norway
UI	Urinary incontinence - inability to control urine
Urgency	Inability to postpone defecation for less than 15 minutes

Introduction

Faecal incontinence

Faecal incontinence (FI) is defined as the inability to control defecation. It is a challenging and frequently occurring condition that can cause tremendous psychological, physical and social impact on a person's life. The term *faecal urgency* is the lack of postponing defecation, while *anal incontinence* (AI) includes the inability to control flatulence (1-3). The prevalence of AI varies between 0.004% to 18% due to a lack of a proper definition of FI, variation between populations, and differences in type of data collected, but the prevalence of FI is approximately 0.7-10% (3-5). The aetiology of FI is multifactorial, but the condition can be seen more often in women with birth related injuries, patients with neurological illness, congenital malformations, sequela after surgery, anatomical factors, systemic illness and others (4).

Many patients experience accompanying pelvic floor dysfunctions with *urinary incontinence* (UI) and *female sexual dysfunction* that also leads to altered lifestyle and reduction in quality of life (6, 7). However, patients treated with SNM for faecal and/or urinary incontinence have reported improvement of sexual function at follow-up, and studies suggest that SNM has an effect in women with sexual dysfunction (8).

FI is a chronic condition that can be challenging to manage and occasionally needs a multidisciplinary approach. As described in international guidelines, the first line of treatment is conservative management that involves pelvic floor training, assisted defecation regimes and regulation of stool consistency. The patient is referred to a surgeon for an operative evaluation if outcome of these measures are inadequate after 3-6 months (1-3, 9).

Conservative treatment in patients with FI proves to be efficient in nearly half of the individuals with the condition, however, some require surgery (10). *Sacral nerve modulation* (SNM) is a minimally invasive treatment for FI when a conservative approach fails (11). It was first described by *Matzel* in 1995 (12) and implemented at the *University Hospital of*

Northern Norway (UNN) in 1999 (13). The success rate during the first year after implantation is 79% with a long-term success rate of 84% after three years (11, 14). Internationally it is now a well-established second line treatment for FI, UI and *double incontinence* (DI; combined faecal and urinary incontinence), and it has also been tested in the management of constipation, lower urinary tract symptoms, chronic pelvic pain and sexual dysfunction in selected patients (1, 3, 8, 11, 13, 15-19).

The surgical procedure of SNM

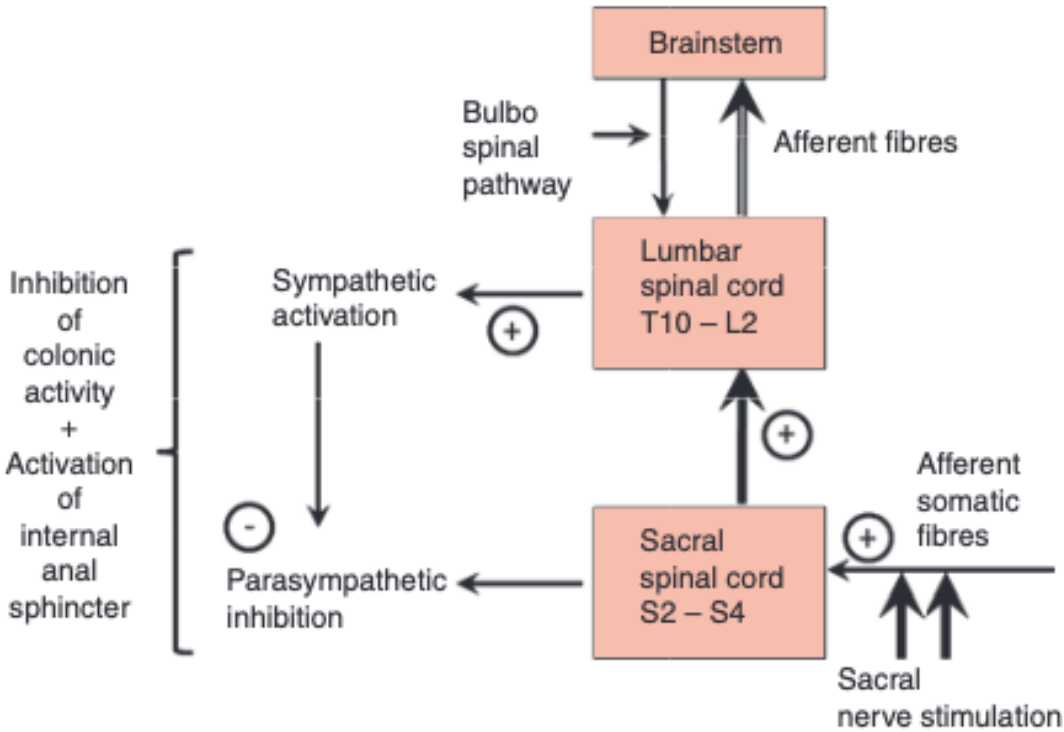
The procedure of SNM is performed in the operating theatre under sedation, general- or local anaesthesia. One or more of the sacral foraminas are cannulated and an electrode is placed through the sacral foramina along the sacral nerve plexus. The electrode is attached to a neurostimulator, providing a pulsating current. An "anal wink" where the external anal sphincter contracts indicates correct placement of the electrode (20, 21). The pacemaker system creates a continuous low threshold voltage that affects the sacral nerve plexus that controls the functions of the pelvic floor (13, 22). Suboptimal placement of the electrodes to the sacral nerve is one of the several factors that may contribute to treatment failure. Therefore, a European group of colorectal surgeons and urologists standardized the surgical method of electrode placement in 2016. Prior to this, the surgical technique varied nationally and internationally (22).

SNM can be performed in a two-step procedure (13, 23) where the first step is a three-week test phase, known as *peripheral nerve evaluation* (PNE). During this phase, the electrode is connected to an external pacemaker. The purpose of this part is to determine whether or not the patient is a suitable candidate for SNM. Successful PNE is defined as a reduction in faecal incontinence episodes of 50%, and the patient is then offered implantation of a permanent pacemaker (13, 22). Due to the high success rate (24) and the international standardization of the surgical method (22), there is currently a multicentre study in Norway and Denmark, known as the *OneStage-study*, where the procedure is performed in one step without PNE (25). This is thought to be more beneficial for the patients as there is one surgical procedure instead of two, in addition to less risk for infection in the site of implantation.

Mechanism of action

SNM is a method of treating bowel and/or bladder dysfunction by electrically stimulating the nerve roots of the sacral spinal in order to modulate the neural pathway (11). The exact mechanism on how SNM works is not fully understood as there are various aetiologies for FI, but there are several hypothesis. The nerve fibres S2-S4 in the sacrum have autonomic activity on the left colon, rectum and internal anal sphincter. The pudendal nerve is controlled by the somatic fibres and there are afferent sensory nerves innervating the internal sphincter and afferent sensory somatic nerves innervating the external sphincter and the pelvic floor (21). SNM can therefore modulate both efferent and afferent somatic and autonomic nerves (figure 1). A thought is that stimulation of the pudendal somatic afferent nerve fibres activate somatic afferent fibres that enhance internal anal sphincter activity and inhibit activity of the colon (21).

Figure 1: Hypothesis on how SNM works (21)



Contraindications and adverse effects

Absolute contraindications for SNM involves need for MRI and inability to control the device when going through the test phase. Relative contraindications are patients with a complete

spinal cord injury, a rapidly progressing neurological illness, pregnancy or abnormal anatomy of the sacrum (11).

SNM is considered as a safe surgical procedure, however, unwanted events do occur. The most common complication is pain in the implant site. This occurs in approximately 30% of patients. Infection in the site of implantation, paraesthesia and pain in the leg or buttock are other less common adverse events of SNM (11, 26).

Evaluation of treatment efficacy

Despite success in the majority of patients receiving SNM, treatment fails in some and there is no defined preoperative examination that can predict outcome (27). Suboptimal placement of the electrodes is one of the several factors that may contribute to treatment failure (22). Another thought is that the current methods of evaluation are uncapable of determining who will have effect with SNM (responders) and efficacy.

The efficacy of SNM is currently evaluated based on different incontinence scores like the St. Mark's score and bowel-habit diaries (6, 28). Several studies use the fixed ≥50 % reduction in incontinence episodes as an indicator for a successful result of SNM (6, 14, 24, 27, 29, 30). Based on this benchmark, a patient defined to have a successful result may experience incontinence episodes which can still greatly interfere with quality of life. By only evaluating reduction in incontinence episodes as a measurement for success, the true efficacy of treatment may not be accurately reflected. A reduction in incontinence score after treatment is also a commonly used method to estimate efficacy, but a defined cut-off value for successful outcome and failure is not defined (6). The lack of standardization in evaluation of outcome makes research on FI challenging (14, 28). Failure to involve patients in the creation of the forms may also exclude important concerns to the patients (31).

The *International Consultation on Incontinence Questionnaire-Bowels* (ICIQ-B) is a relatively new patient-completed questionnaire subdivided into several categories, and is thought to give a more detailed picture of the symptoms and outcome after treatment for FI (attachment 1, table 2).

Objective

The aim of this study was to use the ICIQ-B to evaluate the short-term efficacy of SNM in patients with FI, treated at UNN Tromsø in 2018. Primary endpoint was defined as a change in ICIQ-B score one month after surgical implantation of the pacemaker. In addition, the following secondary endpoints were assessed:

1. Change in St. Mark's score from baseline to one month in all patients with FI treated with SNM.
2. Assess the number of responders versus non-responders using all domains of ICIQ-B compared to St. Mark's score, were non-responders were defined as an unchanged or increased score one month after surgical implantation.

Restrictions to this trial

This study investigated the effect of treatment one month after implantation of the electrical stimulator. Many patients are suffering from DI, but this trial is limited to the effects of SNM on FI. Bowel-habit diaries, Wexner incontinence score and a questionnaire related to urinary incontinence (ICIQ-UI) were completed by the majority of patients as a part of the OneStage-study, but were not investigated in this trial.

Patients and methods

Study design and setting

The present study was a prospective case series under the *Department of Gastroenterological Surgery* at UNN Tromsø, which is affiliated with the *Norwegian National Advisory Unit on Incontinence and Pelvic Floor Health*. The goal of this unit is to facilitate treatment across the various health care professionals while maintaining focus on symptoms, expectations and possible health benefits (32). Since 2012 it has been the leading pelvic floor unit in Norway and is an interdisciplinary centre that treats patients with pelvic floor disorders.

In this study, all surgeries were performed at UNN Tromsø and the eligible patients were followed up at the surgical outpatient clinic in either UNN Narvik or UNN Tromsø.

Table 1: Eligibility criteria

Inclusion criteria	Exclusion criteria
Informed consent 18 years or older St. Mark's score > 8 and weekly episodes of passive and/or urge FI Failed customized conservative treatment over the course of 6 months Peroperative successful stimulation*	Perioperative lack of successful stimulation

* Defined as anal contraction when stimulating three or more electrodes, with one <1,5 volt.

Study population

The study population contained all consenting patients of age 18 or older treated with SNM in 2018 (table 1). A St. Mark's score greater than 8 points with weekly episodes of passive and/or urge FI and failed customized conservative treatment over six months were criteria for inclusion. Patients with peroperative success were also entered in the study. Exclusion criteria was perioperative lack of successful stimulation.

All patients in this trial were a part of the ongoing OneStage-study at UNN Tromsø. Approximately half the patients were randomized (blinded) and given minor stimulation

with the pacemaker the first month according to the OneStage-study design. As the OneStage-study is not completed as the paper is being written, it is not possible to determine what patients received complete stimulation versus minor stimulation.

Variables

ICIQ-B as a method for evaluating treatment effect

ICIQ-B is a psychometric patient-completed questionnaire on FI created by a team of multidisciplinary clinical experts through the ICIQ project (31). This was based on a study to identify items required for a comprehensive symptom and quality of life assessment tool from a patient's point of view. Highlighted issues from patient interviews were unpredictability, toilet location, coping strategies, embarrassment, isolation and social impact (33). The form consists of 21 questions that scores the patient's symptoms based on bowel control, bowel pattern and quality of life, as well as four unscored questions focusing on concerns from a patient or clinical perspective (attachment 1). Every question has a section where the patient can range how bothersome the given symptom is on a score from 0-10. This is a supplement to attain bigger insight to the patient's problem, but is not a part of the final score (31). The ICIQ-B has been translated to Norwegian, but is not yet published.

Formally, ICIQ-B gives a score on the three domains; bowel pattern, bowel control and quality of life. Questions regarding bowel symptoms and sexual functions were included in the making of ICIQ-B due to their clinical efficacy and significance to symptomatic patients, but are not the formal psychometric properties in the questionnaire (31). This study wanted to thoroughly investigate all the aspects, and created therefore five main domains of the ICIQ-B in addition to a subdomain relating to quality of life termed "overall quality of life" (table 2). This works as a *visual analogue scale* (VAS) assessing how much the bowel interfere with everyday life, scored from 0-10 (question number 23 in ICIQ-B). Since the ICIQ-B stands out from other questionnaires on FI by emphasizing on quality of life, it was considered important to look at this part separately. Therefore, this study used a total of six variables covering the ICIQ-B.

Table 2: Variables used in this study

Evaluation methods	Topics covered	Score range*	Number of questions scored
ICIQ-B score			
Bowel pattern	Bowel movements in 24 hours, nightly bowel movements, urgency, use of antidiarrheal medication, pain	0-21	5
Bowel control	Underwear staining, use of pads, leakage of liquid/solid stool, flatus leakage control, mucus incontinence, unexplained incontinence, unpredictability	0-28	7
Other bowel symptoms	Bristol Stool Scale, straining, fear of having a bowel accident	0-15	3
Sexual impact	Restriction on sexual activities	0-5	1
Quality of life	Embarrassment, toilet location awareness, having to plan according to bowels, isolation	0-26	5
Overall quality of life**	Overall interference in everyday life	0-10	
St. Mark's score	Frequency of solid and liquid stool, flatus leakage, change in lifestyle, the use of pads, use of antidiarrheal medication, ability to prolong defecation with 15 minutes	0-24	7

*A higher score indicates increasing symptoms.

**Subdomain of the domain "Quality of Life"; acts as a visual analogue scale (VAS).

St. Mark's score as a method for evaluating treatment effect

St. Mark's score is a validated questionnaire that is based on symptoms the past four weeks, and grades frequency, type of incontinence, use of pads, and to what extent the condition affects lifestyle (28). A score of zero means no leakage and a score of 24 means complete incontinence (attachment 2). This method of evaluating patients is acknowledged internationally and the questionnaire has been translated in Norwegian (34). The St. Mark's score has been used to assess patients treated with SNM, however, it does not incorporate aspects on quality of life (6, 15, 24, 28, 34, 35).

Follow-up and data collection

Scoring of symptoms with ICIQ-B and St. Mark's score was done at the day before the surgery. Patients were either seen at the surgical outpatient clinic or contacted by a trained nurse by telephone one month after implantation to complete ICIQ-B and St. Mark's score.

The patients' electronic journal (DIPS) were investigated to attain the aetiology of the incontinence, in addition to retrieve the scanned file with St. Mark's score. Data were collected prospectively, and the completed ICIQ-B questionnaires were delivered confidentially to the investigator for analysis.

Ethics

This patient group is known to have various degrees of mistrust towards the health care system, and many patients have been struggling with their health for years. Incontinence contributes to intimate and embarrassing problems that can affect relationships, family, work and how they are viewed by society. Treating patients with this unmentionable condition requires discretion, frequent follow-up and high level of clinical experience. Patients were exclusively followed up by specialized nurses in this field.

This trial was a project under the already occurring OneStage-study at UNN Tromsø, and patient consent was retrieved through the OneStage-study (see attachment 3-5). A second form of consent was not created, as this project was a quality assertion on a new questionnaire with no additional data collection. Because this was a part of the OneStage-study and 50% of the patients were treated with minor stimulation initially, it was anticipated to detect a lower reduction in symptom scores than otherwise expected.

Statistical methods

Demographic data was retrieved through descriptive analysis and are presented with frequency tables, mean, standard deviation (SD), median and interquartile range (IQR). Categorical variables are listed with frequency (n) and the respective percentage. When comparing two groups, the paired samples T-test was used to analyse outcome variables and are presented as mean and standard deviation (SD). Difference of mean was presented with 95% confidence interval (CI). Nonparametric tests were used when assumptions were not met. All analysis were completed with SPSS statistical software (version 25) with a significance level of $p < 0.05$.

Responders versus non-responders

A non-responder was defined as unchanged or increase in score one month after surgical implantation in one or more of the domains in the ICIQ-B or St. Mark's score. We expected more non-responders using the ICIQ-B as this questionnaire contains more questions regarding quality of life, and also 50% of the patients were assigned to minor stimulation in the OneStage-study. The domain concerning sexual impact was omitted from the evaluation of responders versus non-responders, as the patients were recommended to avoid sexual intercourse during the first six weeks after surgery.

Wilcoxon Signed Rank Test was used to identify responders versus non-responders by determining if median in the distribution of differences were equal or different than zero. If the difference was equal to zero, it was defined as no difference in treatment prior to surgery compared to after surgery. A negative change in score (negative rank) meant better outcome, as a lower score indicates less symptoms. A positive change in score (positive rank) meant worse outcome, as an increase in score meant more symptoms. In other words, patients with a difference ≥ 0 between baseline at one month were considered non-responders, while patients with a difference <0 were responders to SNM treatment.

Results

Participants

A total of 17 patients received treatment with SNM at UNN Tromsø between February 2018 and October 2018, and all were included in the study. Patients completed the ICIQ-B and St. Mark's score the day of surgery, in addition to one month postoperatively, either at the outpatient clinic or by telephone.

The mean age was 52.8 (SD 14.4) and 16/17 participants were female. Nearly half the study group (47%) had a previous obstetric history as a cause for FI, while 18% had a neurological aetiology (multiple sclerosis, cauda equina syndrome). The remaining 35% of patients had other or idiopathic cause for FI (table 3).

Table 3: Demographic data

	N (%)	Mean (SD)	Median (IQR)
Sex	17		
Female	16 (94)		
Male	1 (6)		
Age (years)		52.8 (14.4)	52.0 (40-68)
Aetiology			
Obstetric	8 (47)		
Neurologic	3 (18)		
Idiopathic FI/other	6 (35)		

n = number of patients, SD = standard deviation, IQR = interquartile range

The primary endpoint in this study was change in ICIQ-B one month after implantation of SNM. All domains, except for the sexual impact score, had significant change in score from baseline to one month (table 4, figure 2). Significant difference in St. Mark's score was also found (table 4, figure 3).

Outcome of ICIQ-B and its respective domains

Bowel pattern score

Patients scored with a mean of 11.7 (SD 2.8) at baseline compared to 9.0 (3.1 SD) at one month, resulting in a mean change of 2.7 (95% CI: 1.2 – 4.2) and proving to be significant with p = 0.002 (table 4, figure 2). Of the 17 patients, 14 patients (82%) showed a score with better outcome one month after surgery. One patient (6%) had no change in score, while two patients (12%) had a worse score after treatment (table 5, figure 5).

Table 4: Differences in ICIQ-B domains and St. Mark's score at baseline and one month

	Baseline		1 month		Mean difference (95% CI)	p-value
Domain	**Mean**	**SD**	**Mean**	**SD**		
Bowel pattern score	11.7	2.8	9.0	3.1	2.7 (1.2 – 4.2)	0.002
Bowel control score	20.9	2.9	14.1	4.4	6.8 (5.0 – 8.6)	< 0.001
Other bowel symptoms score	9.9	1.4	8.2	2.3	1.7 (0.84 – 2.57)	0.001
Sexual impact score	2.9	1.6	2.7	1.7	0.2 (0.3 – 0.7)	0.332
Quality of life score	21.8	3.1	13.7	7.6	8.1 (4.5 – 11.7)	< 0.001
Overall quality of life	8.5	1.4	5.8	3.5	2.7 (1.3 – 4.1)	0.001
St. Mark's score	17.3	2.0	12.8	3.7	4.5 (3.0 – 5.9)	< 0.001

See table 2 for definition and score for the respective domain.
Values are presented as mean and SD (standard deviation). Mean difference (with 95% confidence interval) represents difference in score at baseline and at one month and was achieved by paired samples T-test, where a p-value < 0.05 was considered statistically significant.

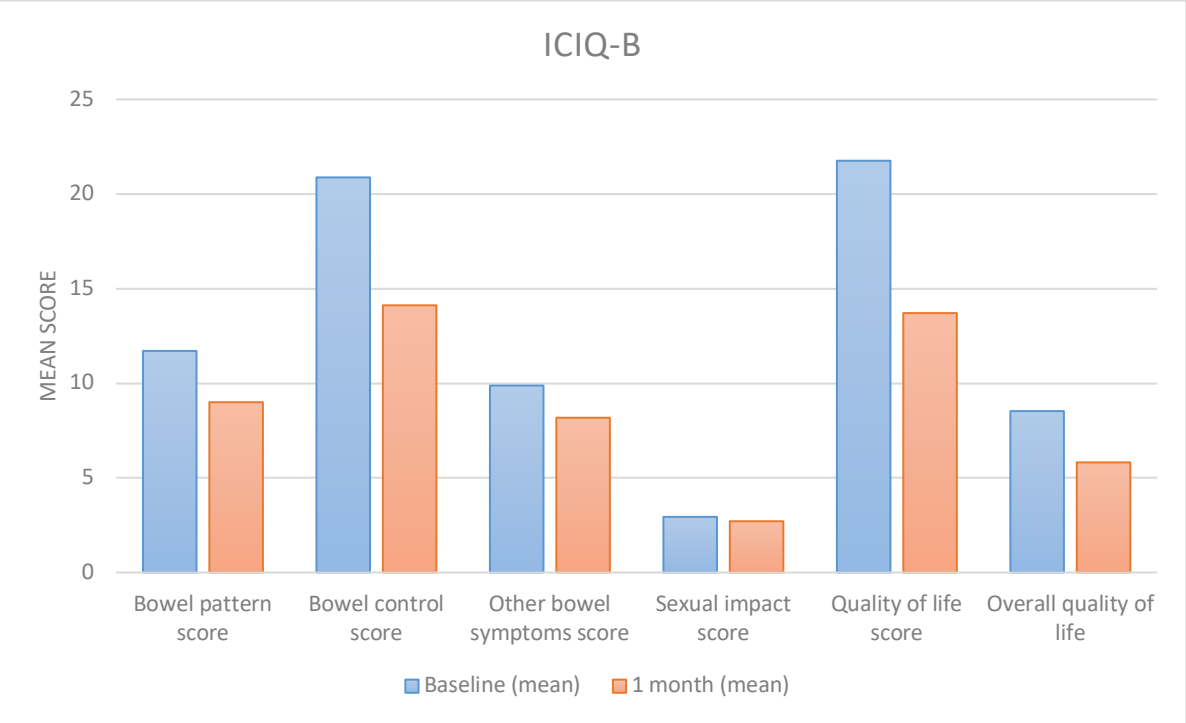
Bowel control score

With a mean of 20.9 (2.9 SD) at baseline and 14.1 (SD 4.4) at one month, there was a significant difference in score of 6.8 (95% CI: 5.0 – 8.6), p < 0.001 (table 4, figure 2). Only one (6%) patient had an unchanged score (6%), while 16 patients (94%) had a lower score one month after treatment (table 5, figure 5).

Other bowel symptoms score

Score at baseline was a mean of 9.9 (SD (1.4) compared to 8.2 (2.3 SD) at one month, resulting in the mean difference of 1.7 (95% CI: 0.84 – 2.57) being significant, p = 0.001 (table 4, figure 2). Two patients (12%) had a better score prior to treatment than after. The reminding 15 patients (88%) had had a score indicating less symptoms at one month (table 5, figure 5).

Figure 2: Mean score of the six various domains in the ICIQ-B at baseline and at one month after SNM



Sexual impact score

The mean score at baseline was 2.9 (SD 1.6) compared to a slightly lower mean of 2.7 (SD 1.7) at one month, showing the mean difference to be 0.2 (95% CI: 0.3 – 0.7). With a p = 0.332 (table 4, figure 2). However, patients were recommended to avoid sexual intercourse six weeks after implantation, confirming the result where ten (59%) did not have a change in score and two patients (12%) had a worse score at one month (table 5). Therefore, this domain was not further analysed with regards to responders versus non-responders.

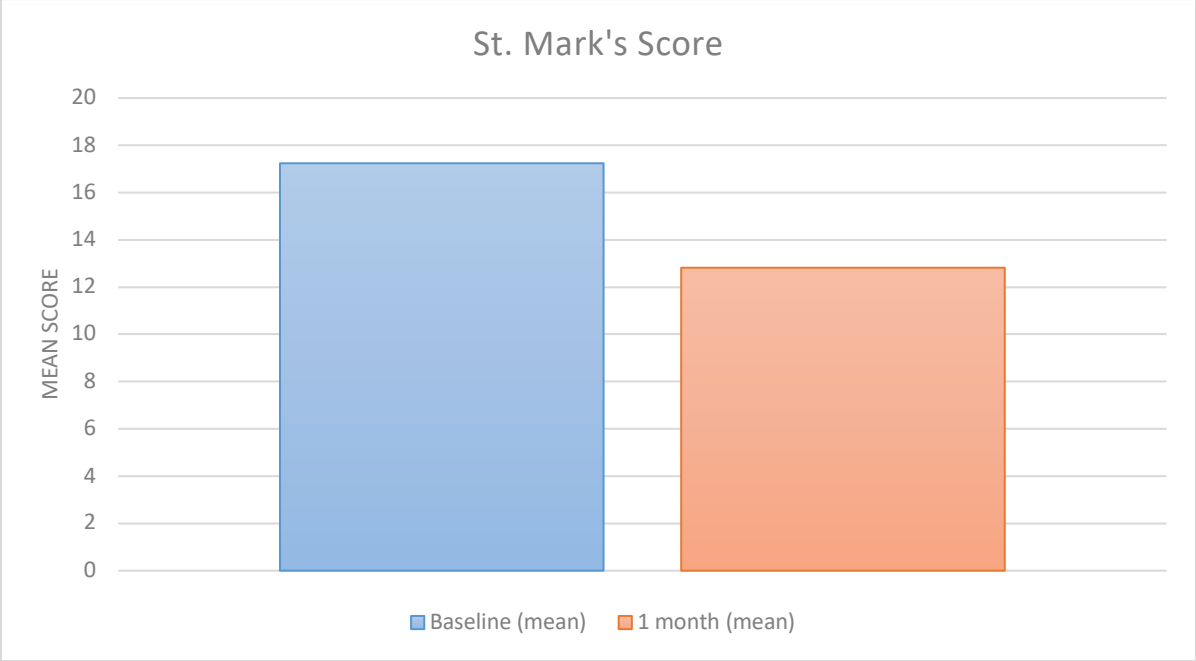
Quality of life score

This score showed the greatest change compared to the other domains. With a mean difference of 8.1 (95% CI: 4.5 – 11.7) provided by a mean at baseline of 21.8 (SD 3.1) and 13.7 (SD 7.6) at one month, there was a significant change in quality of life with $p < 0.001$ (table 4, figure 2). Of the 17 patients, one patient (6%) had the same score, while 16 (94%) were had better outcome at one month (table 5, figure 5).

Overall quality of life

There was a significant change from a mean of 8.5 (SD 1.4) at baseline to 5.8 (SD 3.5) at one month, resulting in a mean difference of 2.7 (95% CI: 1.3 – 4.1), $p = 0.001$ (table 4, figure 2). A total of five patients (29%) showed no response to treatment, where four (24%) of these had an unchanged score at one month. The 12 remaining patients (71%) had better outcome on this subdomain (table 5, figure 5).

Figure 3: Mean score evaluated with the St. Mark's Score at baseline and at one month after SNM



Outcome of St. Mark's score

St. Mark's score showed a change in the mean score at baseline of 17.3 (SD 2.0) and at one month 12.8 (SD 3.7). The mean difference was 4.5 (95% CI: 3.0 – 5.9), and was considered significant with $p < 0.001$ (table 4, figure 3). The majority of patients were responding to

treatment according to this scoring method. Of the 17 patients, 16 (94%) had better outcome at one month, while only one patient (6%) had an increased score after treatment (table 5, figure 5).

Table 5: Ranks of observed differences in the various domains of ICIQ-B and St. Mark's Score

	Bowel pattern score	Bowel control score	Other bowel symptoms score	Sexual impact score	Quality of life score	Overall quality of life	St. Mark's score
Responder (better outcome)	14	16	15	5	16	12	16
Non-responder (no difference)	1 (#6)	1 (#14)	0	10 (#1, 2, 5, 6, 7, 10, 13, 15, 16, 17)	1 (#14)	4 (#1, 2, 9 ,15)	0
Non-responder (worse outcome)	2 (#15, 16)	0	2 (#6, 14)	2 (# 12, 14)	0	1 (#14)	1 (#15)
p-value*	0.003	0.000	0.001	0.340	0.000	0.002	0.000

*Wilcoxon Signed Rank Test.
#: patient number in data bank.

Responders versus non-responders

After detecting the number of responders versus non-responders, the patients who had worse or no difference in outcome were identified and labelled using "#" followed by the patient's given number in the data bank (table 5, figure 4). This was done to see if a patient was non-responding in multiple domains in addition to comparison to responders and non-responders in the St. Mark's score.

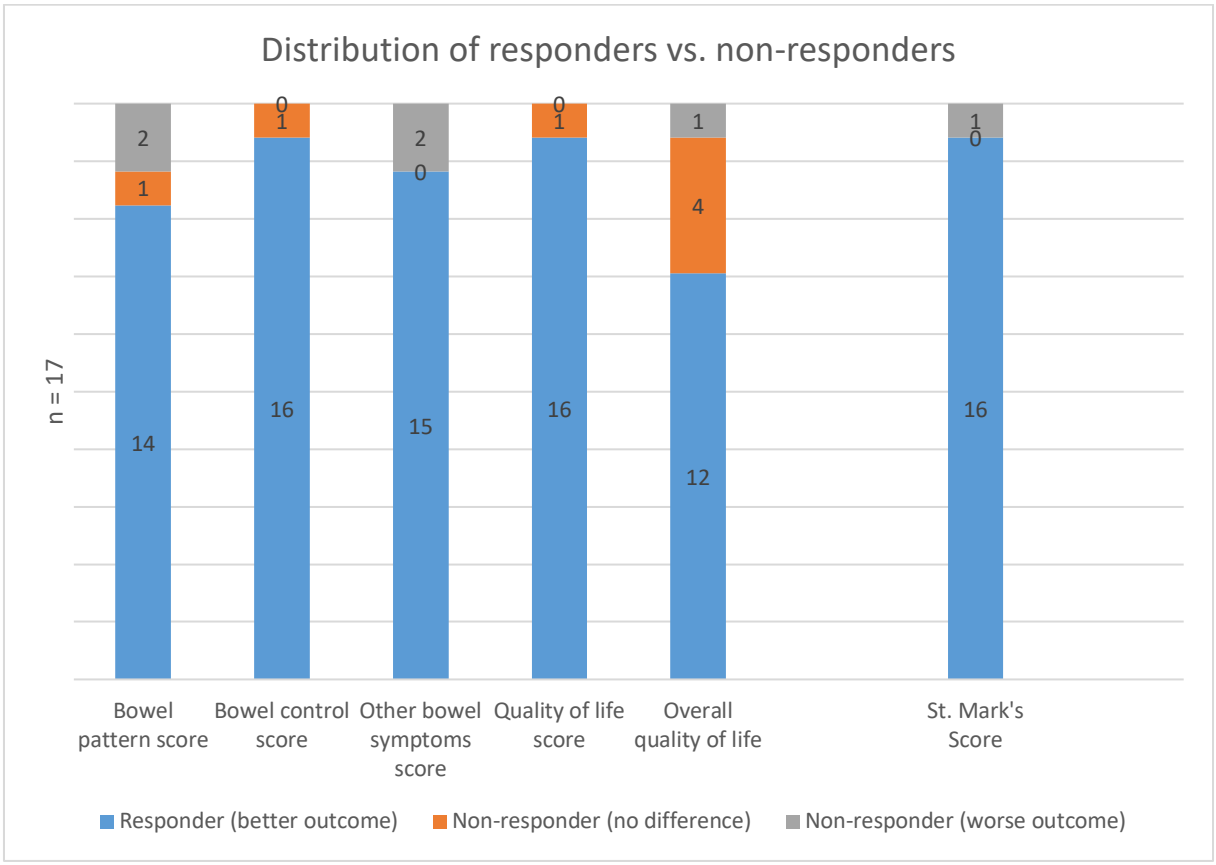
A total of seven patients (41%) were considered non-responders (# 1, 2, 6, 9, 14, 15, 16) in one or more domains using the ICIQ-B compared to one (6%) non-responder (#15) using the St. Mark's score (table 6). The sexual impact score was excluded as previously described.

Table 6: Responders vs. non-responders detected with ICIQ-B and St. Mark's Score

	ICIQ-B	**St. Mark's score**
Responders (%)	10 (59)	16 (94)
Non-responders (%)	7 (41)	1 (6)
Total	17	17

With the five significant domains of the ICIQ-B, a total of four patients (#1, 2, 9, 16) were considered non-responding in one of the domains. Another two patients (#6, 15) were non-responders in two domains, while one patient (#14) had no difference or increased symptoms in four domains. In comparison, St. Mark's score had only one non-responder (#15) in total. This patient was also non-responding in two domains using the ICIQ-B, which was interestingly the bowel pattern score and overall quality of life.

Figure 4: Graphical representation of responders and non-responders after treatment with SNM using ICIQ-B and St. Mark's score



Discussion

To our knowledge, this is the first study evaluating the efficacy of SNM using the ICIQ-B. In this study, we found that five out of six domains in the ICIQ-B showed significant change one month after SNM, except for sexual impact. There was also a significant reduction in St. Mark's score. Seven patients (41%) were non-responders in one or more domains using the ICIQ-B, compared to a single patient (6%) using the St. Mark's score.

ICIQ-B as a method for evaluating efficacy of SNM

Bowel pattern score

With the bowel pattern score focusing on daily and nightly bowel movements, urgency, pain and use of antidiarrheal drugs, more than 80% of patients had a reduction in symptoms one month after treatment. Despite of this, the mean reduction in score was only three out of 21 points (14%). The reduction was lower than expected. It appears in published literature that bowel-habit diaries are mainly used for detecting change in FI episodes to evaluate efficacy of SNM, not change in bowel pattern. Bowel-habit diaries contain information on several of the topics in this domain, like urgency and frequency of bowel movements, but are not used as measures of outcome after SNM (14, 25, 36). The St. Mark's score does not register frequency of bowel movements, but involves urgency where patients can answer "yes" or "no" if they can postpone defecation for 15 minutes (28). The ICIQ-B grades urgency on a scale from 0-4, and gives therefore a more accurate and graded evaluation, but also eventually a lower change in score compared to the St. Mark's score.

The St. Mark's score also includes the use of antidiarrheal drugs, presented in a categorical manner. The ICIQ-B measures the use of antidiarrheal drugs on a scale from 0-5. This contributes to a skew comparison in scores in the same fashion as urgency already described. Moreover, the patients are also supposed to continue conservative treatment including antidiarrheal medications even after SNM. The evaluation of pain as in the ICIQ-B in patients with FI treated with SNM, has to our knowledge not been described previously, but may be an important aspect as some studies have shown that pain is a common complaint after SNM (6).

In summary, the usefulness of the bowel pattern score in the ICIQ-B in the evaluation of efficacy of SNM is unknown. The ICIQ-B gives a more detailed grading of symptoms than the St. Mark's score. Urgency stands out as the important aspect of the bowel pattern score, compared to the remaining topics in this domain which may be less relevant in evaluating the efficacy of SNM. The change in urgency can ultimately be masked amongst less important questions and the associated large width in scale in the bowel pattern domain.

Bowel control score

The bowel control score showed that more than 90% of the patients experienced a decrease in incontinence symptoms like soiling, ability to hold soft or hard stool, ability to control flatulence and mucus, as well as passive leakage. A mean reduction in score was nearly seven out of 24 points (30%). This value appear to be comparable to other studies using the traditional questionnaires like St. Mark's score and *Cleveland Clinic Incontinence Score* (6, 14).

The St. Mark's score includes three of the seven questions in this domain, which are leakage of soft and hard stool and leakage of flatulence. The remaining questions in the ICIQ-B may not contribute to any additional information with regards to treatment efficacy of SNM, but contributes to a more complex and complicated questionnaire to complete for the patients and for interpretation of efficacy.

Other bowel symptoms score

Nearly 90% of patients experienced better outcome in the other bowel symptoms domain, which was the consistency of stool (Bristol Stool Scale), straining and fear of having a bowel accident. With the maximum score of 15, the change after one month was only two points (13%). Perhaps it is too early to evaluate the fear of having a bowel accident at this stage. It is likely that fear is still present in patients with remaining incontinence episodes, even if frequency is reduced or eliminated as it is believed that it takes time to break a negative pattern and trusting the restoring natural functions of the body.

This domain also contains various components on FI that are not related. A large reduction in the Bristol Stool Scale may ultimately mask an unchanged or increased score in fear of

having a bowel accident, although the scale is a target for conservative treatment before surgical intervention and related to use of antidiarrheal medication already evaluated in the bowel pattern score.

The usefulness of ICIQ-B on this domain at one month is unknown. However, it is believed that fear will decrease over time as incontinence episodes diminishes, so this score should be further investigated at one year follow-up.

Sexual impact score

The sexual impact score showed no difference in outcome after one month, and similar findings have been described (24). Prior to surgery, patients were advised to avoid sexual activity during the first six weeks after surgery. It was therefore not expected to get a change in score after one month. A change in the sexual impact score may therefore be determined with a longer period of follow-up. However, research suggest that SNM can alter the pudendal nerve function and can cause an increase in pelvic blood flow via stimulation of parasympathetic fibres that can ultimately improve sexual function (8, 37). Long-term effects of SNM on female sexual dysfunction is still unknown (7, 8, 38).

Involving sexual impact in the questionnaire is an asset with the ICIQ-B as it evaluates more of the dysfunctions of the pelvic floor. However, the ICIQ-B does not take urinary incontinence into consideration. Approximately 75% of women have concomitant UI and SNM is proven to be an effective treatment of both UI and DI (24). Urinary symptoms should have been incorporated in the questionnaire for assessing the efficacy on pelvic floor function as a whole after treatment. Incorporating urinary function as well as sexual function would have given a complete questionnaire to assess pelvic floor function after intervention. Anyhow, the ICIQ advisory board recommend to use other available questionnaires for urinary function (ICIQ-UI) (1).

Quality of life

Of the two domains relating to quality of life, 94% had better outcome on aspects regarding embarrassment, toilet awareness, interference with everyday life and isolation. This domain had a mean reduction of more than eight points, which was the greatest difference in score

of all domains in the ICIQ-B. Quality of life improvement that follows the functional progression of incontinence has been shown to correlate in published literature (6, 14, 39, 40). Comparatively the same can be seen with the quality of life score and the bowel control score in the ICIQ-B. Furthermore, 71% showed an improvement when asked to scale their overall quality of life from 1-10, with a mean change in score of three points (30%).

The quality of life score involves 26 questions with a mean reduction of eight points (31%), whereas the overall quality of life has ten questions with a mean reduction of three points (30%). Interestingly, both scoring methods were reduced with a third of the baseline score. In other words, the comprehensive quality of life score may not offer any additional information relating to treatment efficacy with ICIQ-B compared to the VAS or overall quality of life score. VAS scales have previously been proved accurate on evaluating the impact of urinary incontinence on quality of life (41). Having to answer many questions is tedious and bothersome to the patient. Perhaps this domain does not need all the questions on quality of life, as it appears that the simple VAS scale offers the same result in a single question.

St. Mark's score as a method for evaluating efficacy of SNM

The St. Mark's score showed that 94% of the patients had effect of SNM with a change of nearly five points (21%) in one month. This is less than what has been described previously, but it appears that no study has evaluated outcome at one month specifically, in short-term studies (14, 42). Another explanation for a less favourable outcome after one month is of course that half of the patients received minor stimulation only.

St. Mark's score focuses on the functional aspects of FI, and bases effect on objective measures. It was created by *Vaizey et. al*. as there was no scoring system evaluating the severity of FI with good reproducibility in published literature. In addition, objective comparison of outcome for both conservative and surgical treatments were lacking (28). This scoring method has been used in many recent studies (6, 14, 24, 40), but in comparison with the ICIQ-B, it has a less meticulous grading of symptoms and does not evaluate any quality of life aspects like fear and isolation (table 7).

Anyhow, a reduction in St. Mark's score has been shown to correlate with quality of life (6), but does not solely give a detailed picture on what aspects are challenging like the ICIQ-B does. The St. Mark's score should therefore be used in combination with other methods of evaluating quality of life.

Responders versus non-responders

The ICIQ-B manged to detect more non-responders compared to the St. Mark's score. The ICIQ-B had a total of seven non-responders (41%) compared to a single non-responder (6%) with the St. Mark's score. Interestingly, five non-responders were identified based on the domains specific on quality of life. It is also noteworthy that approximately half of the patients had minor stimulation due to assignment in the OneStage-study, and were expected to be non-responders. This highlights the challenges using any questionnaires evaluating treatment efficacy after intervention for functional disorders like faecal incontinence. It has been reported that approximately 30% of patients with FI have better treatment outcome with SNM based on a substantial placebo effect (6, 36, 43). Due to beliefs and high level of expectation, it is already established that the placebo effect are high in patients with chronic gastrointestinal disorders (36), and might be a confounding factor in this trial as significant effect was found in such a short time.

Comparatively, long-term results show that treatment fails in approximately 30% of patients receiving treatment with SNM (14, 19), similar to what the ICIQ-B revealed at one month. Remarkably, there was only one patient non-responding in the bowel control domain, and one non-responding in the St. Mark's score. One of the main goals of SNM is to treat incontinence episodes, but with the complexity of FI it seems like improvement in incontinence episodes does not solve all the problems for the affected patient. Patients with FI need a multidisciplinary approach where the ICIQ-B can contribute as an important tool in understanding the symptoms and the efficacy of treatment. However, when evaluating efficacy of SNM, it might be too complex and extensive, but further research with more patients and longer follow-up is needed in order to conclude.

Should the ICIQ-B be the new method of evaluating treatment efficacy with SNM?

The ICIQ-B contributes with many key topics that cannot be found in a single questionnaire. It involves important sections that grades urge, assess stool consistency, sexual impact, fear and quality of life (table 7). As this study shows, it detects many other aspects related to FI other than change in incontinence episodes.

Like previously stated, the majority of patients with FI also have UI. The ICIQ-B lack evaluation of these symptoms. Adding assessment of UI would have given a complete questionnaire for assessing the efficacy on pelvic floor function after treatment.

Overall, the ICIQ-B seems to be a too comprehensive method for evaluating efficacy of SNM, but shows significant change in outcome comparable to the St. Mark's score. The questionnaire seems to involve too many questions with high variety that causes important topics to drown amongst insignificant questions in the domain. Also, a long questionnaire can be bothersome to patients and is not suitable for use in follow-up via telephone. The ICIQ-B is an important tool in evaluating incontinence, but not in the evaluation of treatment efficacy at one month. Perhaps the ICIQ-B would be more useful in a multidisciplinary baseline evaluation of complex patients or in treatment failure, compared to standard follow-up after intervention.

Table 7: Strengths and limitations with the ICIQ-B and St. Mark's score.

	ICIQ-B	**St. Mark's score**
Strengths	Patient completed Created with input from patients Evaluates many aspects on quality of life Evaluates sexual impact	Well-established Short questionnaire Suitable for objective comparison
Limitations	Long questionnaire No published studies using the form Not published in Norway Absent evaluation of UI	Limited evaluation on quality of life Absent evaluation of sexual impact Absent evaluation of UI

Strengths of this trial

This study was a prospective evaluation of treatment efficacy using a relatively new questionnaire, ICIQ-B. There are established methods for clinical assessment on FI, like *Pescatori score, Cleveland Clinic Incontinence Score*, bowel-habit diaries and St. Mark's score

(28). All these evaluate the functional problems that patients have based on the clinicians evaluation and expertise. So far, a detailed self-reporting evaluation on experienced symptoms and quality of life is lacking, therefore it has been important to determine if the ICIQ-B can contribute in a more detailed matter in determining the treatment efficacy of SNM.

Limitations of this trial

This study included all patients treated for SNM at UNN Tromsø in 2018, which was a total of 17. This is a small population sample and follow-up time was limited to one month. Most research available on the efficacy of SNM on FI carries out small prospective and retrospective case series with few randomized controlled trial, and follow-up in existing literature is based on a mean follow-up period between six and 12 months (14). This study showed nonetheless a significant decrease in symptoms and increase in quality of life already after one month.

None of the available questionnaires have a defined cut-off value defining success, and efficacy was simply defined as a reduction in score (responder). The St. Mark's score also assess the function over a course of the past four weeks. In order to get a more accurate value of the ICIQ-B, it would be necessary to evaluate each question separately.

In addition, this was a part of an ongoing randomized trial where half of the patients had minor stimulation and were expected to be non-responders. Further analysis after completing the trial and identifying the patients in the non-stimulation group, will give additional information about the genuine value of the questionnaires, with true non-responders and probably greater change in score.

Another limitation is that the validation of the ICIQ-B is not published and available for clinical use in Norway, and the current translation of questions may not correctly represent the original version.

Conclusion

The ICIQ-B showed a significant change in five out of six domains one month after implantation. There was also a substantial reduction in the St. Mark's score for the same duration of follow-up. Seven patients (41%) proved to be non-responders in one or more domains using the ICIQ-B, compared to a single patient (6%) using the St. Mark's score.

Using the ICIQ-B in evaluation of treatment efficacy adds important points on fear, a more detailed evaluation of urgency, consistency of stool, and sexual impact, but lacks assessment of UI. However, the ICIQ-B is more complex to complete for the patients and for interpretation in clinical practice, thus making the clinical applicability uncertain.

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Appendices

Attachment 1: The International Consultation on Incontinence Questionnaire-Bowels

Initial number

ICIQ-B (04/08)

CONFIDENTIAL

DAY MONTH YEAR
Today's date

Many people experience bowel accidents or bowel leakages. We are trying to find out how many people experience these symptoms and how much this bothers them. We would be grateful if you could answer the following questions, thinking about how you have been over the PAST THREE MONTHS.

1 Please write in your date of birth: DAY MONTH YEAR

2 Are you *(tick one)*: Female ☐ Male ☐

Bowel pattern

3 On average how many times do you open your bowels in 24 hours?
(Tick one box for 'usual' and tick one box for 'at worst')

	(a) Usual	(b) At worst
less than once	☐ 1	☐ 1
one to three times	☐ 2	☐ 2
three to ten times	☐ 3	☐ 3
ten or more times	☐ 4	☐ 4

(c) How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 10
not at all — a great deal

4 How often do you open your bowels during the night from going to bed to sleep until you get up in the morning? *(Tick one box)*

	(a)
never	☐ 0
once	☐ 1
twice	☐ 2
three times	☐ 3
four or more times	☐ 4

(b) How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 10
not at all — a great deal

ICIQ-B (04/08)

5 Do you have to rush to the toilet when you need to open your bowels?
(Tick one box)

	(a)
never	☐ 0
rarely	☐ 1
some of the time	☐ 2
most of the time	☐ 3
always	☐ 4

(b) How much does this bother you?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 10
not at all — a great deal

6 **Do you use medications (tablets or liquids) to <u>stop</u> you opening your bowels?**
(Tick one box)

(a)

never ☐ 0
less than once a month ☐ 1
less than once a week ☐ 2
less than once a day ☐ 3
about once a day ☐ 4
several times a day ☐ 5

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

7 **Do you experience pain/soreness around your back passage?** *(Tick one box)*

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Bowel pattern score: sum scores 3a - 7a ☐☐

ICIQ-B (04/08)

Bowel control

8 **Do you experience any staining of your underwear or need to wear pads because of your bowels?** *(Tick one box)*

(a)

never ☐ 0
less than once a month ☐ 1
less than once a week ☐ 2
less than once a day ☐ 3
everyday ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

9 **Are you able to control watery or loose stool leaking from your back passage?**
(Tick one box)

(a)

always ☐ 0
most of the time ☐ 1
some of the time ☐ 2
rarely ☐ 3
never ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

10 **Are you able to control accidental loss of formed or solid stool from your back passage?** *(Tick one box)*

(a)

always ☐ 0
most of the time ☐ 1
some of the time ☐ 2
rarely ☐ 3
never ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

ICIQ-B (04/08)

11 **Are you able to control wind (flatus) escaping from your back passage?** *(Tick one box)*

(a)

always ☐ 0
most of the time ☐ 1
some of the time ☐ 2
rarely ☐ 3
never ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

12 **Are you able to control mucus (discharge) leaking from your back passage?** *(Tick one box)*

(a)

always ☐ 0
most of the time ☐ 1
some of the time ☐ 2
rarely ☐ 3
never ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

13 **Do you have bowel accidents when you have no need to open your bowels?** *(Tick one box)*

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

14 **Are your bowel accidents or leakages <u>unpredictable</u>?** *(Tick one box)*

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Bowel control score: sum scores 8a – 14a ☐☐

Other bowel symptoms

15 **Using the pictures please indicate how your bowel movements are <u>most</u> of the time?** *(Tick all boxes that apply)*

(a)

separate hard lumps like nuts (hard to pass) ☐ 1
sausage-shaped but lumpy  ☐ 2
like a sausage but with cracks on its surface ☐ 3
like a sausage or snake – smooth and soft ☐ 4
soft blobs with clear cut edges (easy to pass) ☐ 5
fluffy pieces with ragged edges, a mushy stool ☐ 6
watery, no solid pieces ☐ 7

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Bristol Stool Form Scale O'Donnell, L.J.D. et al (1990)

ICIQ-B (04/08)

16 **Do you need to strain to open your bowels?** *(Tick one box)*

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

17 **Is the possibility of having a bowel accident on your mind?** *(Tick one box)*

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Sexual impact

18 **Do you restrict your sexual activities because of your bowels?** *(Tick one box)*

	(a)	
never	☐	0
rarely	☐	1
some of the time	☐	2
most of the time	☐	3
always	☐	4
not applicable	☐	5

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Quality of life

19 **Do your bowels cause you to feel embarrassed?** *(Tick one box)*

	(a)	
never	☐	0
rarely	☐	1
some of the time	☐	2
most of the time	☐	3
always	☐	4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

20 **Do your bowels cause you to make sure you know where toilets are?**
(Tick one box)

	(a)	
never	☐	0
rarely	☐	1
some of the time	☐	2
most of the time	☐	3
always	☐	4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

21 **Do your bowels cause you to make plans according to your bowels?**
(Tick one box)

	(a)	
never	☐	0
rarely	☐	1
some of the time	☐	2
most of the time	☐	3
always	☐	4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

22 **Do your bowels cause you to stay home more often than you would like?**
(Tick one box)

(a)

never ☐ 0
rarely ☐ 1
some of the time ☐ 2
most of the time ☐ 3
always ☐ 4

(b) **How much does this bother you?**
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

23. Overall, how much do your bowels interfere with your everyday life?
Please ring a number between 0 (not at all) and 10 (a great deal)

0 1 2 3 4 5 6 7 8 9 **10**
not at all — a great deal

Quality of life score: sum scores 19a -23 ☐ ☐

24 **Please use the space below to describe any worries you have about bowel accidents or leakages, what you think may have caused your bowel accidents or leakages, or anything else you think we should know.**

Thank you very much for answering these questions.

Attachment 2: St. Mark's score

	Never	Rarely	Sometimes	Weekly	Daily
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
				No	Yes
Need to wear a pad or plug				0	2
Taking constipation medicines				0	2
Lack of ability to defer defecation for 15 minutes				0	4

Never = no episodes in the past four weeks
Rarely = 1 episode in the past four weeks
Sometimes = > 1 episode in the past four weeks but < 1 per week
Weekly = 1 or more episodes a week but < 1 per day
Daily = 1 or more episodes a day

Add one score from each row: minimum score 0 = perfect continence; maximum score 24 = totally incontinent

Attachment 3: Approval of main protocol

Regionshuset
Viborg
Regionssekretariatet
Juridisk kontor
De Videnskabsetiske Komiteer
For Region Midtjylland
Skottenborg 26
DK-8800 Viborg
Tel. +45 7841 0183
komite@rm.dk
www.komite.rm.dk

Jakob Jakobsen, Læge, ph.d.
Aarhus Universitetshospital
Mave- og Tarmkirurgi, Analfysiologisk klinik
Tage-Hansens Gade 2
8000 Aarhus C

Dato 16-01-2017
Sagsbehandler Helle Nikkel
komite@rm.dk
Tel. +4578410186
Sagsnr. 1-10-72-321-16

Projekt: Sacral Nerve Stimulation – placebo or clinical effective – a randomized blinded study.

De Videnskabsetiske Komitéer for Region Midtjylland, Komité II, har behandlet projektet på sit møde den 15. december 2016 og I har efterfølgende indsendt revideret materiale. Komitéen har på den baggrund truffet følgende afgørelse.

Afgørelse:

Projektet godkendes i henhold til lov nr. 593 af 14. juni 2011 om videnskabsetisk behandling af sundhedsvidenskabelige forskningsprojekter.

Godkendelsen gælder for de anmeldte forsøgssteder, den anmeldte forsøgsansvarlige i Danmark samt for den angivne forsøgsperiode.

Godkendelsen gælder til den 1. februar 2020 og omfatter følgende dokumenter:

- Forsøgsprotokol, version 01.02, dateret 12. januar 2017.
- Deltagerinformation, version 01.02, dateret 12. januar 2017.
- Samtykkeerklæring, version 01.02, dateret 12. januar 2017.

Såfremt der opnås økonomisk støtte til projektet, skal støttegiver og støttebeløb tilføjes deltagerinformationen. Den opdaterede deltagerinformation skal som orientering indsendes til sekretariatet for De Videnskabsetiske Komitéer.

Godkendelsen omfatter tilladelse til, at der kan videregives oplysninger fra patientjournalen til forsker i henhold til sundhedsloven§ 46, stk. 1. Tilladelsen omfatter videregivelse af de oplysninger, der er oplistet i protokollen.

Iværksættelse af projektet i strid med godkendelsen kan straffes med bøde eller fængsel, jf. komitélovens § 41.

Ændringer:

Foretages der væsentlige ændringer i protokolmaterialet under gennemførelsen af projektet, skal disse anmeldes til komitéen i form af tillægsprotokoller. Ændringerne må først iværksættes efter godkendelse fra komitéen, jf. komitélovens § 27, stk. 1.

Anmeldelse af tillægsprotokoller skal ske elektronisk på *www.drvk.dk* med det allerede tildelte anmeldelsesnummer og adgangskode.

Væsentlige ændringer er bl.a. ændringer, der kan få betydning for forsøgspersonernes sikkerhed, fortolkning af den videnskabelige dokumentation, som projektet bygger på samt gennemførelsen eller ledelsen af projektet. Det kan fx være ændringer i in- og eksklusionskriterier, forsøgsdesign, antal forsøgspersoner, forsøgsprocedurer, behandlingsvarighed, effektparametre, ændringer om de forsøgsansvarlige eller forsøgssteder samt indholdsmæssige ændringer i det skriftlige informationsmateriale til forsøgspersonerne.

Hvor nye oplysninger betyder, at forskeren overvejer at ændre proceduren eller stoppe forsøget, skal komitéen orienteres om det.

Bivirkninger og hændelser:

Løbende indberetning
Komitéen skal omgående underrettes, hvis der under projektet optræder formodet alvorlige, uventede bivirkninger eller alvorlige hændelser, jf. komitélovens § 30, stk. 1.

Indberetningen skal ledsages af kommentarer om eventuelle konsekvenser for forsøget. Det er kun bivirkninger og hændelser forekommet i Danmark, der skal indberettes. Underretning skal ske senest 7 dage efter, at sponsor eller den forsøgsansvarlige har fået kendskab til tilfældet.

Ved indberetning kan anvendes et skema, der findes på *www.dnvk.dk*. Skemaet med evt. bilag skal indsendes elektronisk i pdf-format til *komite@rm.dk*.

Årlig indberetning
Én gang årligt i hele forsøgsperioden skal komitéen have tilsendt en liste over alle formodet alvorlige (ventede og uventede) bivirkninger

og alvorlige hændelser, som er indtruffet i forsøgsperioden sammen med en rapport om forsøgspersonernes sikkerhed, jf. komitélovens § 30, stk. 2. Har der ikke været alvorlige bivirkninger og hændelser skal dette ligeledes indberettes.

Ved indberetning kan anvendes et skema, der findes på *www.dnvk.dk*. Skemaet med evt. bilag skal indsendes elektronisk i pdf-format til *komite@rm.dk*.

Afslutning:

Den forsøgsansvarlige skal senest 90 dage efter afslutningen af projektet underrette komitéen herom, jf. komitélovens § 31, stk. 1. Projektet regnes som afsluttet, når sidste forsøgsperson er afsluttet.

Afbrydes projektet tidligere end planlagt, skal en begrundelse herfor sendes til komitéen senest 15 dage efter, at beslutningen er truffet, jf. komitélovens § 31, stk. 2.

Hvis projektet ikke påbegyndes, skal dette samt årsagen hertil meddeles komitéen.

Komitéen beder om kopi af den afsluttende forskningsrapport eller publikation, jf. komitélovens § 28, stk. 2. Vi skal i den forbindelse gøre opmærksom på, at der er pligt til at offentliggøre både negative, positive og inkonklusive forsøgsresultater, jf. komitélovens § 20, stk. 1, nr. 8.

Tilsyn:

Komitéen fører tilsyn med, at projektet udføres i overensstemmelse med godkendelsen, jf. komitélovens § 28 og § 29.

Følgende komitémedlemmer deltog i mødebehandlingen:

Fagpersoner
- Kasper Jacobsen Kyng (formand)
- Birgitte Brock
- Charlotte Graugaard-Jensen
- Mette Nørgaard

Lægpersoner
- Lone Blume (næstformand)
- Britta Bang
- Claus Kjeldsen
- Sanne Schou
- Steen Jakobsen

Venlig hilsen

Helle Nikkel
Sekretær

Attachment 4: Patient conscent

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

SAKRALNERVEMODULERING FOR AVFØRINGSLEKKASJE

Dette er et spørsmål til deg om å delta i en forskningsprosjekt som har til hensikt at skape ny kunnskap. Vi vil i prosjektet behandle dine plager med ufrivillig avføringslekkasje. Den aktuelle behandling er en videreutvikling av en anerkjent og effektiv behandling av avføringslekkasje. Vi håper at din deltakelse i prosjektet vil kunne være med på å forbedre metoden. Det aktuelle forskningsprosjekt er en del av et skandinavisk samarbeide.

HVA INNEBÆRER PROSJEKTET?

Dersom du takker ja til deltagelse i prosjektet, underskriver du denne samtykkeerklæringen. Du vil etter en henvisning bli innkalt til vanlig rutine utredning av ditt problem ved Utredningspoliklinikken, UNN, Tromsø. Det medfører at du vil bli bedt om fylle ut noe spørreskjemaer og gjennomgå en undersøkelse av endetarmen med kikkert og ultralyd av lukkemusklene. Hvis du etter dette oppfyller kravene vil du bli tilbudt operasjon.

Operasjonene foregår i Narvik. Tradisjonelt har den vært todelt, først med en 3 ukers testfase og deretter en varig operasjon. Den første delen går ut på å teste ut effekten av behandlingen med en ekstern/ytre nervestimulator (pacemaker). Under den andre operasjon får de som har effekt av behandlingen under testen tilbud om en varig nervestimulator som opereres inn på ryggen.

I dette forskningsprosjektet skal vi undersøke effekten av å gjøre hele prosedyren på en gang, uten en forutgående testfase. Du vil bliver utskrivet dagen etter operasjonen og skal da komme til kontroll hver 4. uke i 3 mnd, og deretter 6 og 12 mnd. Ved disse kontroller utfylles samme spørreskjemaer som før operasjon.

I prosjektet vil vi registrere opplysninger om deg. Dette gjelder grad av avføringslekkasje, urinlekkasje og livskvalitet før og etter behandling. I tillegg kommer vi til å registrere opplysninger rundt operasjonen.

MULIGE FORDELER OG ULEMPER

Deltagelse i studien medfører at du må besvare noe ekstra spørreskjemaer og må møte til noen ekstra kontroller. Du må gjennomgå en mindre operasjon i lokalbedøvelse, ikke to som tidligere. Dette tror vi vil redusere risikoen for infeksjon. Du får således ett mer effektivt behandlingsforløp.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dette vil ikke få konsekvenser for din videre behandling). Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte Mona Rydningen, mona.rydningen@unn.no, 776 27044, prosjektleder overlege Steen Buntzen, (telefon 77626527), overlege Stig Norderval (telefon 77669092) gastroenterologisk kirurgisk avdeling, UNN, Tromsø, eller ansvarlig sykepleier Wenche Jenssen, Poliklinikken i Narvik (telefon 76968400/76968438).

HVA SKJER MED INFORMASJONEN OM DEG?

Informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigert eventuelle feil i de opplysningene som er registrert.

Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste.

Prosjektleder har ansvar for den daglige driften av forskningsprosjektet og at opplysninger om deg blir behandlet på en sikker måte. Informasjon om deg vil bli avidentifisert eller slettet senest fem år etter prosjektslutt. Etter studiens avslutning vil all informasjon om deg bli sendt avidentifisert til Danmark for videre analyser.

FORSIKRING

Du er forsikret på vanlig måte gjennom pasientskadeloven og Norsk pasientskadeerstatning.

UTLEVERING AV OPPLYSNINGER TIL ANDRE

Ved å delta i prosjektet, samtykker du også til at opplysninger fra spørreskjema og operasjon kan utleveres til Danmark i avidentifisert form. Koden som knytter deg til dine personidentifiserende opplysninger vil ikke bli utlevert.

OPPFØLGINGSPROSJEKT

Avføringslekkasje er en kronisk tilstand og sakralnervemodulering en livslang behandling som krever oppfølging. Opplysningene vil bli lagret for å kunne følge deg opp på best mulig måte. Det vil bli aktuelt med oppfølging både ved 5 og 10 år.

GODKJENNING

Prosjektet har gjennomgått godkjenning hos personvernombudet ved Universitetssykehuset Nord-Norge.

SAMTYKKE TIL DELTAKELSE I PROSJEKTET

JEG ER VILLIG TIL Å DELTA I PROSJEKTET

Sted og dato	Deltakers signatur
	Deltakers navn med trykte bokstaver

Jeg bekrefter å ha gitt informasjon om prosjektet [Tas med hvis ønskelig og bare i de tilfeller der informasjon gis ansikt til ansikt.]

Sted og dato	Signatur
	Rolle i prosjektet

Attachment 5: Personregister UNN

HELSE NORD

Meldeskjema for Personregister UNN

Dokumentansvarlig: Per Bruvold
Godkjent av: Einar Bugge
Gyldig for: UNN HF

Dokumentnummer: SJ0125
Versjon: 2.2

Meldeskjema for forskningsstudier, kvalitetssikring og annen aktivitet som medfører behandling av personopplysninger som er melde- eller konsesjonspliktig i henhold til helseregisterloven og personopplysningsloven med forskrifter.
Utfylt skjema lagres på disk og sendes som vedlegg til e-post sammen med eventuelt informasjonsskriv. Skjemaet sendes til Personvernombudet@unn.no

UNIVERSITETSSYKEHUSET NORD-NORGE

Bruk F11 til å flytte markøren til neste felt. Ved avkryssingsboks: Dobbelklikk på avkryssingsboksen, velg aktiver og trykk på ok.

1 PROSJEKTETS NAVN/TITTEL	
sakralnervemodulering for avføringslekkasje – placebo eller effektiv behandling?	
2 BESKRIV FORMÅLET MED BEHANDLINGEN/PROSJEKTET[1]	
Formålet med studien er å undersøke grad av placeboeffekt ved sakralnervemodulering og å undersøke om suksessraten kan økes med ettstegs implantasjon fremfor den tradisjonelle tostegs prosedyren. Se vedlagt protokoll	
3 INFORMASJON OM SØKEREN	
A. PROSJEKTLEDER	
Navn og stilling: Steen Buntzen, professor overlege	Klinikk/avdeling hvor prosjektet gjennomføres: Gastrokirurgisk avdeling, UNN, Tromsø
Telefonnummer: 77727443	E-postadresse: Steen.buntzen@unn.no
B. STUDENT OPPGAVE/STUDIE	
Er prosjektet et studentstudie?	☐ Ja ☒ Nei
Dersom **Ja** angi studentnavn, telefon og e-postadresse	
C. MULTISENTERSTUDIE	
Er prosjektet en multisenterstudie?	☒ Ja ☐ Nei
Dersom **Ja** angi øvrige virksomheter som deltar:	Aarhus og Hvidovre Hospital, Danmark
Skal noen av disse også ha kopi av elektronisk database/informasjon som etableres i prosjektet?	☒ Ja ☐ Nei
D. ANNEN DATABEHANDLINGSANSVARLIG ENN UNIVERSITETSSYKEHUSET NORD-NORGE HF[2]	
Er prosjektet organisert fra et legemiddelfirma eller annen ekstern virksomhet?	☐ Ja ☒ Nei
Dersom **Ja** angi virksomhetens navn (Kopi av konsesjonen/godkjenning skal sendes personvernombudet, og prosjektet skal meldes til personvernombudet som meldepliktig prosjekt, dvs skjemaet fylles ut med unntak av punkt 5.4):	

[1] Behovet for konsesjonmelding er knyttet opp til hvilket formål man har med behandlingen av personopplysningene. Pasientjournalsystemet er meldt i sin helhet, og har lovhjemlet formål. Når informasjon i journalsystemet skal benyttes til andre formål, kommer behovet for konsesjon, alternativt ny melding, opp, og man må angi formålet med den nye bruken/behandlingen av personopplysningene. Formulering av formålet er derfor viktig. Tilsvarende gjelder for annen innsamling og behandling av pasient-/personopplysninger. Formålet må samsvare med det som beskrives i samtykket fra hver enkelt person som deltar i studien.

[2] For alle studier som startes i regi av Universitetssykehuset Nord-Norge HF (UNN) og som bruker pasientdata som utgår fra UNN vil normalt databehandlingsansvarlig være UNN.

Skal den eksterne også ha koblingsnøkkelen over deltakere? ☐ Ja ☒ Nei

4 RETTSLIG GRUNNLAG FOR BEHANDLING AV PERSONOPPLYSNINGENE[3]

4.1 SAMTYKKE

Skal det innhentes skriftlig samtykke fra den registrerte? ☒ Ja ☐ Nei

Hvis nei, begrunn hvorfor:

Skal det innhentes skriftlig samtykke fra andre enn den registrerte? ☐ Ja ☒ Nei

Hvis ja, av hvem?

Hvis barn inkluderes, angi alder

Skal det søkes om unntak fra taushetsplikt? ☐ Ja ☒ Nei

ELLER

4.2 INTERN KVALITETSSIKRING AV PASIENTBEHANDLING. DETTE ER IKKE KVALIFISERT SOM FORSKNING.

☒ Ja, prosjektet oppfyller helsepersonelloven § 26. Opplysningene må være slettet eller anonymisert før eventuell publisering av resultater. Må publiseres som kvalitetssikring, ikke som forskning. I prinsippet skal all bruk av pasientopplysninger ha en hjemmelsgrunnlag. Kvalitetsstudier er i så måte ikke unntatt dette kravet, men kan fraviles , jf.r. HPL §26. Unntaket må i såfall begrunnes. Personopplysningsloven § 33 4. ledd gir unntak for konsesjon, men krever melding. Pasienter som har reservert seg mot slik bruk av opplysningene skal respekteres.

ELLER

4.3 ANNET SOM HJEMLER MELDING, ANGI ÅRSAK/HJEMMEL:

5 FREMLEGGINGSPLIKT M.M.

☐ Fremleggingsplikt for De regionale komiteer for medisinsk forskningsetikk

☐ Søknadsplikt til Statens legemiddelverk

☐ Registrering i clinicaltrials.gov

☐ Bioteknologiloven kommer til anvendelse (det utføres genetiske undersøkelser hvor deltakeren gis tilbakemelding om resultatet)

☐ UTPRØVING AV MEDISINSK TEKNISK UTSTYR SOM SKAL GODKJENNES AV HELSEDIREKTORATET

6 PROSJEKTPERIODE

Studiestart (dd.mm.åååå):	Studieslutt (dd.mm.åååå)[4]:	Sletting/anonymisering av data (dd.mm.åååå)[5]: 31.12.2024
01.11.2016	31.12.2019	Beskriv hvordan data vil bli slettet/anonymisert: data slettes fem år etter studiens avslutning

7 HUMANT, BIOLOGISK MATERIALE

Medfører prosjektet bruk av humant, biologisk materiale som tas kun for denne studien eller fra en diagnostisk biobank? ☐ Ja ☒ Nei

Dersom ja (OBS FYLL UT FELT NEDENFOR):

Opprettes forskningsbiobanken fra en eksisterende biobank? ☐ Ja ☐ Nei

Hvis **ja**, angi

[3] Som hovedregel skal informert samtykke innhentes.

[4] Når prosjektet er ferdigstilt. Dette inkluderer innsamling, analyse/vurdering, artikkelskrivingkonklusjon.

[5] Data skal lagres i en viss tid etter at prosjektet er ferdigstilt (analyse er gjennomført) for mulig etterprøving. I forskningsstudier skal data lagres 5 år (Norsk Lægemiddelforening) etter publisering, og for klinisk utprøving skal data lagres i minst 15 år etter innsendt sluttrapport til SLV. Enkelte større tidsskrifter krever 10 års oppbevaring for etterprøving. Data kan ikke oppbevares etter prosjektslutt for kvalitetssikring. Dersom forskningsprosjektet er finansiert av Norges forskningsråd, skal sluttrapport og prosjektdata arkiveres på betryggende måte i minimum 10 år etter avslutning av prosjektet (se punkt 5.3 i Norges forskningsråds generelle kontraktsvilkår).

navn på biobank:

biobankregisternr.:

Ansvarshavende person for biobanken (Biobankloven §7):

Forskningsbiobankens innhold (vev, blod og lignende):

Ved avsluttet prosjekt

Hva skjer med biobankmaterialet?: ☐ Materialet destrueres

☐ Materialet føres tilbake til eksisterende biobank

Annet:

Hva skjer med forskningsdata utledet av biobankmaterialet?:

8 DETALJER OM PROSJEKTETS INFORMASJONSBEHANDLING

Det minnes om følgende ansvar ifm innsamling, registrering og bruk av personopplysninger:

- **opplysningene skal være tilstrekkelige og relevante i forhold til formålet med den planlagte databehandling**
- **opplysningene skal være korrekte og oppdaterte**

8.1 TYPE PERSONOPPLYSNINGER BEHANDLINGEN SKAL OMFATTE:

8.1.1

Hvis det benyttes kobling mot forskriftsregulerte registre, som for eksempel fødselsregister, kreftregister eller dødsårsaksregister, eller interne konsesjonsbelagte registre, angi hvilke registre: *NRA (nasjonalt register for anal inkontinens9*

Angi totalt antall inkluderte: 25 ved hvert senter, totalt 75

Angi antall år opplysningene vil bli lagret, inkludert oppbevaring for utlevering: 5

8.1.2 Ikke-sensitive personopplysninger

8.1.2.1 Identifikasjonsopplysninger

☒ Navn, adresse, fødselsdato
☒ Fødselsnummer (11 siffer)
☐ Fingeravtrykk, iris
☐ Annet:

8.1.2.2

8.1.2.3 Opplysninger om tredjepersoner

☐ Navn, adresse, fødselsdato
☐ Fødselsnummer (11 siffer)
☐ Annet:

8.1.2.4 Adferdsopplysninger

☐ Loggføring av adferd
☐ Preferanser (ønsker , behov og lignende)
☐ Annet:

8.1.3 Sensitive personopplysninger (jf. personopplysningsloven § 2 nr. 8)

8.1.3.1 Prosjektet omfatter opplysninger om

☐ rasemessig eller etnisk bakgrunn, eller politisk, filosofisk eller religiøs oppfatning
☐ at en person har vært mistenkt, siktet, tiltalt eller dømt for en straffbar handling
☒ helseforhold
☐ seksuelle forhold
☐ fagforeningstilhørighet

Presiser nærmere:

Behandles spesielt inngripende opplysninger, i såfall hvilke?

8.2 UTVALG

Behandlingen omfatter opplysninger om (beskriv også eventuell kontrollgruppe):

☐ Ansatte i egen virksomhet ☐ Elever/studenter/ barnehagebarn ☒ Pasienter ☐ Tilfeldig utvalgte

☐ Adgangskontrollerte ☐ Medlemmer ☐ Pårørende ☐ Seleksjonsutvalgte

☐ Friske frivillige Dersom det skal gis godtgjørelse, beskriv nærmere:

8.3 INNSAMLING AV OPPLYSNINGENE

Hvordan samles personopplysningene inn?

☒ Manuelt ☐ Elektronisk (bilde og tekst) ☐ Videoopptak ☐ Lydopptak ☐ Annet (beskriv hvordan):

Hvor innhentes personopplysningene fra? ☒ Fra den registrerte selv
☐ Annet (beskriv hvor fra):

Hvordan oppnås kontakt med de som skal inkluderes? Etter utført konservativ behandling, hvor man ikke er kommet i mål, kontaktes pasienten via utredningspoliklinikken, UNN, Tromsø

Hvis innsamling av personopplysninger skal gjøres fra andre virksomheter, hvordan skal dette gjennomføres?

8.4 UTLEVERING AV OPPLYSNINGENE

Blir personopplysningene gjort tilgjengelige/utlevert til andre virksomheter? ☒ Ja ☐ Nei

Dersom ja:

Oppgi mottakerens navn og adresse: Jakob Duelund-Jakobsen, Analfysiologisk klinik Aarhus Sygehus, THG, Tage-Hansens Gade 2, 8000 Århus C

Er virksomheten innenfor EU/EØS: ☒ Ja ☐ Nei

Vil den eksterne virksomheten brukes som ressurs/laboratorium/annet for denne studien? ☐ Ja ☒ Nei

Vil mottakeren ha eget formål/studie? ☒ Ja ☐ Nei

Hva blir overført?

☐ Informasjon med navn, personnummer eller annet som entydig angir det enkelte individ

☐ Anonymisert informasjon

☒ Avidentifisert informasjon. Forklar i så fall hvordan krysireferanseliste beskyttes dersom dette ikke er likt som i pkt 8.6:

Hvordan oversendes informasjonen?

☐ Personlig overlevering

☐ CD sendt med rekommandert post

☒ Registreres på sikret web-side hos mottaker

☐ Legges ut på sikret område for nedlasting av mottaker

☒ Annet Nærmere beskrivelse: Initialt samles data på papir som oppbevares i låst skrivebords På låst kontor. Opplysningene vil i ettertid bli registrert på en sikret webside, deretter vil spørreskema i papir makuleres.

8.5 LAGRING OG BEHANDLING AV OPPLYSNINGER

Hvordan lagres opplysningene?

☒ Forskningsserver på UNN

☒ O:\Forskning

☐ På frittstående PC. Forklar hvordan denne sikres mot uvedkommende:

☐ På papir. Forklar hvordan dette sikres mot uvedkommende:

☐ På video, tape eller annet opptak. Beskriv hvordan dette er sikret og om personen kan identifiseres:

☐ Annet (for eksempel andre virksomheters nettverk)[6]. Forklar:

Hvem skal ha tilgang til datasene?

Navn/ Brukerkonto (eks: Per Bruvold/ edbpeb)

Mona Rydningen, Steen Buntzen, Stig Norderval; SBU006, KIRSTN, mr0301unn

Gastroenetrologisk kirurgisk Avdeling, UNN, Tromsø

8.6 GJENFINNING AV OPPLYSNINGENE

Hvordan gjenfinnes opplysningene? (Bruk av direkte identifisering som personnummer og navn skal forsøkes unngått)

☐ Opplysningene lagres med navn, personnummer eller annet som entydig angir det enkelte individ

☒ Opplysningene lagres avidentifisert (ved bruk av krysslister, kodelister, løpenummer eller lignende)

Hvordan er krysslister/kodelister beskyttet/lagret? Forklar: se punkt 8.5

9 DATO FOR UTFYLLING

Meldeskjemaet er forelagt klinikk-/avdelingssjef / forskningsansvarlig ☒ Ja

Sted og dato	Utfylt av:
Unn Tromsø 26.10.16	Steen Buntzen, Prof. , overlege, Gastrokir avd, UNN Tromsø

[6] Krever gjennomføring og godkjenning av risikovurdering.

Grade 1

<table>
<tr><td colspan="3">Reference: Thin NN, Horrocks EJ, Hotouras A, Palit S, Thaha MA, Chan CL, et al. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. Br J Surg. 2013;100(11):1430-47.</td><td>Design: Systematic review
Level of documentation: 2b
GRADE: B</td></tr>
<tr><td>Objective</td><td>Material and method</td><td>Results</td><td>Discussion/comments</td></tr>
<tr><td>Various neuromodulation therapies have been used in treating patients with faecal incontinence (FI) over the past 18 years, and sacral nerve stimulation (SNS) is the most recognised method. Other methods are percutaneous tibial nerve stimulation (PTNS) and transcutaneous tibial nerve stimulation (TTNS)

The goal of this systematic review is to evaluate the clinical effectiveness of the various types of neuromodulation in treating FI.

Conclusion

SNS is a useful therapy in treating patients with FI and is proven to have a long-term effect. PTNS is proven to be efficient in treating FI, but no evidence supports its validity after 12 months. There is still uncertainty of the clinical effectiveness of TTNS due to lacking evidence. Standardization of outcome measures is recommended for a more accurate comparison in research on this topic.

Country

Various

Year of data collection

January 1995 – July 2012</td><td>This was a systematic review that utilized Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework.

PubMed, MEDLINE, Embase and Evidence-Based Medicine reviews was used in reviewing literature.

Inclusion criteria was studies from 1995 – 2012 with permanent SNS, PTNS, and TTNS treatment. Non-English papers were only used if they provided an abstract with appropriate information. Each study included needed to have at least 10 patients treated with permanent neuromodulation, and had to provide at least one outcome measure, as well as a clear follow-up interval. Exclusion was PNE or chronic testing phase of SNS.

Primary outcome was the success rate of the given therapy where FI-episodes were reduced with ≥50%. Secondary outcome was cure rates (100% reduction in FI-episodes).</td><td>Authors used the PRIMSA-framework in order to keep a clear guidance on the methodology to diminish bias and provides for dependable conclusions.

61/321 articles on SNS were included in this review. 7 articles on PTNS and 4 on TTNS were also included.

Intention-to-treat, the median success rates for SNS were for short terms 63, medium terms 58 and 54 for long term. For PTNS the success rate was 59% after 12 months of follow-up. It was shown that SNS lost 10% of its effectiveness after 5 years.

There was an increase in quality-of-life measures and Cleveland Clinic Incontinence Score in all of the neuromodulation techniques.</td><td>This review presents summaries of the available therapy options in neuromodulation and the scores on short-, medium- and long-term basis. With a proven effectiveness of PTNS, it can be seen as a more cost-effective alternative in treating patients with FI without improvement after a conservative approach.

Authors demonstrate a table of the different studies included in this review, and it shows that the majority of the studies are case series.

Authors identify the risk of selection bias due to inclusion criteria of studies containing >10 patients, as well as only English written articles. They argue that this prevents bias as it eliminates patient subpopulations and inexperienced investigators.

There was a big heterogeneity in outcome measure, as well as different reporting styles. Authors comment that this made statistical formal synthesis impossible to accomplish.

The evidence base for PTNS and TTNS was poor since it consisted mostly of case series involving few patients and a limited follow-up period.

Two of the authors are advisers to Medtronic, a medical company producing stimulators in SNS therapy.</td></tr>
</table>

Grade 2

<table>
<tr><td colspan="3">Reference: Knowles CH, Horrocks EJ, Bremner SA, Stevens N, Norton C, O'Connell PR, et al. Percutaneous tibial nerve stimulation versus sham electrical stimulation for the treatment of faecal incontinence in adults (CONFIDeNT): a double-blind, multicentre, pragmatic, parallel-group, randomised controlled trial. Lancet. 2015;386(10004):1640-8.</td><td>Design: RCT</td></tr>
<tr><td colspan="3"></td><td>Level of documentation: 1b</td></tr>
<tr><td colspan="3"></td><td>GRADE: C</td></tr>
<tr><th>Objective</th><th>Material and method</th><th>Results</th><th>Discussion/comments</th></tr>
<tr>
<td>Percutaneous tibial nerve stimulation (PTNS) is an alternative to sacral nerve stimulation that is believed to be less invasive, more cost effective and is thought to lead to similar changes in the anorectal neuromuscular function in patients with faecal incontinence (FI). Data suggests it has beneficial outcomes in 50-80% of patients treated, but its effectiveness has never been investigated to sham electical stimulation (placebo). The study wants to investigate short-term afficacy of PTNS compared to sham electrical stimulation in adults with FI.
Conclusion
PTNS was not proven to have better clinical benefit compared to sham electrical stimulation treating adults with FI.
Country
United Kingdom
Year of data collection
2012-2013</td>
<td>The study was a double-blind, multicentre, pragmatic, parallel-group, RCT that included 17 hospital units in the UK. Inclusion criteria was participants over 18 years of age with FI where a conservative approach has failed.

Patients were randomly assigned to either PTNS or sham stimulation once per week for 12 weeks. Primary outcome was a clinical response to treatment (>50% reduction in FI-episodes per week). This was evaluated after 12 treatment sessions by patients´ own bowel-habit diaries.</td>
<td>227 out of 373 screed patients were randomly assigned into two groups to receive either PTNS (n=115) or sham stimulation (n=112). 12 patients withdrew from the study as they were not able to commit to the treatment programme, 2 patients withdrew due to unrelated problems.

<table>
<tr><th></th><th>PTNS</th><th>Sham</th><th>Adjusted odds ratio (95% CI)</th><th>p-value</th></tr>
<tr><td>≥ 25% reduction</td><td>51/103 (50%)</td><td>46/102 (45%)</td><td>1.264 (0.730-2.190)</td><td>0.404</td></tr>
<tr><td>≥ 50% reduction</td><td>39/103 (38%)</td><td>32/102 (31%)</td><td>1.283 (0.722-2.281)</td><td>0.396</td></tr>
<tr><td>≥ 75% reduction</td><td>26/103 (25%)</td><td>17/102 (17%)</td><td>1.615 (0.770-3.388)</td><td>0.205</td></tr>
<tr><td>100% reduction</td><td>11/103 (11%)</td><td>7/102(7%)</td><td>1.635 (0.592-4.514)</td><td>0.344</td></tr>
</table>

38% of the patients had a fully completed bowel-habit diary in the PTNS group, and showed to have a >50% reduction in weekly FI episodes, compared to 31% of the patients in the sham group.

Patients and investigators involved in evaluation of clinical outcome were masked to treatment allocation during the course of the involvement of the trial. Investigators performing the treatment procedure was not masked.</td>
<td>Authors comment that placebo effect is high in patients with chronic deliberating gastrointestinal illnesses as they have higher levels of expectations. The authors had predicted this (estimated 35% vs. 31% in the study). Bowel-habit diaries can also lead to bias if unmasked.

Authors discuss limitations that might relate to the negative outcome, such as a undefined outcome measure for FI. Prior to the study, all patients had received conservative therapy which was not formally standardized which might have created a variety in baseline characteristics. Also, patients could still use antidiarrheal drugs during the course of the study, and could ultimately affect the results of the study.

Authors conclude that there is no significant difference in treating patients with PTNS compared to sham electrical stimulation. Previous systematic reviews have proven the contrary. This study focused on short term outcome, and therefore authors comment that if would be appropriate with further studies exploring long-term effects, as well as benefits in patients subgroups.</td>
</tr>
</table>

Grade 3

<table>
<tr><td colspan="3">Reference: Vallet C, Parc Y, Lupinacci R, Shields C, Parc R, Tiret E. Sacral nerve stimulation for faecal incontinence: response rate, satisfaction and the value of preoperative investigation in patient selection. Colorectal Dis. 2010;12(3):247-53.</td><td>Design: Prospective cohort study
Level of documentation: 2b
GRADE: B</td></tr>
<tr><th>Objective</th><th>Material and method</th><th>Results</th><th>Discussion/comments</th></tr>
<tr><td>Prior to treatment with sacral nerve stimulation (SNS) for faecal incontinence (FI), patients were examined with electrophysiologic, dynamic and morphologic tests. The objective of the study was to assess the value of these tests in patient selection to predict who would have greatest benefit of the treatment.

Conclusion
The study concludes that tests for faecal incontinence prior to treatment with SNS, does not facilitate patient selection, nor can it predict outcome.

Country
France

Year of data collection
June 2001 – January 2007</td><td>Patients were included in the study and treated with SNS if they were between 18-75 years of age, had involuntary passage of solid or liquid faces minimum once per week, and refractory to medical treatment and biofeedback therapy. Previous surgery, malformations, IBD, stoma, chronic diarrhoea, and likelihood of non-compliance were exclusion criteria. Data was collected prospectively.

Preoperative evaluation was based on patient characteristics. Physical examination and bowel habit diaries were completed over at least 15 days. Patients were also scored on urgency and the severity of FI with the Cleveland Clinic Continence scoring System. Endoanal ultrasonography, anorectal manovolumometry and electrophysiologic perineal examinations were also performed in every patient. Initial assessment lasted 10 days after implementation of temporary sacral nerve electrodes. Selection for permanent implantation was based on patient satisfaction and improvement based on bowel habit diaries. Patients were followed up at 3 months by 6 monthly intervals.

For statistics, the Mann-Witney U-test, Student’s t-test and X^2 tests were used. For analysis, Statview Software was used.</td><td>41 females and 4 males with FI underwent treatment with SNS. Of the 45 patients, 10 (22%) failed the temporary test, while testing was unsuccessful in 3 (7%). Temporary stimulation was effective in 32 patients (71%) and proceeded to permanent implantation. 23 patients (51%) had a functioning neuromodulator after 33 months (median follow-up).

There was no statistically significant difference between the preoperative evaluation of patients undergoing permanent implantation (n = 32) and not (n = 13), and those with (n = 23) or without (n = 13) a functioning stimulator.

The results were considered good in 12 of the 23 patients with a functioning stimulator. 5 patients reported satisfactory result and 6 reported poor result. No statistically significant difference in patient characteristics was proved between patients with a good result (n = 12) and the rest (n = 32).</td><td>Patients included in the study had met the criteria of FI and was refractory to other medical treatment. The study population consisted of men and women separated in to groups based on aetiology, which was obstetric or surgical trauma, idiopathic, neurologic or radiotherapy. Data was collected prospectively with follow-up after 3 months and at 6 monthly intervals subsequently, with a mean follow-up time of 3 years or more. The study describes well the comparison in patient satisfaction.

The authors discuss the complication rate of 34% and justifies the possible causes well. They also bring up the short test phase of 10 days, which is at the shorter end of the range of 10-21 days recommended by other researchers on this topic.

The authors also discuss how a preoperative selection would be cost-effective, but how they failed with the pre-treatment investigations used in this study.

The authors refer to other studies that suggest that there are other methods of predicting outcome with temporary stimulation, but a discrepancy between objective success and subjective satisfaction has to be considered nevertheless.</td></tr>
</table>

Grade 4

Reference: Duelund-Jakobsen J, van Wunnik B, Buntzen S, Lundby L, Baeten C, Laurberg S. Functional results and patient satisfaction with sacral nerve stimulation for idiopathic faecal incontinence. Colorectal Dis. 2012;14(6):753-9.	**Design:** Cohort study	
	Level of documentation:	2b
	GRADE	B

Objective	Material and methods	Results	Discussion/comments
Patient satisfaction has never been considered as a method of evaluation in treatment with sacral nerve stimulation (SNS). This study investigates patients with faecal incontinence (FI) treated with SNS to see if there is a relationship between patient satisfaction and clinical outcome assessed by symptom scores and bowel-habit diaries.	Patients treated with SNS for idiopathic faecal incontinence (IFI) in Denmark and The Netherlands were included in the study. Patients were considered to have IFI if they had no previous history of anorectal surgery, neurological disorders, diabetes, spinal cord injury, thyroid diseases or larger sphincter defects. A total of 158 patients were considered to have IFI out of the total of 342 patients with faecal incontinence (remaining non-idiopathic patients). 129 of the 158 IFI patients were receiving active SNS therapy at the most recent follow-up, and these data were compared to baseline data from the European Sacral Nerve Stimulation Database and the Maastricht University Medical Centre local database. Follow-up was performed at 1, 3, 6 and 12 months after implantation and yearly thereafter. Treatment outcome was evaluated based on incontinence/bowel scores and patients were asked if they were satisfied with the treatment. Mann-Whitney U-test and Fisher´s exact test were used for statistical comparison between groups. Correlation between improvement in incontinence episodes and patient self-reported satisfaction with bowel function, social function and quality of life was assessed by the Pearson correlation coefficient and 95% CI.	The results showed that the number of FI episodes were undoubtedly related to patient satisfaction. Patients that obtained complete continence after SNS treatment were all satisfied. Satisfaction rate decreased with an increasing number of FI episodes. Interestingly, 46%of patients with more FI episodes at the time of follow-up than at baseline were still satisfied. These patients reported a better social life after SNS treatment, but previous evaluation would consider these patients to have failed outcome. A reduction of more than 50% in FI episodes was reported in 74.7% of the patients receiving active SNS treatment, where 10.3% of them were not satisfied after a median of 46 months of follow-up.	The patients with IFI were clearly selected with justified requirements out of a large group of 342 patients with FI. The patients were a part of an international two-centre retrospective analysis of prospectively collected data in Denmark and The Netherlands. The authors clearly stated the definition of IFI and the exclusion criteria. A total of 129 patients were receiving active treatment with SNS, and the remaining 29 were identified. A systematic flow chart was presented to identify patients lost through the study and why. Patients were followed-up with a median of 46 months. The authors state that a weakness with this study was that it was not possible to evaluate patient satisfaction and the relation to the bowel-habit diary as a function of time. The authors use both intention-to-treat and per-protocol analysis and explains that the method of analysis has to be clearly stated in the future as it would make comparison from different centres more accurate. The authors present four options on how to optimize functional outcome and improve patient satisfaction with SNS therapy. Social behaviour is not addressed in the bowel-habit diary. The authors recommend that this should be included in future research as this study showed that SNS treatment increased patient satisfaction despite an increase in incontinence episodes at follow-up, compared to baseline.
Conclusion The authors conclude that there is a clear relationship between improved continence and patient satisfaction. 57.3% of patients with SNS therapy were satisfied at follow-up, and 46% of patients with more FI episodes at follow-up then at baseline were also satisfied. Therefore, bowel-habit diaries and bowel scores cannot be the sole evaluation method for functional outcome of SNS therapy.			
Country Denmark, The Netherlands			
Year of data collection 2000 - 2009			

Grade 5

<table>
<tr><td colspan="3">Reference: Rydningen M, Dehli T, Wilsgaard T, Rydning A, Kumle M, Lindsetmo RO, et al. Sacral neuromodulation compared with injection of bulking agents for faecal incontinence following obstetric anal sphincter injury - a randomized controlled trial. Colorectal Dis. 2017;19(5):O134-O44.</td><td>Design: RCT</td></tr>
<tr><td colspan="3"></td><td>Level of documentation: 1b</td></tr>
<tr><td colspan="3"></td><td>GRADE: B</td></tr>
<tr><td>Objective</td><td>Material and method</td><td>Results</td><td>Discussion/comments</td></tr>
<tr><td>The study aims to compare the effects of sacral nerve modulation (SNM) versus submucosal injection of collagen (Permacol) in women with previous obstetric anal sphincter injuries (OASIS) that has led to faecal incontinence (FI).

Conclusion

Authors conclude that SNM is a better alternative in treatment of FI in women with OASIS than Permacol. This is based on reduction in St. Mark’s score and scores evaluating quality of life and urinary incontinence.

Permacol should not be considered when treating women with FI with a pervious history of OASIS.

Country

Norway

Year of data collection

2012-2014</td><td>The study included women with FI related to OASIS (3rd or 4th degree tears) from two different hospitals in Norway.

Inclusion criteria was FI defined by a St. Mark’s score >8 and weekly episodes FI despite conservative management.

Women with a positive percutaneous nerve evaluation test (3 weeks testing with ≥50% reduction in FI episodes) were randomly divided into a SNM-group and a Permacol-group.

A change in St. Mark´s score between baseline and 6 months was the primary outcome, and changes in scores of quality of life and urinary incontinence was secondary outcome.</td><td>58 women was eligible for the study, where 30 were treated with SNM and 28 were treated with Permacol.

In the SNM-group there was an 11.2 (SD 5.3) reduction in St. Mark’s score between baseline and 6 months. The Permacol-group showed a reduction of 2.3 (SD 5.0) in St. Mark’s score.

There was also a reduction in St. Mark’s score with regards to the secondary outcomes (quality of life and urinary incontinence).</td><td>This is the first single blinded, parallel RCT that compares SNM and perianal bulking injections for treatment of FI following OASIS. The objective of the study is well defined. The women with a positive PNE-test were randomized into two groups (n = 30, n = 28), and then treated with either SNM or Permacol.

Eligible women included in the study are presented in a flow-chart, and the authors justifies the women not included to the enrolment and randomization.

The minor adverse effects of the two treatments are accounted for.

Authors identify bias in favour of SNM since a positive PNE is an inclusion criteria. They describe additional analysis performed to overcome inherent selection bias via a worst-case scenario, which did not affect outcome.

It is also mentioned that there was an imbalance in recruitment between the two hospitals, but an additional sensitivity analysis did not show change in outcome.

The study focused on FI, but discovered that SNM could be used in treatment for double incontinence, as well as sexual dysfunction.</td></tr>
</table>