NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of self-expanding implant insertion into the intersphincteric space for faecal incontinence

Faecal incontinence can happen when 2 rings of muscle (sphincters) around the anus cannot control the passing of faeces. Faeces can leak out or pass suddenly, without control. In this procedure small implants (usually 6 or 10) are inserted next to each other, through small cuts, into tissue between the 2 sphincters (the intersphincteric space). The implants expand and press together, forming a ring that creates an artificial sphincter. The aim is to give the person more control over passing faeces.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2019 and updated in November 2020.

Procedure name

- Self-expanding implant insertion into the intersphincteric space for faecal incontinence.

Professional societies

- Association of Coloproctology of Great Britain and Ireland
- The Pelvic Floor Society.

Description of the procedure

Indications and current treatment

Faecal incontinence is an inability to control bowel movements, resulting in the involuntary passage of faeces. The process of defaecation and its control is complex. Causes of incontinence include problems in the colon and rectum (including constipation and diarrhoea), problems with the sphincter muscles (such as damage caused by childbirth or surgery), or nerve damage (such as multiple sclerosis, stroke or spina bifida). Faecal incontinence can also be caused by loss of higher level cerebral control in conditions such as dementia or severe learning disability.

NICE's guidance on faecal incontinence in adults states that there is no consensus on methods of classifying the symptoms and causes of faecal incontinence. It is most commonly classified according to symptom, character of the leakage, patient group or presumed primary underlying cause. For many people faecal incontinence is the result of a complex interplay of contributing factors, some of which may be relatively simple to reverse. Therefore, a detailed initial assessment and structured approach to management is needed, starting with addressing reversible factors and, only if this fails to restore continence, progressing to specialised management.

Initial management of faecal incontinence includes interventions related to diet, bowel habit and toilet access, and medication. Specialised management options depend on the underlying cause and include pelvic floor muscle training, bowel retraining, specialist dietary assessment and management, biofeedback, electrical stimulation and rectal irrigation. The main surgical treatment is anal sphincter repair. Sacral nerve stimulation may be offered to people for whom sphincter surgery is not appropriate. If a trial of sacral nerve stimulation is unsuccessful, a neosphincter may be considered (stimulated graciloplasty or an artificial anal sphincter).

What the procedure involves

Self-expanding implant insertion into the intersphincteric space for faecal incontinence is done using local or general anaesthesia, with ultrasound guidance. About 6 to 10 small (2 mm) incisions are made in the perianal skin, equidistant to each other, about 2 cm from the anal margin. An introducer is inserted into each incision in turn, pushed through a short subcutaneous tunnel and into the intersphincteric space. The implant is deployed in the desired position within the intersphincteric space. This is repeated around the entire circumference of the internal anal sphincter. The incisions are sutured with resorbable material. Patients are advised to avoid any heavy physical activity for a few days after surgery. One type of implant is a solid polyacrylonitrile cylinder (non-biological) that becomes thicker, shorter and softer over 1 to 2 days after implantation. The implants expand and press together, forming a ring that creates an artificial sphincter. The aim is to give the person more control over their ability to control defaecation.

Outcome measures

Wexner Continence Grading Scale (Cleveland Clinic Fecal Incontinence) score

The Wexner Continence Grading Scale (Cleveland Clinic Fecal Incontinence) score is a 5-point scale that measures incontinence over 4 weeks. The 5 items measured are: incontinence of solid stool, incontinence of liquid stool, incontinence of flatus, the need to wear a pad, and lifestyle alterations. Each item is scored from 0 to 4, depending on the frequency, from always or daily (4) to never (0). The sum of the 5 items gives the total score, which ranges from 0 indicating full continence, to 20 indicating complete incontinence.

St Mark's (Vaizey) score

The St Mark's (Vaizey) score is an 8-point scale. The 8 items measured are incontinence of solid stool, incontinence of liquid stool, incontinence of flatus, alteration in lifestyle, the need to wear a pad or plug, taking constipating medicines, lack of ability to control defaecation for 15 minutes, and frequency of faecal incontinence episodes. The total score ranges from 0 to 24, with 0 indicating full continence and 24 indicating complete incontinence.

Fecal Incontinence Quality of Life scale

The Fecal Incontinence Quality of Life Scale has 29 items from 4 scales. These are lifestyle (10 items), coping and behaviour (9 items), depression and self-perception (7 items), and embarrassment (3 items). Each of the scale's scores range from 1 to 5 and are the average response to all items on the scale. A lower score shows a lower functional status and a worse quality of life.

Efficacy summary

Improved continence

In a case series of 54 patients, 56% (30/54) of patients' faecal incontinence improved at least 75% and 13% (7/54) of patients had full anal continence. The median number of episodes of soiling reduced from 4.0 per week before the procedure to 0.2 per week at 1-year follow-up ($p<0.001$). The median number of incontinence episodes for gas, liquid and solid stool reduced from 7.0, 0.8 and 0.5 per week, respectively, to 0 per week for all 3 at 1-year follow-up ($p=0.015$, 0.003 and 0.011 respectively). The Cleveland Clinic Fecal Incontinence (CCFI), Vaizey and American Medical Systems (AMS) scores improved from 13, 15 and 94 before the procedure to 4, 4 and 32.5 respectively at 1-year follow-up ($p<0.001$ for all 3). At baseline, 37% (20/54) of patients reported soiling at least once a day but at 1-year follow-up, 85% (46/54) of patients had soiling never or less than once a week. At baseline, 57% (31/54) of patients could defer defaecation for less than 5 minutes but at 1-year follow-up, 80% (43/54) could defer defaecation for at least 5 minutes.[1]

In a case series of 49 patients, 48% (23/49) of patients were considered to have responded to the procedure (defined as improvements of at least 50% of the baseline Vaizey score during the first 6 months). The mean Vaizey score improved from 13.5 at baseline to 7.7 at a mean follow-up of 2.7 years ($p<0.001$).[2]

In a case series of 14 patients, the mean number of major faecal incontinence episodes per week reduced from 7.1 before the procedure to 0.4 at a mean follow-up of 33.5 months. The proportion of patients with no soiling improved from 21% (3/14) to 69% (9/13, $p=0.028$). The ability to defer defaecation improved from 6 minutes to 22 minutes ($p<0.031$). The mean CCFI and Vaizey scores improved from 12.7 and 15.4 at baseline to 5.1 and 6.9 at the last follow-up ($p<0.001$ and 0.01 respectively).[3]

In a case series of 13 patients, mean CCFI score improved from 12.46 before the procedure to 8.91 at 6-month follow-up ($p<0.05$). The total number of episodes of faecal incontinence per week reduced from 5.38 to 1.57 ($p<0.05$).[4]

In a case series of 16 patients, the mean CCFI, St Mark's and AMS scores improved from 11, 16 and 82 before the procedure to 3, 6 and 43 at 12-month follow-up ($p=0.001$, <0.001 and <0.001, respectively). The proportion of patients who could defer defaecation for more than 5 minutes increased from 25% before the procedure (4/16) to 75% after the procedure (12/16, $p=0.25$).[6]

In a case series of 7 patients, the mean number of major faecal incontinence episodes per month reduced from 6.8 to 3.0 at 1-month follow-up, 4.1 at 3-month follow-up and 5.1 at 12-month follow-up ($p<0.05$). The mean Wexner scale score improved from 16.0 at baseline to 10.1 at 12-month follow-up ($p<0.01$). Clinical improvement (defined as a minimum of 50% reduction in the Wexner scale score or the rate of episodes of incontinence relative to baseline) was reported for 43% (3/7) of patients.[7]

In a case series of 42 patients with mean follow-up of 16 months, 5 patients (12%) became fully continent. The proportion of patients who never or rarely experienced post-defaecation soiling episodes increased from 7% (3/42) at baseline to 55% (23/42) at last follow-up ($p<0.001$). The CCFI and Vaizey scores improved from 12.0 and 14.6 at baseline to 7.6 and 10.2 at last follow-up ($p<0.001$ and 0.001).[9]

In a case series of 20 patients, the mean CCFI score improved from 12.4 at baseline to 4.9 at 36-month follow-up ($p<0.0001$).[11] In a case series of 27 patients with median follow-up of 12 months, the St Mark's incontinence scale score changed from 15 at baseline to 10 after the procedure ($p<0.00016$). Of the

27 patients, 14 (52%) had a clinically meaningful improvement as defined by a 50% or more reduction in symptom score.[12]

Quality of life

In the case series of 54 patients, all Fecal Incontinence Quality of Life (FIQL) questionnaire items (lifestyle, coping and behaviour, depression and self-perception, and embarrassment) were statistically significantly improved at 1 year (p=0.01, p=0.001, p=0.029, p=0.001 respectively). There were no statistically significant differences in generic health status at 1 year compared with baseline (measured by SF-36 questionnaire).[1]

In the case series of 14 patients, there were statistically significant increases in the mean scores of physical function (p=0.002), role physical (p=0.001), general health (p=0.01), social function (p<0.001), role emotional (p<0.001) and mental health domains (p=0.001) for the SF-36 at the last follow-up (mean 33.5 months). All FIQL questionnaire items showed a statistically significant improvement in values at final follow-up compared with baseline. These were lifestyle (p=0.001), coping and behaviour (p<0.001), depression and self-perception (p<0.001) and embarrassment (p=0.001).[3]

In the case series of 13 patients, there were no statistically significant changes in FIQL subgroup scores at 6-month follow-up.[4] In the case series of 16 patients, the FIQL scores for lifestyle, coping and behaviour, self-perception and embarrassment improved from 2.6, 1.7, 3.2 and 2.3 at baseline to 3.3, 2.4, 3.8, and 3.2 at 12-month follow-up, respectively (p=0.10, 0.06. 0.03 and 0.06).[6]

Anorectal pressure measurement

In the case series of 14 patients, there were no statistically significant changes in mean anal manometric values during follow-up compared with baseline.[3] In the case series of 13 patients, mean anorectal manometry maximum resting pressure increased from 21.3 millimetres of mercury (mmHg) before the procedure to 31.8 mmHg at 6-month follow-up (p<0.05). The mean anorectal manometry maximum squeeze pressure was 83 mmHg before the procedure and 88.5 mmHg after (p=not significant).[4]

In the case series of 16 patients, intraluminal pressure during average maximum voluntary contraction increased from 45.8 mmHg before the procedure to 60.4 mmHg at 12-month follow-up (p=0.017). Muscle tension increased from 233.2 to 490.8 millinewtons per cm^2 (p<0.001).[6]

Safety summary

Infection

Implant migration and perianal abscess were described in 1 patient in a case report. The patient presented with perianal pain and swelling 2 years after the implants were inserted. A perianal abscess was diagnosed, which was treated by incision and drainage (1 of the implants was described as popping out of the abscess cavity).[8]

Implant extrusion or dislodgement

Intraoperative extrusion was reported in 6% (3/54) of patients in the case series of 54 patients. In these patients, a single implant came out spontaneously immediately after placement and was replaced. Dislodgment of a single implant during follow-up was reported in 6% (3/54) of patients in the same study.[1] Migration of implants during follow-up happened to 52% (25/49) of patients in the case series of 49 patients.[2] Implant extrusion after 1 month was reported in 15.4% (2/13) of patients in the case series of 13 patients. Anterior dislocation (an implant not at the same level as other implants) was detected in 1 patient 6 months after the procedure.[4] Implant displacement was reported in 71% (5/7) of patients) at 3 months in the case series of 7 patients. This was 57% (24/42) of the implants. At 1-year follow-up there was no migration of the other implants but 6 of the implants that had already been noted as displaced at 3 months had migrated further. One patient needed to have an implant removed because it was protruding through the perianal skin, almost at the point of spontaneous extrusion.[7]

Anal discomfort or pain

Anal discomfort or pain was reported in 13% (7/54) of patients in the case series of 54 patients. The mean duration was 4.4 days and it was treated with non-steroidal anti-inflammatory drugs.[1] Anal discomfort was reported in 1 patient 1 week after the procedure in the case series of 10 patients. This was attributed to a 1 cm distal dislocation of a single implant within the intersphincteric space. It was treated with local and systemic painkillers and symptoms resolved 1 week later.[5] Pain or discomfort was reported in 1 patient in the case series of 7 patients. The patient needed analgesia for 4 days.[7]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and

about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts listed sepsis, migration of implant and pain as anecdotal adverse events. They considered that the following was a theoretical adverse event: obstructive defaecation syndrome.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to self-expanding implant insertion into the intersphincteric space for faecal incontinence. The following databases were searched, covering the period from their start to 21 September 2020: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with faecal incontinence.
Intervention/test	Self-expanding implant insertion.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 270 patients from 10 case series, 1 non-randomised comparative study of 2 devices and 1 case report.[1 to 12]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on self-expanding implant insertion into the intersphincteric space for faecal incontinence

Study 1 Ratto C (2016)

Details

Study type	**Case series**
Country	Italy, Denmark, Austria, Germany
Recruitment period	2011 to 2013
Study population and number	**n=54** Patients with faecal incontinence
Age and sex	Mean 66 years; 69% (37/54) female
Patient selection criteria	Age between 18 and 80 years; faecal incontinence onset at least 6 months previously; faecal incontinence episodes (soiling or incontinence to liquid or solid stool) happening more than once a week and resistant to other conservative treatments (pharmacological and behavioural); endoanal ultrasonography (EAUS) evaluation showing intact anal sphincters, or a lesion only of the internal anal sphincter, with a maximum circumferential extension of 60°. Exclusion criteria: EAUS evidence of an internal anal sphincter lesion larger than 60° or any external anal sphincter lesion; previous anal surgery for faecal incontinence (including injection or implantation of another bulking agent); active perianal sepsis; severe anal scarring; inflammatory bowel disease with anorectal involvement; anal or rectal cancer undergoing active treatment; uncontrolled endocrine, metabolic or neurological disease; congenital anorectal malformation.
Technique	Device: Gatekeeper (THD SpA, Italy) The procedure was done under local, locoregional or general anaesthesia. Six skin incisions (2 mm) were made in the perianal area, 2 cm from the anal verge and 6 implants were inserted. Antibiotics were prescribed for 3 days. Patients were advised to avoid any anal trauma and distress, as well as sexual intercourse for the first 48 hours after implantation.
Follow-up	**1 year**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: No patients were lost to follow-up. Clinical evaluation and EAUS were scheduled at 1, 3 and 12 months after surgery.

Study design issues: Prospective multicentre case series. For each follow-up visit, patients kept a 14-day continence diary and the Cleveland Clinic Faecal Incontinence Score (CCFIS; ranging from 0 to 20), Vaizey score (ranging from 0 to 24) and American Medical Systems score (AMS; ranging from 0 to 120) were determined. Clinical success was defined as an improvement of 75% or more in all the following faecal incontinence parameters: total number of faecal incontinence episodes per week, number of episodes of soiling per week, number of episodes of incontinence to gas per week, number of episodes of incontinence to liquid per week, number of episodes of incontinence to solid stool per week.

Study population issues: Mean duration of faecal incontinence was 3 years (range 1 to 19). The median CCFIS was 12 at baseline (range 3 to 20). There was no sphincter injury in 89% (48/54) of patients and an isolated internal anal sphincter defect (range 30 to 60°) in 6 (11%) patients at baseline.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **54**

At 1-year follow-up, 56% (30/54) of patients had improvement of at least 75% in all faecal incontinence parameters and 7 patients (13%) obtained full anal continence.

At baseline, 37% (20/54) of patients reported soiling at least once a day but at 1-year follow-up, 85% (46/54) of patients had soiling never or less than once a week.

At baseline, 57% (31/54) of patients could defer defaecation for less than 5 minutes but at 1-year follow-up, 80% (43/54) of patients could defer defaecation for at least 5 minutes.

Number of episodes of soiling and incontinence per week and faecal incontinence severity scores for patients with at least 75% improvement (n=30); median (range)

	Baseline	1 month	3 months	1 year	p
Soiling	4.0 (0 to 49)	0.4 (0 to 22)	0.3 (0 to 20)	0.2 (0 to 21)	<0.001
Gas	7.0 (0 to 49)	2.5 (0 to 49)	1.0 (0 to 49)	0 (0 to 49)	0.015
Liquid stool	0.8 (0 to 49)	0 (0 to 3)	0 (0 to 4)	0 (0 to 21)	0.003
Solid stool	0.5 (0 to 49)	0 (0 to 3)	0 (0 to 4)	0 (0 to 21)	0.011
CCFIS	13 (3 to 20)	5 (0 to 17)	4 (0 to 19)	4 (0 to 22)	<0.001
Vaizey score	15 (3 to 24)	5 (0 to 19)	4 (0 to 19)	4 (0 to 22)	<0.001
AMS score	94 (28 to 120)	40.5 (0 to 94)	32 (0 to 182)	32.5 (0 to 120)	<0.001

Number of episodes of soiling and incontinence per week and faecal incontinence severity scores for patients with less than 75% improvement (n=24); median (range)

	Baseline	1 month	3 months	1 year	p
Soiling	2.5 (0 to 21)	1.5 (0 to 21)	0.8 (0 to 14)	0 (0 to 10)	0.217
Gas	10 (0 to 40)	2.5 (0 to 35)	5.5 (0 to 35)	0.1 (0 to 35)	0.114
Liquid stool	1 (0 to 20)	0 (0 to 3)	0 (0 to 3)	0 (0 to 4)	0.008
Solid stool	0 (0 to 3)	0 (0 to 0.5)	0 (0 to 1)	0 (0 to 7)	0.015
CCFIS	9 (3 to 20)	7 (0 to 16)	6 (0 to 16)	5 (1 to 16)	0.002
Vaizey score	12 (5 to 21)	8.5 (0 to 18)	8.5 (0 to 18)	8 (2 to 17)	0.012
AMS score	82 (27 to 113)	64.5 (1 to 87)	38 (0 to 80)	59 (1 to 105)	<0.001

Quality of life

All FIQL questionnaire items (lifestyle, coping and behaviour, depression and self-perception, and embarrassment) were statistically significantly improved at 1 year (p=0.01, 0.001, 0.029 and 0.001 respectively). There were no statistically significant differences in generic health status at 1 year compared with baseline (measured by SF-36 questionnaire).

Safety

Intraoperative complications

- Implant extrusion=6% (3/54) (a single implant was extruded spontaneously immediately after placement, and was replaced)

There were no postoperative complications.

- Anal discomfort or pain=13% (7/54) (mean duration 4.4 days, treated with non-steroidal anti-inflammatory drugs)
- Dislodgement of single implant during follow-up=6% (3/54) (replacement was not needed)

At 1- and 3-month and 1-year follow-up endoscopic anal ultrasound confirmed that neither acute nor chronic inflammation was present around the implants.

Abbreviations used: AMS, American Medical Systems; CCFIS, Cleveland Clinic Faecal Incontinence Score; FIQL, Faecal Incontinence Quality of Life Scale; SF-36, Short Form 36 Health Survey

Study 2 Trenti L (2017)

Details

Study type	**Case series**
Country	Spain and Germany (4 centres)
Recruitment period	2010 to 2015
Study population and number	**n=49** Patients with faecal incontinence
Age and sex	Mean 63 years; 78% (38/49) female
Patient selection criteria	Patients diagnosed with idiopathic faecal incontinence or faecal incontinence secondary to sphincter lesions less than 120°. Some patients with low anterior resection syndrome (LARS) refractory to conservative management for more than 12 months were included. All patients had symptoms that had failed to respond to conservative management (diet modification, anti-diarrhoeal medication and biofeedback). Patients with external sphincter injury 120° or more, with altered cognitive status that prevented collaboration, or who refused to have the procedure were excluded from the study.
Technique	Device: THD Gatekeeper Delivery System (THD SpA, Italy). Antibiotics were offered before the procedure and for 3 days afterwards. All patients had 2 enemas before the surgery. Implantation was done under general or spinal anaesthesia. The mean number of implants was 6. Most patients had 6 implants inserted in a standardised technique. At the beginning of the study, 3 patients had 4 implants because the initial device was designed for 4 implants. Patients with LARS had between 8 and 12 implants inserted. Patients were advised to rest in bed during the first 48 hours after surgery, avoid any anal trauma as well as enemas or anal sexual intercourse and to adopt a fibre-rich diet to avoid faecal impaction.
Follow-up	**Mean 2.7 years**
Conflict of interest/source of funding	One of the authors is a trainer for the Gatekeeper procedure.

Analysis

Follow-up issues: Patients were followed up in the outpatient clinic 30 days after surgery. Faecal continence status was assessed at least every 6 months during the first year after surgery in the outpatient clinic or by phone. One patient was excluded from the analysis because of a psychiatric disorder diagnosed 1 year after surgery. Outcomes were reported for 94% (46/49) of patients at the 1-year and last visit follow-up.

Study design issues: Retrospective, multicentre, longitudinal study. All data were collected and registered prospectively as consecutive cases in an electronic database. Faecal incontinence status was assessed using the Vaizey score. Patients were classified as responders when improvements of at least 50% of the baseline Vaizey score were observed during the first 6 months. Patients who did not improve were classified as non-responders.

Study population issues: The mean baseline Vaizey score was 13.5.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **49**

Vaizey scores at baseline and follow-up

	Baseline n=48	6 months n=48	1 year n=46	Last visit n=46	p
Incontinence for solid stool					
Never	12 (25.0%)	26 (54.2%)	27 (58.7%)	29 (63.0%)	0.004
Rarely	8 (16.7%)	8 (16.7%)	10 (21.7%)	5 (10.9%)	
Sometimes	11 (22.9%)	8 (16.7%)	3 (6.5%)	4 (8.7%)	
Weekly	9 (18.8%)	6 (12.5%)	4 (8.7%)	6 (13.0%)	
Daily	8 (16.7%)	0 (0%)	2 (4.4%)	2 (4.4%)	
Incontinence for liquid stool					
Never	10 (20.8%)	11 (22.9%)	17 (37.0%)	22 (47.8%)	0.001
Rarely	2 (4.2%)	14 (29.2%)	12 (26.1%)	8 (17.4%)	
Sometimes	5 (10.4%)	13 (27.1%)	9 (19.6%)	6 (13.0%)	
Weekly	18 (37.5%)	5 (10.4%)	6 (13.0%)	7 (15.2%)	
Daily	13 (27.1%)	5 (10.4%)	2 (4.4%)	3 (6.5%)	
Incontinence for gas					
Never	5 (10.4%)	7 (14.6%)	11 (23.9%)	10 (21.7%)	0.031
Rarely	2 (4.2)%	9 (18.8%)	12 (26.1%)	10 (21.7%)	
Sometimes	5 (10.4%)	12 (25.0%)	10 (21.7%)	4 (8.7%)	
Weekly	15 (31.2%)	9 (18.8%)	5 (10.9%)	8 (17.4%)	
Daily	21 (43.8%)	11 (22.9%)	8 (17.4%)	14 (30.4%)	
Need to wear a pad					
No	11 (22.9%)	25 (52.1%)	26 (56.5%)	23 (50.0%)	0.01
Yes	37 (77.1%)	23 (47.9%)	20 (43.5%)	23 (50.0%)	
Alteration in lifestyle					
Never	6 (12.5%)	21 (43.8%)	23 (50.0%)	24 (52.2%)	0.001
Rarely	12 (25.0%)	14 (29.2%)	10 (21.7%)	6 (13.0%)	
Sometimes	14 (29.2%)	3 (6.3%)	7 (15.2%)	10 (21.7%)	
Weekly	9 (18.8%)	9 (18.8%)	5 (10.9%)	4 (8.7%)	
Daily	7 (14.6%)	1 (2.1%)	1 (2.2%)	2 (4.4%)	
Taking constipating medicines					
No	40 (83.3%)	40 (83.3%)	37 (80.4%)	39 (84.8%)	1.00
Yes	8 (16.7%)	8 (16.7%)	9 (19.6%)	7 (15.2%)	
Faecal Urgency					
No	19 (39.6%)	34 (70.8%)	33 (71.7%)	32 (69.6%)	0.004
Yes	29 (60.4%)	14 (29.2%)	13 (28.3%)	14 (30.4%)	
Total Vaizey score, mean (SD)	13.5 (3.9)	8.2 (4.9)	7.0 (5.5)	7.7 (6.2)	<0.001

23 (48%) patients were classified as responders and 25 (52%) were non-responders.

Mean Vaizey scores in patients classified as responders

- Baseline=13.3 (SD 3.8)
- 6 months=4.3 (SD 2.1), p<0.001 between baseline and 6-month follow up
- 12 months=4.2 (SD 3.6)
- Long-term follow-up (mean 2.7 years)=5.7 (SD 5.3)

Safety

There were no intraoperative or short- or long-term complications such as infection, bleeding, fistula or foreign body reaction. No patients experienced long-term discomfort or proctalgia secondary to the implants.

Migration of implants during follow-up=52% (25/49)

The mean number of migrated implants during follow-up was 1.7. Two days after surgery, 1 patient had extrusion of 3 implants that were reinserted in a second operation. In the other 24 patients, the number of migrated implants was: 1 in 5 patients, 2 in 2 patients and more than 2 in 17 patients.

Characteristics of responder and non-responder patients

	Responders n=23	Non-responders n=25	p
Gender, n (%)			
Male	5 (50)	5 (50)	1.0
Female	18 (47.4)	20 (52.6)	
Age (mean, SD)	67 (15.5)	62.1 (11.1)	0.213
Aetiology of faecal incontinence			
Sphincteric lesions (<120°)	9 (56.2)	7 (43.8)	0.156
Passive	12 (46.2)	14 (53.8)	
LARS	-	-	
Others	2 (100)	-	
Baseline Vaizey score (mean, SD)	13.3 (3.8)	13.7 (4.1)	0.771
Number of implants (mean, SD)	5.9 (0.5)	6.4 (1.7)	0.146
Number of migrated implants			
Mean (SD)	1.1 (1.6)	2.4 (2.6)	0.045
0	14 (60.9%)	9 (39.1%)	0.132
1 to 2	4 (50%)	4 (50%)	
>2	5 (29.4%)	12 (70.6%)	

Abbreviations used: LARS, low anterior resection syndrome; SD, standard deviation

Study 3 Ratto C (2011)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2005 to 2008
Study population and number	**n=14** Patients with faecal incontinence
Age and sex	Mean 64 years (range 28 to 83); 57% (8/14) female
Patient selection criteria	Inclusion criteria: patients with at least a 6-month history of episodes of faecal incontinence (soiling or incontinence to liquid or solid stools) occurring at least once a week that had failed to improve with conservative measures. Exclusion criteria: isolated incontinence to gas, risk of significant postoperative complications, including uncontrolled diabetes, anal sepsis, inflammatory bowel diseases with anorectal involvement or any colorectal cancer with active treatment. Patients with an isolated external anal sphincter defect demonstrated on endoanal ultrasound were also excluded.
Technique	Device: Gatekeeper prostheses (THD, Italy) All procedures were done as a day case, under local anaesthesia using a posterior perineal block. Four implants were inserted (at 3, 6, 9 and 12 o'clock positions) in the perianal area 2 cm from the anal verge. After the procedure, patients were discharged home with advice to avoid heavy physical activity for at least 48 hours. All patients were offered oral antibiotic prophylaxis for 3 days.
Follow-up	**Mean 33.5 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were reviewed in outpatients at 7, 30 and 90 days, and 6 months thereafter. All patients were recalled for further evaluation at the time of study closure.

Study design issues: Prospective single centre case series. Consecutive patients were enrolled. The primary endpoint was safety of the technique assessed as intraoperative and postoperative complications, implant displacement and any other morbidity. Secondary endpoints were therapeutic efficacy in terms of improvement in faecal incontinence symptoms, changes in manometric parameters, and changes in health status and quality of life.

Study population issues: The mean duration of faecal incontinence at baseline was 11.6 months. At baseline, the mean Vaizey score was 15.4 and the mean CCFIS score was 12.7. Of the 14 patients, 8 had no sphincter injury, 4 had an isolated internal anal sphincter defect and 2 patients had a combined internal anal sphincter and external anal sphincter defect (both patients had an episiotomy during childbirth).

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 14

Clinical success=92.9% (13/14)
In 1 patient with an internal anal sphincter defect secondary to lateral internal sphincterotomy, the number of episodes of faecal incontinence remained relevant (12 per week at 3 months compared with 28 at baseline). The patient had successful sacral nerve stimulation 5 months after the implant insertion and was excluded from further analysis.

Mean number of major faecal incontinence episodes per week, (SD)
• Baseline=7.1 (7.4)
• 1 month=1.4 (4.0)
• 3 months=1.0 (3.2)
• Last follow-up=0.4 (0.6), p=0.002

Absence of postevacuation soiling
• Baseline=21.4% (3/14)
• Last follow-up=69.2% (9/13), p=0.028

Ability to defer defaecation (minutes), mean (SD)
• Baseline=6.1 (4.9)
• Last follow-up=21.9 (13.8), p<0.031

Mean CCFIS and Vaizey scores, (SD)
<table>
<tr><th>Follow-up period</th><th>CCFIS</th><th>Vaizey</th></tr>
<tr><td>Baseline</td><td>12.7 (3.3)</td><td>15.4 (3.3)</td></tr>
<tr><td>1 month</td><td>4.1 (3.0)</td><td>7.1 (3.9)</td></tr>
<tr><td>3 months</td><td>3.9 (2.6)</td><td>4.7 (3.0)</td></tr>
<tr><td>Last follow-up</td><td>5.1 (30)</td><td>6.9 (5.0)</td></tr>
<tr><td>p value</td><td><0.001</td><td>0.01</td></tr>
</table>
There were no statistically significant changes in mean anal manometric values during follow-up compared with baseline.

Quality of life
At the last follow-up, there were statistically significant increases in the mean scores in the physical function (p=0.002), role physical (p=0.001), general health (p=0.01), social function (p<0.001), role emotional (p<0.001) and mental health domains (p=0.001) of the SF-36.
All FIQL questionnaire items showed a statistically significant improvement in values at final follow-up compared with baseline: lifestyle (p=0.001), coping and behaviour (p<0.001), depression and self-perception (p<0.001) and embarrassment (p=0.001).
</td><td>
There were no intraoperative or postoperative complications. None of the patients had local or systemic sepsis, fever or pain.
There was no evidence of any acute or chronic inflammatory response around the implants (assessed by digital examination and endoanal ultrasound).
Neither implant dislodgement (assessed by endoanal ultrasound) nor mucosal or skin alteration (fistula, ulceration) were noted.
Patients had no anal discomfort either at rest or during defaecation.
</td></tr>
<tr><td colspan="2">Abbreviations used: CCFIS, Cleveland Clinic faecal incontinence score; FIQL, Faecal Incontinence Quality of Life; SD, standard deviation</td></tr>
</table>

Study 4 La Torre M (2019)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2016 to 2018
Study population and number	**n=13** Patients with faecal incontinence
Age and sex	Age not reported; 77% (10/13) female
Patient selection criteria	Age over 18 years; faecal incontinence (incontinence to liquid or solid stools) that started at least 6 months before; episodes of faecal incontinence that happened more than once a week and resistant to conservative treatments (such as stool bulking or constipating agents); endoanal ultrasound assessment showing intact anal sphincters or a sphincter injury (internal, external or both). Exclusion criteria: malignant neoplasms, rectal bleeding of unknown cause, congenital anorectal malformations, inflammatory bowel disease, sepsis, obstructive defaecation syndrome, neurological disease and coagulation disorders.
Technique	Device: SphinKeeper prostheses (THD SpA, Italy) The procedures were done under general or spinal anaesthesia. All patients had 10 implants inserted. Intravenous antibiotic prophylaxis was given to all patients. Patients were instructed to avoid constipation and hard stools, so behavioural changes were advised, and dietary fibre supplements were prescribed after surgery. All patients were advised to have bed rest or to move slowly from bed to chair for the first 48 hours to minimise early implant dislocation.
Follow-up	**6 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: The implants were checked with endoanal ultrasound at 1 week, 1 month and 6 months after surgery. Patients kept a continence diary during the study and data were compiled at the end of the follow-up.

Study design issues: Prospective case series. Consecutive patients were enrolled. The primary endpoint was to evaluate the safety of the procedure in terms of intraoperative and postoperative adverse events and complications. The secondary endpoint was to assess the effectiveness of the procedure in terms of improvement of faecal incontinence, manometric parameters and quality of life.

Study population issues: The mean CCFIS at baseline was 12.5 (range 10 to 15). Of the 13 patients, 3 had an internal anal sphincter lesion, 1 had an external anal sphincter lesion, 4 had both internal and external anal sphincter lesions, 2 had internal anal sphincter inhomogeneity and 3 had external/internal anal sphincter inhomogeneity. There were no sphincter lesions greater than 120°.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **13**

	Preoperative	Postoperative	p
Anorectal manometry maximum resting pressure (mmHg); mean (range)	21.3 (10 to 30)	31.84 (20 to 41)	<0.05
Anorectal manometry maximum squeeze pressure (mmHg); mean (range)	83 (30 to 105)	88.53 (40 to 106)	NS
CCFIS; mean (range)	12.46 (10 to 15)	8.91 (6 to 12)	<0.05
FIQL score			
Lifestyle; mean (range)	2.62 (2.2 to 3.1)	3.2 (2.9 to 3.5)	NS
Coping and behaviour; mean (range)	1.97 (1.7 to 2.2)	2.37 (2 to 2.6)	NS
Depression and self-perception; mean (range)	2.96 (2.7 to 3.2)	3.39 (3.1 to 3.6)	NS
Embarrassment; mean (range)	2.46 (2 to 2.8)	3 (2.7 to 3.4)	NS
Total number of episodes of faecal incontinence per week	5.38 (2 to 11)	1.57 (1 to 5)	<0.05

Safety

There were no intraoperative or in-hospital complications.

There were no reports of anorectal pain or discomfort during follow-up.

Implant extrusion 1 month after surgery=15.4% (2/13)

(there was 1 posterior extrusion in a male patient and 1 anterior extrusion in a female patient)

Anterior dislocation (defined as an implant not at the same level as other implants) = 7.7% (1/13)

(detected 6 months after surgery)

Abbreviations used: CCFIS, Cleveland Clinic faecal incontinence score; FIQL, faecal incontinence quality of life; NS, not significant

Study 5 Ratto C (2016)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2014 to 2015
Study population and number	**n=10** Patients with faecal incontinence
Age and sex	Median 58 years (range 20 to 75); 50% (5/10) female
Patient selection criteria	Age between 18 and 80 years, faecal incontinence onset at least 6 months before the implant, more than 1 episode of faecal incontinence per week, willingness to perform baseline and follow up schedule evaluations and to sign an informed consent. Exclusion criteria: malignancies under treatment, rectal bleeding of unknown origin, chronic diarrhoea unresponsive to medical treatment, inflammatory bowel disease unresponsive to medical treatment, acute anorectal sepsis, concomitant rectal prolapse, obstructive defaecation syndrome, neurological disease, coagulation disorder.
Technique	Device: SphinKeeper prostheses (THD SpA, Italy) All procedures were done under local anaesthesia. All patients had 10 implants inserted. Intravenous antibiotic prophylaxis was given to all patients. All patients were advised to have bed rest or to move slowly from bed to chair for the first 48 hours to minimise early implant dislocation. Patients were told about the importance of avoiding constipation and hard stool; a diet rich in water and fibre, and stool softeners were prescribed during the first postoperative month.
Follow-up	**3 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Implants were checked for dislocation with endoanal ultrasound at 1 week, 1 month and 3 months after the procedure. All patients completed follow-up.

Study design issues: Prospective single centre case series. The aim of the study was to record intraoperative and postoperative adverse events to obtain data about technical feasibility and safety.

Study population issues: The median duration of faecal incontinence at baseline was 9 years (range 3 to 21). Of the 10 patients, 3 had an internal anal sphincter lesion, 4 had an external anal sphincter lesion, 5 had internal anal inhomogeneity and 5 had external anal inhomogeneity. Seven patients had a history of perineal surgery and 3 had previous surgery for faecal incontinence. One patient had had pelvic radiotherapy for endometrial cancer. At baseline, the median CCFI score was 10 (range 5 to 17) and the median Vaizey score was 13 (range 7 to 16).

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **10** No efficacy data were reported.	There were no intraoperative complications or early postoperative complications reported during the hospital stay. At 1 week, 1 patient had anal discomfort that was attributed to a 1 cm distal dislocation of a single implant within the intersphincteric space. This was treated with local and systemic painkillers and symptoms resolved 1 week later. There was no acute sepsis at the site of implantation documented within 90 days after the procedure. No patient had long-lasting symptoms, including anorectal pain and discomfort, directly or indirectly related to the implants.
Abbreviations used: CCFI, Cleveland Clinic faecal incontinence	

Study 6 Grossi U (2019)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2011 to 2015
Study population and number	**n=16** Women with faecal incontinence
Age and sex	Median 69 years; 100% (16/16) female
Patient selection criteria	Inclusion criteria: symptoms of faecal or flatus incontinence for at least 6 months before recruitment and happening at least once a week, and failure of conservative management (lifestyle changes or pharmacological agents). Exclusion criteria: patients with isolated flatus incontinence, inflammatory bowel disease, uncontrolled diabetes, anal sepsis, history of gastrointestinal cancer, history of anal surgery for faecal incontinence (including injection of bulking agents), internal anal sphincter defects >45°.
Technique	Device: Gatekeeper delivery system (THD SpA, Italy).
Follow-up	**12 months**
Conflict of interest/source of funding	One author pioneered Gatekeeper in patients with faecal incontinence; he has served as a speaker, consultant, and proctor during several congresses and training courses on Gatekeeper.

Analysis

Study design issues: Retrospective analysis of prospectively collected data. The aim of the study was to compare external anal sphincter contractility before and after the procedure.

Study population issues: There may be some patient overlap with Ratto C et al., 2016 (study 5). There were no isolated internal anal sphincter defects and 10 patients had degeneration or atrophy. Isolated external anal sphincter defects or degeneration/atrophy were found in 2 (12.5%) and 8 (50%) patients respectively. One patient had both external anal sphincter abnormalities. Combined internal and external anal sphincter abnormalities were found in 8 (50%) patients.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **16**

External anal sphincter contractility at baseline and 12 months after implant

Parameter	Baseline	After implant	p
Intraluminal pressure during average maximum voluntary contraction, mmHg	45.8 (26.5 to 75.8)	60.4 (43.1 to 88.1)	0.017
Inner radius of the external anal sphincter, mm	12.4 (11.5 to 13.4)	18.7 (17.3 to 19.6)	<0.001
External anal sphincter thickness, mm	2.7 (2.5 to 2.8)	2.5 (2.2 to 2.8)	0.31
Muscle tension, millinewtons per cm^2	233.2 (123.8 to 303.2)	490.8 (286.9 to 562.5)	<0.001

Change in symptoms and quality of life score from baseline to 12 months after implant, median (first and third quartiles)

	Baseline	After implant	p
CCFI	11 (8, 14)	3 (2, 7)	0.001
St Mark's incontinence score	16 (14, 18)	6 (3, 9)	<0.001
American Medical Systems score	82 (72, 89)	43 (19, 62)	<0.001
FIQL (n=12)			
Lifestyle	2.6 (1.5, 3.6)	3.3 (2.4, 3.9)	0.10
Coping/behaviour	1.7 (1.2, 2.1)	2.4 (2.2, 3.3)	0.06
Self-perception	3.2 (2.0, 3.9)	3.8 (2.5, 4.3)	0.03
Social embarrassment	2.3 (1.0, 3.2)	3.2 (2.1, 4.0)	0.06

Proportion of patients who could defer defaecation for more than 5 minutes

- Baseline=25% (4/16)
- 12 months=75% (12/16), p=0.25

Safety

No safety data were reported.

Abbreviations used: CCFI, Cleveland Clinic faecal incontinence; FIQL, faecal incontinence quality of life

Study 7 de la Portilla F (2017)

Details

Study type	**Case series**
Country	Spain
Recruitment period	Not reported
Study population and number	**n=7** Patients with faecal incontinence
Age and sex	Mean 56 years; 6 females, 1 male
Patient selection criteria	All patients had passive faecal incontinence, secondary to an internal anal sphincter lesion extending for less than 60° of the anal circumference.
Technique	Device: Gatekeeper (THD, Italy) Each patient had 6 implants inserted. All procedures were done on an outpatient basis.
Follow-up	**12 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Patients were assessed with endoanal 3-dimensional ultrasound at 1, 3 and 12 months after the procedure.

Study design issues: Prospective case series. The main aim of the study was to assess the degree to which displacement of the implants may occur and to determine whether this is associated with patient outcomes. A minimum of 50% reduction in the Wexner scale score or the rate of incontinence episodes (determined by a defaecation diary) relative to baseline were considered to denote clinical improvement.

Study population issues: The mean duration of faecal incontinence was 6 years.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 7 **Mean number of major faecal incontinence episodes per month** • Baseline=6.8±2.6 • 1-month follow-up=3.0±1.7 • 3-month follow-up=4.1±2.0 • 12-month follow-up=5.1±2.2, p<0.05 **Mean Wexner scale score (ranging from 0 to 20, where 0 denotes perfect continence and 20 complete incontinence)** • Baseline=16.0±4.0 • 1-month follow-up=10.7±3.2 • 3-month follow-up=10.4±3.2 • 12-month follow-up=10.1±3.1, p<0.01 **Mean Wexner scale score for patients with implant displacement** • Baseline=15.2±3.1 • 1-month follow-up=8.0±2.8 • 3-month follow-up=6.8±2.1 • 12-month follow-up=6.6±2.0, p<0.05 **Quality of life** There were no statistically significant changes in quality of life compared with baseline (assessed using the FIQL questionnaire). **Manometry** There were no changes in the key manometric parameters of pressure and volume compared with baseline. **Clinical improvement (defined as a minimum of 50% reduction in the Wexner scale score or the rate of incontinence episodes relative to baseline) = 42.9% (3/7)** This improvement was detected from 1 month onwards, remained stable up to 1 year, and was unaffected by implant migration.	There were no immediate intraoperative or postoperative complications. One patient needed analgesia for 4 days because of discomfort at the implantation site. Displacement of implants at 3 months=71.4% (5/7) of patients; 57.1% (24/42) of implants Of these, 15 implants had migrated to a lower level and 9 had migrated to an upper level of the anal canal and rectum. At 1-year follow-up, there was no migration of the other implants but 6 of the implants that had already been noted as displaced at 3 months had migrated further. One patient needed to have an implant removed because it was protruding through the perianal skin, almost at the point of spontaneous extrusion.
Abbreviations used: FIQL, faecal incontinence quality of life	

Study 8 Al-Ozaibi L (2014)

Details

Study type	**Case report**
Country	United Arab Emirates
Recruitment period	2012
Study population and number	n=1 Patient with faecal incontinence
Age and sex	52-year-old male
Patient selection criteria	Not applicable
Technique	Device: Gatekeeper 6 implants were inserted at 1, 3, 5, 7, 9 and 11 o'clock positions. The patient was advised to take rest for 1 week and to avoid any physical exercise for another 3 weeks.
Follow-up	**2 years**
Conflict of interest/source of funding	None

Key safety findings

Case report: implant migration and perianal abscess The patient presented with passive soiling since 2007 (>10 episodes per week). The CCFI score was 4. Physiotherapy was advised because his anal sphincter tone was normal and there was no underlying pathology. The symptoms did not improve, and the patient had self-expanding implant insertion in 2012. There was some improvement after 3 months: soiling decreased to 3 episodes per week and the CCFI score was 3. At 1-year follow-up, frequency of soiling had returned to >10 episodes per week. Endorectal ultrasound revealed the migration of the implants from the intersphincteric region. In 2014, the patient presented with perianal pain and swelling and a perianal abscess was diagnosed. Incision and drainage was done and 1 of the prostheses popped out of the abscess cavity.
Abbreviations used: CCFI, Cleveland Clinic faecal incontinence

Study 9 Litta F (2020)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2016 to 2018
Study population and number	**n=42** Patients with faecal incontinence
Age and sex	Mean 67 years; 86% (36/52) female
Patient selection criteria	Inclusion criteria: age between 18 and 85 years; faecal incontinence for at least 6 months; conservative treatment had failed; faecal incontinence episodes more than once a week; sphincter defect affecting no more than 120° of the internal or external sphincter, or both; able to consent to participate and attend all scheduled follow-up visits. Exclusion criteria: current diagnosis of cancer; rectal bleeding of unknown origin; chronic diarrhoea unresponsive to medical treatment; inflammatory bowel disease; acute anorectal sepsis; concomitant rectal prolapse; obstructive defaecation syndrome; neurological disease; coagulation disorder; previous rectal resection; and sphincter(s) defects of the internal or external anal sphincter, or both, of more than 120° of anal canal circumference.
Technique	Device: Sphinkeeper (THD SpA, Italy) For details, see Ratto C et al. (2016) – study 5 in overview
Follow up	**Mean 16 months (range 6 to 33)**
Conflict of interest/source of funding	One author received travel reimbursement from THD to attend conferences.

Analysis

Follow-up issues: An additional 3 patients were originally included in the study but were lost to follow-up after the first postoperative visit, leaving 42 for evaluation.

Study design issues: Prospective single-centre observational study. The primary aim was to assess the efficacy of the procedure in patients with faecal incontinence. Secondary endpoints were quality of life evaluation, safety of implantation, and frequency of prosthesis displacement. A prosthesis was considered adequately placed when at least two-thirds of it were found within the target area. Prosthesis placement was considered adequate when most of the prostheses (at least 6 of 10) were found in the target area. Symptoms of faecal incontinence were evaluated using a daily diary of faecal incontinence episodes over 2 weeks, ability to defer defaecation, need to wear pads or take constipating drugs, and validated Cleveland Clinic Fecal Incontinence Score (CCFIS) and Vaizey score. Quality of life and health status were assessed using the Faecal Incontinence Quality of Life Scale (FIQL) and Short Form 36 (SF-36) questionnaires. Anorectal manometry and endoanal ultrasonography were used for both the assessment of anorectal function and morphology, and evaluation of the location of the prostheses after implantation.

Study population issues: At baseline, the mean duration of faecal incontinence was 7 years. The mean CCFIS score was 12.

Key efficacy and safety findings

Efficacy

Number of patients analysed: 42

Number of soiling and incontinence episodes per week, and faecal incontinence severity scores at baseline and during follow-up; mean (standard deviation)

	Baseline n=42	3 months n=42	6 months n=42	12 months n=28	Last follow-up n=42	p
Soiling (episodes per week)	8.2 (6.4)	5.2 (4.7)	3.0 (3.6)	3.1 (3.8)	3.2 (3.8)	<0.001
Incontinence to gas (episodes per week)	13.9 (12.4)	9.6 (7.8)	7.1 (6.7)	7.0 (6.7)	7.5 (7.1)	0.001
Incontinence to liquid stools (episodes per week)	2.9 (3.4)	2.1 (3.0)	1.1 (1.8)	1.1 (1.6)	1.4 (1.9)	0.005
Incontinence to solid stools (episodes per week)	2.0 (2.1)	1.3 (1.5)	0.9 (1.5)	0.6 (1.4)	0.8 (1.5)	0.003
CCFIS	12.0 (3.7)	10.1 (3.8)	7.8 (4.1)	7.7 (4.2)	7.6 (4.1)	<0.001
Vaizey score	14.6 (4.4)	13.0 (4.7)	10.2 (5.0)	10.0 (4.5)	10.2 (4.7)	0.001

5 patients became fully continent.

Proportion of patients who never or rarely experienced postdefaecation soiling episodes:

- Baseline=7.1% (3/42)
- Last follow-up=54.8% (23/42), p<0.001

Proportion of patients able to defer defaecation for more than 5 minutes:

- Baseline=33.3% (14/42)
- Last follow-up=69.0% (29/42), p=0.001

All domains of the FIQL improved after the procedure, but only physical functioning improved on the SF-36 questionnaire.

Mean maximum squeeze pressure (mmHg)

- Baseline=80.7 (68.5)
- Last follow-up=90.1 (48.7), p=0.006

There was no statistically significant difference in maximum resting pressure and rectal sensory thresholds.

At the last follow-up, endoanal ultrasound assessment of prosthesis position found that implantation was adequate in 54.8% (23/42) of patients, with at least 6 of 10 prostheses placed in the target area. Patients with adequate placement had improved outcomes and CCFIS compared with those with inadequate placement.

Safety

There were no intraoperative or postoperative complications.

Abbreviations used: CCFIS, Cleveland Clinic Fecal Incontinence Score

Study 10 Grossi U (2020)

Details

Study type	**Non-randomised comparative study of 2 devices**
Country	Italy
Recruitment period	February to March 2018 and May to October 2016
Study population and number	**n=20 (10 SphinKeeper, 10 GateKeeper)** Female patients with faecal incontinence
Age and sex	Median 52 years (SphinKeeper) and 53 years (GateKeeper)
Patient selection criteria	The selection criteria for the study were onset of passive faecal incontinence with or without urge-related symptoms at least 6 months before the first clinical evaluation and symptoms being refractory to all standard conservative measures (pharmacological, behavioural, and pelvic floor rehabilitation). Exclusion criteria: internal anal sphincter lesion >60° or EAS lesion >90° identified on ultrasound, active perianal sepsis, severe anal scarring, inflammatory bowel disease with anorectal involvement, and active treatments for anal or rectal cancer.
Technique	Device: SphinKeeper or GateKeeper (THD SpA, Italy)
Follow up	**12 months**
Conflict of interest/source of funding	None

Analysis

Study design issues: Retrospective non-randomised comparative study of 2 devices. All consecutive female patients who had a SphinKeeper implant between February and March 2018 were case matched by selecting the first 10 consecutive female patients (matched for age ±5 years) who had a GateKeeper implant between May and October 2016. The main aim was to evaluate the change in muscle tension after the procedure with each device. The secondary aim was to assess whether changes in muscle tension correlated with symptom improvement.

Study population issues: The 2 groups were similar with regard to baseline demographic and clinical characteristics. The median duration of faecal incontinence was 3 years. Of the 20 patients, 4 (20%) had a previously implanted sacral neurostimulator that remained in situ for the total length of the study (2 in each group) and 4 patients had a history of pudendal nerve neuropathy.

Key efficacy and safety findings

Efficacy

Number of patients analysed: 20

Prosthetic displacement was observed in 8 patients, 4 in each group.

CCFIS before and after the procedure

Device	Baseline	Follow-up	p
SphinKeeper	13 (11 to 13)	4 (3 to 4)	0.005
GateKeeper	12 (11 to 14)	6 (5 to 6)	0.005

External anal sphincter contractility at baseline and 12 months after surgery; median (first and third quartiles)

Device	Parameter	Baseline	Follow-up	p
GateKeeper	Intraluminal pressure during average maximum voluntary contraction, mmHg	100.0 (97.5 to 112.5)	110.0 (103.8 to 112.5)	0.071
	Inner radius of the external anal sphincter, mm	13.0 (12.1 to 13.5)	18.2 (18.1 to 18.3)	0.005
	External anal sphincter thickness, mm	2.5 (2.5 to 2.7)	2.3 (2.3 to 2.4)	0.005
	Muscle tension, mN $(cm^2)^{-1}$	508.1 (478.8 to 568.0)	864.4 (827.0 to 885.8)	0.005
SphinKeeper	Intraluminal pressure during average maximum voluntary contraction, mmHg	110.0 (105.0 to 112.5)	110.0 (108.8 to 118.5)	0.348
	Inner radius of the external anal sphincter, mm	12.8 (12.0 to 13.3)	19.2 (19.0 to 19.3)	0.005
	External anal sphincter thickness, mm	2.6 (2.5 to 2.7)	2.1 (2.0 to 2.1)	0.005
	Muscle tension, mN (cm2)-1	546.6 (472.7 to 576.7)	999.2 (968.6 to 1077.2)	0.005

Linear and Poisson regression models to examine the extent of change in muscle tension and CCFIS after SphinKeeper versus GateKeeper

Change in muscle tension	Coefficient	Standard error	p	95% CI
SphinKeeper	158.3	23.1	<0.001	109.6 to 207.0
Muscle tension at baseline	-0.6	0.2	0.004	-1.0 to -0.2
Constant	662.8	99.2	<0.001	453.6 to 872.1
Change in CCFIS	**Incidence rate ratio**	**Standard error**	**p**	**95% CI**
SphinKeeper	1.33	0.22	0.088	0.96 to 1.85
CCFIS at baseline	1.10	0.07	0.101	0.98 to 1.24
Constant	1.90	1.41	0.384	0.45 to 8.10

Safety

There were no side effects or complications reported within the first 12 months after the procedure.

Abbreviations used: CCFIS, Cleveland Clinic Fecal Incontinence Score; CI, confidence interval

Study 11 Brusciano L (2020)

Details

Study type	**Case series**
Country	Italy
Recruitment period	2014 to 2016
Study population and number	**n=20** Patients with faecal incontinence
Age and sex	Median 59 years (range 24 to 77); 100% (20/20) female
Patient selection criteria	Selection criteria for the study were based on patient's clinical history, with onset of faecal incontinence at least 6 months before the first visit and symptoms being refractory to all standard conservative measures (pharmacologic, behavioural, and pelvic floor rehabilitation). Exclusion criteria: internal anal sphincter lesion >60° or external anal sphincter lesion >90° identified on ultrasound; active perianal sepsis; severe anal scarring; inflammatory bowel disease with anorectal involvement; active treatment for anal or rectal cancer.
Technique	Device: Gatekeeper (THD Sp, Italy). Spinal anaesthesia was used, and 4 to 6 implants were inserted. Patients were discharged on the same day and recommended to avoid any trauma or sexual practice during the first 48 hours after implantation. A 5-day course of antibiotics was prescribed.
Follow up	**36 months**
Conflict of interest/source of funding	None

Analysis

Follow up issues: Clinical and symptomatologic evaluations were scheduled at 1, 3, 6, 12, 24, and 36 months after implantation. There were no losses to follow-up.

Study design issues: Prospective single centre case series. The main outcome measure was the CCFIS.

Population issues: Of the 20 patients, 4 (20%) had a history of pudendal nerve neuropathy, and 3 (15%) had a previously implanted sacral nerve stimulator that remained in situ and switched on for the total length of the study.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 20

Mean CCFIS
• Preoperative=12.4±1.8
• 3 month follow-up=4.9±1.5, p<0.0001
• 36 month follow-up=4.9±1.7, p<0.0001

Subgroup analysis of CCFIS
<table>
<tr><th>Patient subgroups</th><th>Baseline</th><th>36 months</th><th>p</th></tr>
<tr><td>Patients with pudendal neuropathy (n=4)</td><td>10.4±1.9</td><td>5.8±1.1</td><td><0.0001</td></tr>
<tr><td>Patients without pudendal neuropathy (n=16)</td><td>12.1±1.8</td><td>4.5±1.0</td><td></td></tr>
<tr><td>Patients with a sacral neurostimulator (n=3)</td><td>10.3±1.7</td><td>4.0±1.4</td><td><0.0001</td></tr>
<tr><td>Patients without a sacral neurostimulator (n=17)</td><td>10.4±1.9</td><td>5.9±1.2</td><td></td></tr>
<tr><td>4 prostheses (n=4)</td><td>11.2±1.6</td><td>6.0±1.2</td><td><0.0001</td></tr>
<tr><td>6 prostheses (n=16)</td><td>11.9±1.8</td><td>4.4±1.0</td><td></td></tr>
</table>
At 2 months after surgery, endoanal ultrasound showed normal prostheses localisation in 16 patients (80%) and dislocation in the upper part of the anal canal in 2 patients (10%) and in the extrasphincteric space (ischioanal fossa) in 2 patients (10%).

High-resolution anorectal manometry parameters at baseline and 3 months after surgery
<table>
<tr><th>Patient subgroups</th><th>Anal resting pressure, mean±SD, mmHg</th><th>Maximum squeeze increment, mean±SD, mmHg</th><th>Anal canal length, cm</th></tr>
<tr><td>Baseline (n=20)</td><td>46.5±6.5</td><td>102.2±13.2</td><td>3.4±0.7</td></tr>
<tr><td>3 month follow-up (n=20)</td><td>57.8±7.5
p<0.05 compared with baseline</td><td>110.4±11.2
p<0.05 compared with baseline</td><td>3.9±0.6</td></tr>
<tr><td>Patients with pudendal neuropathy (n=4)</td><td>50.2±4.2
p<0.05 compared with baseline</td><td>102.5±3.7
p<0.05 compared with baseline</td><td>3.7±0.8</td></tr>
<tr><td>Patients without pudendal neuropathy (n=16)</td><td>63.4±8.1
p<0.05 compared with baseline</td><td>111.8±10.4
p<0.05 compared with baseline</td><td>3.9±0.9</td></tr>
<tr><td>Patients with a sacral neurostimulator (n=3)</td><td>56.2±4.3</td><td>103.5±5.8</td><td>3.8±0.7</td></tr>
<tr><td>Patients without a sacral neurostimulator (n=17)</td><td>58.1±8.8</td><td>111.2±9.9
p<0.05 compared with baseline</td><td>3.9±0.7</td></tr>
<tr><td>4 prostheses (n=4)</td><td>55.4±3.7</td><td>110.5±8.8</td><td>3.9±0.8</td></tr>
<tr><td>6 prostheses (n=16)</td><td>61.5±7.4
p<0.05 compared with baseline</td><td>110.8±7.9</td><td>3.9±0.6</td></tr>
</table>
</td><td>There were no adverse effects or complications.</td></tr>
<tr><td colspan="2">Abbreviations used: CCFIS, Cleveland Clinic Fecal Incontinence Score; SD, standard deviation</td></tr>
</table>

Study 12 Leo CA (2020)

Details

Study type	**Case series**
Country	UK (2 centres)
Recruitment period	2016 to 2019
Study population and number	**n=27** Patients with faecal incontinence
Age and sex	Median 57 years (range 27 to 87); 67% (18/27) female
Patient selection criteria	All patients had exhausted nurse-led conservative management. The decision to do self-expanding implant insertion was discussed and agreed by the local pelvic floor multidisciplinary team. The procedure was only considered to be suitable if patients had at least moderate symptoms of faecal incontinence (>10 on the St Mark's incontinence scale).
Technique	Device: SphinKeeper (THD SphinKeeper, THD SpA, Italy). All procedures were done under general anaesthesia. Intravenous broad-spectrum antibiotic prophylaxis was used. Ten equally spaced 2 mm perianal skin incisions were made 2 cm from the anal verge on the anoderm side, avoiding the 12 o'clock position to prevent any possibility of injury to the vagina or urethra. The introducer was inserted under digital or ultrasonography guidance. Postoperatively, all patients were instructed to minimise mobilisation for at least 48 hours to reduce the risk of early prosthesis dislocation. Lidocaine gel and systemic painkillers were prescribed as needed for postoperative pain. A 5-day course of oral antibiotics was used postoperatively. Postoperative imaging was used to confirm positioning of the prostheses, using either endo-anal ultrasound scan, CT, or MRI depending on centre preference.
Follow up	**Median 12 months (range 3 to 26)**
Conflict of interest/source of funding	None

Analysis

Follow up issues: All patients were followed up at least once within 3 months of surgery. Postoperative imaging was done in 96% (26/27) of patients.

Study design issues: Retrospective analysis of prospectively collected data. Patients were treated in 2 major tertiary referral hospitals. For efficacy data, 'success' was defined as reduction of 50% or more in the St Mark's incontinence scale after treatment.

Study population issues: Of the 27 patients, 12 (44%) had previous pelvic floor surgery, and 56% (10/18) of female patients had a history of obstetric anal sphincter injury. 75% of patients had symptoms of faecal incontinence for more than 2 years. Five patients had had an initial trial of sacral nerve stimulation that had failed. Mixed symptoms of faecal incontinence (urge and passive) were reported in 78% (21/27) of patients and 22% (6/27) had passive faecal incontinence in isolation. Median preoperative St Mark's incontinence scale score was 15 (range 11 to 24). Degeneration or disruption of the internal anal sphincter was present in 12 (44%) patients and disruption of the external anal sphincter in 10 (37%) patients.

Other issues: The authors noted that there was a technical issue with deployment of prostheses as evidenced by radiologically absent or misplaced prostheses in a high proportion of patients.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 27

In 30% of the patients, the firing device jammed and not all prostheses were delivered.

St Mark’s incontinence scale score; median (range)
• Preoperative=15 (11 to 24)
• Postoperative=10 (3 to 22)
• Change=-6 (-12 to 3), p<0.00016

51.9% (14/27) of patients had a clinically meaningful improvement as defined by a 50% or greater reduction in symptom score at short-term follow-up.

Radiological prostheses location; median (range)
• Total prostheses visualised=7 (0 to 10)
• Ideal placement=5 (0 to 10)
• Suboptimal placement=2 (0 to 7)

Contingency table showing no relationship between numbers of optimally placed prostheses and outcomes based on 50% or greater reduction in St Mark’s incontinence scale score (p=0.79)
<table>
<tr><th></th><th>≥50% reduction in score</th><th><50% reduction in score</th><th>Total</th></tr>
<tr><td>≥50% ideal placement</td><td>10</td><td>8</td><td>18</td></tr>
<tr><td><50% ideal placement</td><td>4</td><td>4</td><td>8</td></tr>
<tr><td>Total</td><td>14</td><td>12</td><td>26</td></tr>
</table>
</td><td>There were no intraoperative complications and all patients were discharged the same or following day.</td></tr>
</table>

Validity and generalisability of the studies

- Only small case series were identified; there were no comparative studies.
- Most of the data were from Europe. One case series reported data from UK patients.
- Two small studies reported longer-term outcomes; 1 had a mean follow-up of 2.7 years and the other had a mean follow-up of 33.5 months.
- The inclusion criteria varied between the studies, particularly in external anal sphincter lesions.
- In 1 study, fibre supplements were prescribed after the surgery, which may have had an effect on efficacy outcomes.[4]
- All studies used either the Gatekeeper or Sphinkeeper device.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Insertion of a magnetic bead band for faecal incontinence. NICE interventional procedures guidance 483 (2014). Available from http://www.nice.org.uk/guidance/IPG483
- Percutaneous tibial nerve stimulation for faecal incontinence. NICE interventional procedures guidance 395 (2011). Available from http://www.nice.org.uk/guidance/IPG395

- Endoscopic radiofrequency therapy of the anal sphincter for faecal incontinence. NICE interventional procedures guidance 393 (2011). Available from http://www.nice.org.uk/guidance/IPG393
- Transabdominal artificial bowel sphincter implantation for faecal incontinence. NICE interventional procedures guidance 276 (2008). Available from http://www.nice.org.uk/guidance/IPG276
- Injectable bulking agents for faecal incontinence. NICE interventional procedures guidance 210 (2007). Available from http://www.nice.org.uk/guidance/IPG210
- Stimulated graciloplasty for faecal incontinence. NICE interventional procedures guidance 159 (2006). Available from http://www.nice.org.uk/guidance/IPG159
- Sacral nerve stimulation for faecal incontinence. NICE interventional procedures guidance 99 (2004). Available from http://www.nice.org.uk/guidance/IPG99
- Artificial anal sphincter implantation. NICE interventional procedures guidance 66 (2004). Available from http://www.nice.org.uk/guidance/IPG66

Medical technologies

- Peristeen transanal irrigation system for managing bowel dysfunction. Medical technologies guidance 36 (2018). Available from http://www.nice.org.uk/guidance/mtg36

NICE guidelines

- Faecal incontinence in adults: management. NICE clinical guideline 49 (2007). Available from http://www.nice.org.uk/guidance/CG49

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two professional expert questionnaires for self-expanding implant insertion into the intersphincteric space for faecal incontinence were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 1 company who manufactures a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Ongoing trials
  - Anal Sphinkeeper in patients with faecal incontinence: a multicentre prospective evaluation in the UK (ISRCTN61603070). Observational case series; May 2018 to January 2020.
  - Treatment of Anal Incontinence With Intersphincteric Implants (NCT03080753); Sweden; single group assignment; n=52; estimated study completion date December 2022.

References

1. Ratto C, Buntzen S, Aigner F et al. (2016) Multicentre observational study of the Gatekeeper for faecal incontinence. British Journal of Surgery 103: 290–9
2. Trenti L, Biondo S, Noguerales F. (2017) Outcomes of Gatekeeper™ prosthesis implantation for the treatment of fecal incontinence: a multicenter observational study. Techniques in Coloproctology 21: 963–70
3. Ratto C, Parello A, Donisi L et al. (2011) Novel bulking agent for faecal incontinence. The British Journal of Surgery 98: 1644–52
4. La Torre M, Lisi G, Milito G et al. (2019) Sphinkeeper™ for faecal incontinence: a preliminary report. Colorectal Disease doi: 10.1111/codi.14801
5. Ratto C, Donisi L, Litta F et al. (2016) Implantation of SphinKeeper™: a new artificial anal sphincter. Techniques in Coloproctology 20: 59–66
6. Grossi U; De Simone V; Parello A; et al. (2019) Gatekeeper improves voluntary contractility in patients with fecal incontinence. Clinical Innovation 26: 321–7
7. de la Portilla F, Reyes-Diaz ML, Maestre MV et al. (2017) Ultrasonographic evidence of Gatekeeper™ prosthesis migration in patients treated for faecal incontinence: a case series. International Journal of Colorectal Disease 32: 437–40
8. Al-Ozaibi L, Kazim Y, Hazim W et al. (2014) The Gatekeeper™ for fecal incontinence: Another trial and error. International Journal of Surgery Case Reports 5: 936–8
9. Litta F, De Simone V, Parello A et al. (2020) Long-term outcome of sphinkeeper for the treatment of fecal incontinence. Techniques in Coloproctology 24: 366
10. Grossi U, Brusciano L, Tolone S et al. (2020) Implantable agents for fecal incontinence: an age-matched retrospective cohort analysis of GateKeeper versus SphinKeeper. Surgical Innovation DOI: 10.1177/1553350620934932
11. Brusciano L, Tolone S, Del Genio G et al. (2020) Middle-term outcomes of Gatekeeper implantation for fecal incontinence.Diseases of the Colon and Rectum 63: 514-519
12. Leo CA, Leeuwenburgh M, Orlando A et al. (2020) Initial experience with SphinKeeperTM intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit. Colorectal

Disease: the Official Journal of the Association of Coloproctology of Great Britain and Ireland doi: 10.1111/CODI.15277

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	21/09/2020	Issue 9 of 12, September 2020
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	21/09/2020	Issue 9 of 12, September 2020
International HTA database (INAHTA)	21/09/2020	
MEDLINE (Ovid)	21/09/2020	1946 to September 18, 2020
MEDLINE In-Process (Ovid)	21/09/2020	1946 to September 18, 2020
MEDLINE Epubs ahead of print (Ovid)	21/09/2020	September 18, 2020
EMBASE (Ovid)	21/09/2020	1974 to 2020 Week 38

Trial sources searched June 2019

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched June 2019

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Fecal Incontinence/
2 ((faecal* or fecal* or faeces or feces or faecally or anal or anally or stool* or bowel* or double or defecat* or defaecat*) adj4 (incontin* or urge* or leak* or soil* or seep* or impact*)).tw.
3 FI.tw.

4	or/1-3
5	"Prostheses and Implants"/ae, mt [Adverse Effects, Methods] (4590)
6	Artificial anal sphincter.tw.
7	Transanal Endoscopic Surgery/
8	Transanal endoscop* surger*.tw.
9	intersphinct* space*.tw.
10	((self expand* or self-expand*) adj4 (prothes* or implant*)).tw.
11	(intersphinct* or anal*).tw.
12	10 and 11
13	sphincteroplast*.tw.
14	5 or 6 or 7 or 8 or 9 or 12 or 13
15	4 and 14
16	Sphinkeeper.tw.
17	PTQ implant.tw.
18	InterStim.tw.
19	16 or 17 or 18
20	15 or 19
21	animals/ not human/
22	20 not 21

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Cavazzoni A, Rosati E, Zavagno V et al. (2015) Simultaneous Delorme's procedure and inter-sphincteric prosthetic implant for the treatment of rectal prolapse and faecal incontinence: preliminary experience and literature review. International Journal of Surgery 14: 45–8	Case series n=3 Follow-up=12 months	Gatekeeper implant is feasible and safe when associated with surgical procedures such as Delorme's prolapse resection. A simultaneous treatment of faecal incontinence should always be considered when doing surgery for rectal prolapse.	Larger studies are included.