National Institute for Health and Care Excellence

IP1764 Self-expanding implant insertion into the intersphincteric space for faecal incontinence

IPAC date: 12 November 2020

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 NHS Professional	**General**	Dear Sirs and Madams, We read with the interest the full draft guidance for Sphinkeeper. This is a relatively new product so the global engagement with and status of this treatment for faecal incontinence is constantly changing. At St Mark's we have been using this treatment since 2016 and have found the insertion of this device relatively straight forward given our previous experience with injectable anal bulking agents. It has also proved to be safe in our hands and generally well tolerated by patients. There is, however, an issue of poor placement of the inserts or post-insertion migration. These are difficult to distinguish as the implants are less palpable / visible on ultrasound at the time of insertion than they are after they have expanded in vivo. We have recently published an interesting review of a cohort of patients who underwent Sphinkeeper procedure at St Mark's Hospital and The Royal London Hospital in the UK and our results match with those previously published by other authors. Although a refined technique is necessary to achieve optimal outcomes, the figures reported in our prospective study have	Thank you for your comments about your clinical experience and about the life-changing nature of the condition. The review (Leo et al.) was identified in the post consultation literature search and will be added to table 2 of the overview.

			confirmed that this is a safe alternative procedure for patients suffering from faecal incontinence. It should be taken in consideration that faecal incontinence is a life changing condition. Patients undergoing this procedure have exhausted valid alternative procedures and are close to the end of their treatments options. In some patients this treatment is an alternative to a stoma which is a body imaging-changing intervention.	
2	Consultee 1 NHS Professional	**Section 1**	Clearly any patient who is a candidate for SphinKeeper should be discussed at a pelvic floor MDT and only surgeons in tertiary centres and with high expertise in pelvic floor diseases should perform this procedure. Entry onto a database is also ideal but, considering its safety record, its suitability for the very old and its position at the end of the treatment ladder entry into a trial may not be suitable for all patients.	Thank you for your comments about patient selection by an MDT and the expertise required to perform the procedure. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee.
3	Consultee 1 NHS Professional	**General**	Finally, the following four most recent publications should be considered in the final guidance: 1.Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of GateKeeper versus SphinKeeper. Grossi U, Brusciano L, Tolone S, Del Genio G, Di Tanna GL, Gambardella C, Docimo L. Surg Innov. 2020 Jun 16:1553350620934932. doi: 10.1177/1553350620934932. Online ahead of print. PMID: 32543984. 2.Sphinkeeper™ for faecal incontinence: a preliminary report. La Torre M, Lisi G, Milito G, Campanelli M, Clementi I. Colorectal Dis. 2020 Jan;22(1):80-85. doi: 10.1111/codi.14801. Epub 2019 Aug 16. PMID: 31373152. 3.Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre	Thank you for your comment. Grossi et al. was identified in the updated literature search and will be added to table 2 of the overview. La Torre et al. is included in table 2 of the overview. Leo et al. was identified in the updated literature search and will

			retrospective clinical audit. Leo CA, Leeuwenburgh M, Orlando A, Corr A, Scott SM, Murphy J, Knowles CH, Vaizey CJ, Giordano P. Colorectal Dis. 2020 Jul 19. doi: 10.1111/codi.15277. PMID: 32686233. 4.Efficacy of Sphinkeeper™ implant in treating faecal incontinence. Litta F, Parello A, De Simone V, Campennì P, Orefice R, Marra AA, Goglia M, Moroni R, Ratto C. Br J Surg. 2020 Apr;107(5):484-488. doi: 10.1002/bjs.11558. Epub 2020 Feb 17. Thank you for taking these comments in consideration. Yours Faithfully, [redacted] [redacted] Declaration of interest: [redacted] has no declarations of interest in relation to this particular product has been paid to run courses for THD. She also has share options in Renew Medical and has been paid Consultancy Fees, Lecture Honoraria and fees for running courses for Medtronic. [redacted] has no declarations of interest. In relation to this particular product has received few funding to attend two international conferences in the past.	be added to table 2 of the overview. Litta et al. will be added to table 2 of the overview. Papers added to the overview will be considered by the committee.
4	Consultee 2 Overseas health care professional Associate Professor in General Surgery	**General**	**"Self-expanding implant insertion into the intersphincteric space for faecal incontinence In development [GID-IPG10137]"** [redacted] Associate Professor in General Surgery, Department of Surgery, [redacted]	Thank you for identifying and summarising these papers. Litta et al. (ref 1) will be added to table 2 of the overview.

			Director of Proctology Unit, University Hospital Foundation [redacted] DISCLOSURES: I have had a deep involvement in the project and practice of the self-expanding implant insertion into the intersphincteric space for faecal incontinence from the beginning of its introduction, when this method was named Gatekeeper (GK), and, then, later with its latest evolution named SphinKeeper (SK). Moreover, I cooperate with THD spa, Company producing those devices in improving their clinical and scientific application. In my following comments I have tried all my best to report data as appeared in the papers commented, avoiding at the best personal considerations related to my potential conflict of interest. COMMENTS: Results of my previous clinical data have already been included in the Overview of this Project (see references # 1, 3, 5 and 6). It could be of interest for NICE Institution to update the available data taking in consideration my more recent published (or submitted for publication) results, specifically concerning the SphinKeeper procedure. They are: **(1)** Efficacy of Sphinkeeper™ implant in treating faecal incontinence. Litta F, Parello A, De Simone V, Campennì P, Orefice R, Marra AA, Goglia M, Moroni R, Ratto C. Br J Surg. 2020 Apr;107(5):484-488. doi: 10.1002/bjs.11558. **(2)** Implant of SphinKeeper in fecal incontinent patients improves external anal sphincter contractility. Litta F, Marra AA, Ortega Torrecilla N, Orefice R, Parello A, De Simone V, Campennì P, Goglia M, Ratto C. Submitted for publication on Dis Colon Rectum. Moreover, I have found very interesting the results recently published in two papers: **(3)** Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit. Leo CA, Leeuwenburgh M,	Reference 2 is not yet published. Leo et al. was identified in the updated literature search and will be added to table 2 of the overview. Grossi et al. was identified in the updated literature search and will be added to table 2 of the overview. Brusciano et al. was identified in the updated literature search and will be added to table 2 of the overview. Papers added to the overview will be considered by the committee.

			Orlando A, Corr A, Scott SM, Murphy J, Knowles CH, Vaizey CJ, Giordano P. Colorectal Dis. 2020 Jul 19. doi: 10.1111/codi.15277. **(4)** Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of GateKeeper versus SphinKeeper. Grossi U, Brusciano L, Tolone S, Del Genio G, Di Tanna GL, Gambardella C, Docimo L. Surg Innov. 2020 Jun 16:1553350620934932. doi: 10.1177/1553350620934932. Finally, another paper recently appeared concerning GK, the precursor of SK: **(5)** Middle-term Outcomes of Gatekeeper Implantation for Fecal Incontinence. Brusciano L, Tolone S, Del Genio G, Grossi U, Schiattarella A, Piccolo FP, Martellucci J, Schiano di Visconte M, Docimo L. Dis Colon Rectum. 2020 Apr;63(4):514-519. doi: 10.1097/DCR.0000000000001559. In the **study (1)**, patients with a sphincter defect affecting no more than 120° of the internal or external sphincter, or both were selected, while those with sphincter(s) defects of the internal or external anal sphincter, or both, of more than 120° of anal canal circumference were excluded. Forty five consecutive patients (36 women; mean(s.d.) age 66·6(10·6), range 38–85 years) underwent SK implantation (10 prostheses placed into the intersphincteric space of the upper-middle anal canal, under the guide of the endoanal ultrasonography - EAUS); 42 of them were available for follow up (mean follow-up was 15·9(8·6) (range 6–33) months). Neither intra- nor postoperative complication was registered. Compared with baseline values, faecal incontinence of all types decreased (see Table below). Five patients became fully continent. **Table.** Number of soiling and incontinence episodes per week, and faecal incontinence severity scores at baseline and during follow-up	

	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	2·0(2·1)	1·3(1·5)	0·9(1·5)	0·6(1·4)	0·8(1·5)	0·003

solid stools (episodes per week)						
CCFIS score	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

Values are mean(s.d.). CCFIS, Cleveland Clinic Fecal Incontinence Score.

* Comparison between baseline and data collected at last follow-up session (Wilcoxon test).

The number of patients who never or rarely experienced post-defaecation soiling episodes increased significantly from 3 at baseline to 23 at date of last follow-up (P < 0·001). The ability to defer defaecation improved significantly, with 14 patients able to defer for more than 5 min at baseline, compared with 29 at last follow-up (P = 0·001). The mean(s.d.) CCFIS changed from 12·0(3·7) at baseline to 7·6(4·1) at last follow-up (P < 0·001); similarly, the Vaizey score decreased from 14·6(4·4) to 10·2(4·7) (P < 0·001).

			Concerning the evaluation of patients' quality of life (QoL), all domains of the FIQL questionnaire improved after the SK procedure; while only the physical functioning improved on the SF-36® questionnaire. Maximum squeeze pressure increased, from mean(s.d.) 80·7(68·5) mmHg at baseline to 90·1(48·7) mmHg at last follow-up (P = 0·006), with no difference in maximum resting pressure and rectal sensory thresholds. At the last follow-up, EAUS assessment of prosthesis position found that SK implantation was adequate in 23 of the 42 patients, with at least six of ten prostheses placed in the target area. Patients with adequate SK placement had improved outcomes and CCFIS compared with those with inadequate placement. Fourteen patients (all women; mean age 67·4(9·3) years) with faecal incontinence and anal sphincter defects underwent SK implantation. The range of sphincter defect extension was 30–120° for the internal anal sphincter and 30–120° for the external anal sphincter. After SK placement, eight of 14 patients showed an over 50 per cent reduction in the total number of faecal incontinence episodes per week. In summary, this paper has demonstrated an improved incontinence in the majority of patients submitted to SK implant, during the early postoperative phase and long-term follow-up, regardless of the type of faecal incontinence treated. **Study (2)** was aimed to evaluate external anal sphincter contractility changes after SphinKeeper implantation (10 prostheses placed into the intersphincteric space of the upper-middle anal canal, under the guide of the endoanal ultrasonography - EAUS), comparing them to clinical outcomes. Thirty-nine patients (34 females; median age 68 years) were included in the study. Along the FU (at 1, 3, 6 months and, then, annually), patients underwent full clinical and instrumental examinations, including 3D-EAUS and ARM, to assess not only the morpho-functional	

			features of the anal canal but also the prostheses position. As previously described, an implant was considered as “adequate” when at least 6 out of 10 prostheses were located in the upper two thirds of the anal canal. The external anal sphincter muscle-tension (Tm, measured in milliNewton per square centimeter, mN/cm2) was evaluated using the equation Tm=P*ri/tm, where P is the maximum voluntary squeeze pressure, ri is the inner radius of the external anal sphincter muscle, and tm is its thickness. For the calculation of the external anal sphincter muscle-tension and changes in Tm, we considered ARM and EAUS data obtained at baseline and at the last FU visit (named, "last-FU"), as showed in Figures 1 and 2. In all patients, the maximum squeeze pressure and the inner radius and thickness of the external anal sphincter were measured at the level of the middle anal canal. The change in Tm (ΔTm) was evaluated as difference between external anal sphincter muscle-tension after the SK implantation and that at baseline. Based on the ΔTm median value, patients were divided in two subgroups: subgroup 1 concerning patients with ΔTm higher than median value; subgroup 2 concerning those with ΔTm lower than median value. FI symptoms were assessed with CCFIS and Vaizey score. No morbidity was registered. After a median follow-up period of 14 months, both the median maximum voluntary squeeze pressure and the median inner radius of the external anal sphincter significantly increased. A statistically significant increase of external anal sphincter muscle tension was detected. A decrease of any faecal incontinence symptom and an improvement in severity scores were observed at the last follow-up examination. The external anal sphincter contractility was significantly higher in patients reducing incontinence episodes to solid stool by more than 50% and improving ability to defer defecation for more than 15 minutes.	

			In conclusion, this study showed that SK implantation improved the external anal sphincter muscle-tension; a positive correlation between its increase and the clinical outcome has been noted. In the **study (3)**, two major tertiary referral UK centres - Royal London and Whipps Cross Hospitals (part of Bart's Health NHS Trust: hereafter 'BARTS') and St Mark's Hospital (SMH) (part of London North West University Healthcare NHS Trust) – enrolled 27 patients who underwent the SK procedure: 19 at BARTS and 8 at SMH. Five patients had undergone an initial trial of sacral nerve stimulation that had failed. Preoperative EAUS showed degeneration or disruption of the internal anal sphincter in 12 of the 27 patients (44%), and disruption of the external anal sphincter in 10 of 27 patients (37%). At BARTS, 19 consecutive patients were treated with the placement of SK prostheses under digital guidance. In 10 procedures, the device was noted to misfire for technical reasons intraoperatively. At SMH, in which prostheses were placed under ultrasound guidance during surgery, difficulties with device misfire also occurred, although the number of occasions this happened was not recorded (to be noted that these technical adverse events were not reported in my as well other experiences; they did not alter the clinical conditions of the patients). There were no intraoperative complications other than device misfire; moreover, no postoperative complication was registered. St. Mark's incontinence score (SMIS, also known as "Vaizey score") significantly improved from baseline (median -6 points [range -12 to +3]; $p < 0.00016$) with 14/27 (51.9%) patients achieving a 50% reduction in SMIS score. On postoperative imaging, a median of 7 prostheses (range 0 – 10) were identified with a median of 5 (range 0 - 10) optimally placed. There was no relationship between number of well-sited prostheses on postoperative imaging and categorical success based on 50% reduction in SMIS (Chi2 test: $p = 0.79$).	

			In summary, from in study SK appears to be a safe procedure for faecal incontinence. Overall, about 50% patients achieved a meaningful improvement in symptoms. The **study (4)** was aimed to evaluate morpho-functional changes of the sphincter complex after GateKeeper (GK) and SphinKeeper (SK) procedures and correlate these with symptom improvement. Ten consecutive females undergoing SK implant were age-matched with a cohort of 10 females who previously underwent the GK procedure. The external anal sphincter muscle-tension (Tm) was calculated in this study using the same formula of **study (2)** and the Cleveland Clinic Fecal Incontinence Score (CCFIS) was used to evaluate the incontinence severity. Although not reaching statistical significance, symptom improvement after SK was 33% above that observed after GK (P = 0.088). Compared to the baseline, a significant increase in Tm was observed in both groups at 12 months (GK, 508.1 [478.8-568.0] vs 864.4 [827.0-885.8] mN (cm2)-1; SK, 528.0 [472.7-564.0] vs 858.6 [828.0-919.6] mN (cm2)-1, P = .005). Compared to the GK group, Tm was significantly higher in patients after SK implant (158.3 mN (cm2)-1 [95% confidence interval, 109.6-207.0]; P < .001), after controlling for baseline values, at 12-month post-implantation. In this study, both GK and SK were safe and effective treatments for FI with good short-term clinical outcomes. Comparative analysis showed superiority of SK over GK in terms of gain in Tm, with borderline significantly better improvement in symptoms. In the **study (5)**, 20 patients (all women; median age, 59 y) were enrolled, and submitted to GK implantation (4-6 prostheses). All procedures were not complicated. Postoperative endoanal ultrasonography showed normal prosthesis localization in 16 patients (80%). At anorectal manometry, mean anal resting pressure significantly improved	

			(57.8 ± 7.5 mm Hg; p = 0.0004). Mean preoperative Cleveland Clinic Fecal Incontinence score was 12.4 ± 1.8, with significant improvements initially documented at 3 months (4.9 ± 1.5; p < 0.0001) and sustained up to 36 months (4.9 ± 1.7; p < 0.0001). Patients receiving only 4 (compared with 6) prostheses and those experiencing pudendal neuropathy (compared with those who did not) showed significantly higher Cleveland Clinic Fecal Incontinence score values in the middle term. In conclusion this study showed that initial improvements after GK implantation for FI are sustained in the middle term. All the more recent studies, together with those already taken in consideration in the NICE Overview of this Project, demonstrated consistently the high safety and significant clinical efficacy of both GK and SK in treating patients affected by faecal incontinence (the latter one with additional potentials also in patients with sphincter lesions). Further studies (in particular, RCTs) will definitely elucidate the therapeutic role and the correct indications for this approach. The NICE recognition will boost the clinical application and scientific research in UK.	
5	Consultee 3 Overseas health care professional Colorectal surgeon	**General**	<u>Setting and clinical activity description:</u> [redacted], myself, is a Colorectal Surgeon with more that 15 years of experience in proctology and pelvic floor anatomical and functional diseases. I'm a research Professor at [redacted] school of medicine and I currently head coloproctology clinics in Perugia and Milan with more than 700 patients/year evaluated for benign and malignant affections of the anorectum. Among those patients about 10% complain with a Faecal Incontinence (FI) condition, both active or passive. We directly provide clinical and instrumental evaluation, including EAUS, Manometry, Defecography and clinical assessment and Scoring for FI in the initial patient assessment.	Thank you for your comments and conclusions about your clinical experience of using this procedure.

			Percentage of Fi patients considered for Sphin Keeper (SK) implant: Among FI patients, about 40-50% are considered for surgical implant of inter-sphincteric prosthesis. Indications for the procedure are: passive faecal incontinence, EAS damage, status post Radio Therapy sphincter damage, primary or age related Hypotone of EAS-IAS complex, OASIS, Anterior resection syndrome. Treated patients: To date, I treated more than 20 patients suffering with FI with the application of the SK device. Methodology: All patients were treated according with the original technique described by Carlo Ratto, including the use of intra operative EAUS before and after the insertion of every prosthesis in order to encircle the IAS and deploy the prosthetic material in the inter-sphincteric space. Seven to 10 prosthesis were used in the personal patients cohort. Intra operative observations: The SK procedure needs a relatively short training and learning curve, being a superficial procedure with few simple and precise rules to follow. Experience in EAUS is important as well as a complete knowledge of the anatomical details of the anal sphincter complex. The operation usually never exceed 50-60 minutes and can be performed by a single surgeon. Minimal difficulties in implanting the prosthesis can be found in case of very short anal canal, especially in elderly women, extremely relaxed and hypotonic pelvic muscles, diffuse scaring	

			of the EAS. In such cases the implant should be more careful in order to obtain the correct axial placement and hight of the prosthesis in the inter sphincteric space. Immediate extrusion of the implant during placement can happen in less than 5% of the deployments, in such cases an immediate replacement is indicated and completely feasible. Perforation in the anal lumen is an extremely rare event, and to my knowledge has never be followed by septic complications. Bleeding or other intra operative adverse events were never experienced in our series. <u>Post operative observations:</u> SK implant is an extremely safe procedure, post operative pain is minimal to completely absent and the only principal advice in the immediate post operative period is to avoid excessive movements, exercise or straining in the first two-three days after the implant to reduce the chance of early prosthesis displacement. No infections, bleeding or other complications were experienced in the treated patients. In particular, we never registered septic complications, both early or late. Misplacement of one or more prosthesis can be observed, as it is widely described in the literature, and in our series it happened in less than 5% of the implants. Dissipation (the prosthesis cannot be found anywhere at follow up) never happened in our experience, and it is mainly due to the prosthetic characteristics. Cranial migration (the prosthesis is found above the Pubo Rectalis plane) has never been experienced also in our series. Extrusion (the prosthesis is found below the level of the implant) is the only kind of migration that we truly found in the follow up period with the need of removal of a single prosthesis from the under skin area in only one patient. <u>Efficacy:</u>	

			Our results are in line with the published data, with more than 70% of patients experiencing a positive results starting from the immediate post operative period. In particular, a significant drop of the St Marks scoring value when compared with the preoperative assessment is the commonest result found at follow up. QOL, impact on the daily life is one of the main parameter that is expected to improve, followed by a reduction of the incontinence episodes. Manometric data can improve especially when the implant is followed by a pelvic floor rehabilitation. <u>Conclusions:</u> SK is an extremely safe procedure, that should be performed by a surgeon with a good experience in anorectal procedures and trans-anal surgery. Nevertheless the learning curve is short and intra operative complications are extremely rare and unlikely to be significant. EAUS is important to obtain a precise implant especially in difficult cases. Passive incontinence is the main indication, if a sphincter rupture is present, the higher is the degree of the muscle loss and scar, the higher will be the difficulty in correctly implanting the prosthesis. Considering the feasibility of the procedure, the very low rate of complications and the expected results, SK should be always considered as a valid option in the initial treatment of Faecal Incontinence.	
6	Consultee 4 NHS Professional	**General**	Sir/ Madam, I am writing regarding "Self-expanding implant insertion into the intersphincteric space for faecal incontinence In development [GID-IPG10137]". I have pioneered the use of the Gatekeeper and Sphinkeeper in the UK in 2012, being the first surgeon in Scotland to use this device, following the appropriate training. I also run courses at my hospital ([redacted]), training consultant colorectal surgeons on	Thank you for your comment. Thank you for your comment about your clinical experience of using this procedure. We note you have a paper in preparation and have presented findings at various meetings. IPAC only considers evidence on efficacy from peer-reviewed journal papers. IPAC will

			this operation. I have also visited various hospitals in the UK, such as Poole, Liverpool and Dundee in order to train local surgeons. I have carried out in excess of 40 operations using both the Gatekeeper and Sphinkeeper, with reasonably good results and a very low complication rate. A paper detailing both the short-term as well as the long-term results of this procedure is in preparation. The results had been presented in various meetings such as the ACPGBI and the ESCP and published in abstract form. I have written on the indications and technique of this procedure in a book chapter, recently published.	consider evidence on safety from conference abstracts and other sources.
7	Consultee 4 NHS Professional	**Section 1**	I strongly support the use of this procedure in clinical practice, and not just as a research tool. However my strong view is that this is a specialised operation that should be carried out by colorectal surgeons who have undergone the appropriate training. The indications for its use are clearly defined. Careful patient selection is key to a successful outcome. The results of this operation should be audited. In fact, the pelvic floor society is collecting prospective data on the Sphinkeeper. I am happy to discuss this further if deemed necessary.	Thank you for your comments about surgeon expertise and patient selection. Consultee disagrees with main recommendation. Consultee reports that the pelvic floor society are collecting prospective data on the device. The Committee considered this comment but decided not to change the guidance.
8	Consultee 5 NHS Professional	**General**	I believe there is a consultation process about the above technique and I would like the opportunity to provide some comments on that. I was one of the experts initially asked to provide some evidence on the technique being probably one of the largest UK users of the device. We have also just published a two UK Centres experience with the newest generation of the device, the Sphinkeeper. Although it is just a relatively small retrospective series, most of the data were collected	Thank you for your comment. The cited paper (Leo et al.) was identified in the updated literature search and will be added to table 2 of the overview for consideration by the committee.

			prospectively as part of prospective audits registered locally. This study is the first UK evidence on the subject and probably at the present provides the best snapshot about it. I have attached the paper for your interest. https://onlinelibrary.wiley.com/doi/pdf/10.1111/codi.15277  codi.15277-Sphinkeeper.pdf	
9	Consultee 5 NHS Professional	**General**	I would also like to provide further comments on the subject that you may find useful. 1. In my experience the technique is safe, easy to perform and well tolerated by the patients 2. Although its real effectiveness remains to be stablished it is likely that a proportion of the patients do benefit from the treatment (50-55%). 3. Our data represents the initial experience with the technique and are likely to reflect our learning curve. We have now recognised and addressed some of the pitfalls of the procedure with the hope to further improve clinical outcomes 3. The population to be treated should be carefully selected and only treated in recognised Pelvic Floor centres with specific experience about the technique and as part of ongoing audits 4. This population represents patients who have failed other treatment options for faecal incontinence and may benefit from this simple option that I believe should be available to them, provided is delivered in the right centre by the right person. These patients may have no other treatment options 5. All patients treated should be included in the National Register now available on line to all	Thank you for your comments about your clinical experience. Consultee reports that a national register is now available to all. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee.
10	Consultee 5 NHS Professional	**General**	I would also like to comment on the fact that the main Author of some of the study published on the technique (Carlo Ratto) has had and maybe still has strong financial interest with the company that produces the device. A couple of years ago his	Thank you for your comment.

			nomination to the presidency of the Italian Society of Colorectal Surgery was rejected by the board because of his very strong commercial links with this particular company. I am indeed extremely surprised to see that he has never declared any conflict of interest in any of the published study on the subject. Finally I have to add that I do have a conflict of interest to declare since I am an official trainer for THD UK running the only Royal College Of Surgeons accredited training course.	The overview describes conflicts of interest as reported in the published studies.
11	Consultee 6 NHS Professional Colorectal Pelvic Floor Nurse Specialist	**General**	Morning My name is [redacted] I am the Colorectal Pelvic Floor Nurse Specialist at [redacted] Hospital my role involves helping patients with severe bowel issues. A long side my two colleagues [redacted] and [redacted] we have been using the sphinkeeper to improve our patients faecal incontinence and their lives, this issue is something that is not really talked about and gives our patients a very miserable and restricted life style which impacts on their lives greatly. I have discussed with some of my patients the difference this procedure has made to their lives. They have all given permission for me to share their comments with you. I asked all patients Had This procedure made a difference to their lives. A score of one to five, five been highest. Would they recommend this procedure to friends and family And any improvement's that could be made. Difference to life 100% Score 5 Yes would definatly recommend Patient said this procedure had "changed her life completely she can no lead a normal life without any worries about working ,socialising etc". Difference to life yes a small amount but glad he had it done Score 2 Would recommend for the right patient Patient said he still has to use Rectal Irrigation and is having on going physio so is hoping things will still improve.	Thank you for your comments and for providing this collated feedback from your patients, including what difference it has made to them, their self-rated score out of 5, and whether they would recommend it. The Committee very much welcomes hearing from patients who have had this procedure.

			Difference to life Partly Score 4 Would recommend Has improved lifestyle somewhat and reduced his anxiety about normal day to day things Difference to life no Score 1 Would you recommend for right person Feels that her chroins/ colitis has been the problem why this hasn't improved her life Diffrence to life yes Score 3 Would definatly recommend Urgency isn't as bad more manageable does take Imodium occasionally Happy without come life is better Score 3 Would recommend Has made life more bearable. These were picked out on a random basis to give a subjective outcome. Things that were recomended were if feel more for us as a surgical team such as maybe a scan/test to see if things still inplace and maybe more physio. It also highlighted that after procedure some manomertery should be conducted so that the patient can see the difference the procedure has actually made.	
12	Consultee 7 Company THD UK	**General**	Further to reading the recent draft guidance ("Self-expanding implant insertion into the intersphincteric space for faecal incontinence In development [GID-IPG10137]") I would like to make some comments on the guidance (please see attached document). I am a registered stake holder and notifier of the proposed IPG. I also work for the manufacturer of the technologies which are used to carry out the procedures.	Thank you for your comment and identifying additional references. Litta et al. will be added to table 2 of the overview. Brusciano et al. was identified in the updated literature search and

			I have attached a document commenting on the draft publication and highlighting recently published data which was not included in the initial assessment but is highly relevant. • Litta F, Parello A, De Simone V et al. (2020) Efficacy of Sphinkeeper™ implant in treating faecal incontinence. Br J Surg;107(5):484-488. doi:10.1002/bjs.11558. • Zino S, Camilleri-Brennan J. Effectiveness of Polyacrilonitrile ('Gatekeeper') Anal Implants in the Treatment of Passive Faecal Incontinence: a Prospective Study. Poster presentation. (Poster attached) • Brusciano, Luigi M.D., Ph.D.1; Tolone, Salvatore M.D., Ph.D.1; Del Genio, Gianmattia M.D., Ph.D.1; Grossi, Ugo M.D.2; Schiattarella, Antonio M.D.1; Piccolo, Francesco Pio M.D.1; Martellucci, Jacopo M.D., Ph.D.3; Schiano di Visconte, Michele M.D.4; Docimo, Ludovico M.D., Ph.D.1. (2020). Middle-term Outcomes of Gatekeeper Implantation for Fecal Incontinence, Diseases of the Colon & Rectum: - Volume 63 - Issue 4 - p 514-519 doi: 10.1097/DCR.0000000000001559. • Ugo Grossi, Luigi Brusciano, Salvatore Tolone, Gianmattia Del Genio, Gian Luca Di Tanna, Claudio Gambardella, Ludovico Docimo, Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of GateKeeper versus SphinKeeper, Surgical Innovation, 10.1177/1553350620934932, (155335062093493), (2020). • Leo, C.A., Leeuwenburgh, M., Orlando, A., Corr, A., Scott, S.M., Murphy, J., Knowles, C.H., Vaizey, C.J. and Giordano, P. (2020), Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit. Colorectal Dis. Accepted Author Manuscript. doi:10.1111/codi.15277	will be added to table 2 of the overview. Grossi et al. was identified in the updated literature search and will be added to table 2 of the overview. Leo et al. was identified in the updated literature search and will be added to table 2 of the overview. Conference abstracts and poster presentations are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview unless they contain important safety data.
13	Consultee 7 Company THD UK	**1.1**	**Summary of Evidence on the Efficacy and Safety of THD Gatekeeper™ and Sphinkeeper™ Implants for the Treatment of Patients with Faecal Incontinence**	Thank you for your comment. Consultee disagrees with main recommendation.

			1. Background The THD Gatekeeper® (GK) and THD Sphinkeeper® (SK) methods are minimally invasive surgeries that can be used in the treatment of patients with faecal incontinence. Both procedures involve making small incisions in the perianal skin, before an implant is deployed at the desired position within the intersphincteric space. The implants can expand and contract within this space, and form a ring that creates an artificial sphincter. These procedures can be carried out in a short amount of time in a day-case setting, and are capable of restoring sphincter control to patients suffering from this disabling condition [1]. Assessment of the two procedures was carried out as part of the National Institute for Health and Care Excellence's (NICE's) Interventional Procedures Programme (*Interventional Procedure Overview of Self-Expanding Implant Insertion into the Intersphincteric Space for Faecal Incontinence* [2]). A recommendation for use of the procedure(s) only in the context of research was made, but on the basis of existing evidence (much of which was not considered in the initial assessment) and previous recommendations around similar procedures, we would suggest that a 'standard arrangements' or 'special arrangements' recommendation is more fitting to support future evaluations of the intervention. We present our rationale for this position in the following report.	The Committee considered this comment but decided not to change the guidance.
14	Consultee 7 Company THD UK	**General**	**2. Response to NICE Interventional Procedure Overview** NICE carried out a rapid review of the medical literature available at the time (September 2019), supplemented by input from professional experts (none of whom have direct experience in	Thank you for your comment. Consultee has presented the data summarised in the overview and provided their own commentary on

			performing the procedure), in order to make their original assessment based on the safety and efficacy of the intervention [2]. As noted in their assessment overview, the main outcome measures used to assess efficacy of the intervention, and related procedures, are the Cleveland Clinic Fecal Incontinence Score (CCFIS), the Vaizey score (both of which examine incontinence severity), and the Fecal Incontinence Quality-of-Life Scale (FIQL). In the NICE rapid review, 7 case series and 1 case report were identified focussing on the safety and/or efficacy of a self-expanding implant insertion for the treatment of faecal incontinence (GK or SK procedure) [2]. Although all studies were relatively small case series with limited follow-up, the safety and efficacy of the procedure (GK or SK), both in terms of reduction of symptoms of incontinence and improvement in quality-of-life, were clearly demonstrated (key findings summarised in Table 1). Focussing on two of the studies with the largest number of patients and longest periods of follow-up (Ratto et al. (2016) [3] & Trenti et al. (2017) [4]), the patient benefits associated with the procedure are evident. In a case series analysis of 54 patients, Ratto et al. (2016) found that 56% of included patients had at least a 75% improvement in incontinence at 1 year follow-up, with 13% of patients achieving full anal continence [3]. Incidents of soiling, and ability to defer defaecation, were also significantly improved at 1 year, while quality-of-life was improved across all domains of the FIQL. In another case series involving 49 patients (Trenti et al. 2017), 48% of patients were classified as a responder within the first 6 months of having undergone the procedure (based on an improvement of at least 50% in Vaizey score) [4]. Mean Vaizey scores were found to be considerably reduced at 6 months (4.3 (SD 2.1)), 12 months (4.2 (SD 3.6) and in a longer-term follow up of 2.7 years on average (5.7 (SD 5.3) compared to baseline (13.3 (SD 3.8)). Additionally, neither case series identified considerable complications associated with the procedure. Ratto et al. (2016) reported that 6% of patients experienced implant extrusion, 13% of patients experienced anal discomfort and 6% of patients experienced dislodgement of a single implant during follow-up [3].	this, to support their statement in comment 13. The table submitted by the consultee is included in the appendix at the end of this document.

			No post-operative complications were identified, while at all follow-up points there was no acute or chronic inflamation around the implants. Trenti at al. (2017) also reported that there were no intra-operative, short- or long-term complications identified amongst the 49 patients included [4]. While all other studies reviewed by the NICE group involved much smaller patient numbers, a similar trend in terms of improved clinical efficacy and minimal safety issues associated with the procedure(s) were noticeable. As noted in the overview presented by NICE, key limitations associated with the identified studies included the fact that none were conducted in a UK setting, and the follow-up duration was limited in most cases. The evidence, which is now available since this initial assessment, presented in Section 3, overcomes these limitations. **Table 1.** Safety and efficacy findings detailed in NICE assessment	
15	Consultee 7 Company THD UK	**General**	**3. Evidence around safety and efficacy not considered in initial assessment** A number of additional studies have been conducted since the original assessment of the procedure(s), which add to the evidence base; clinical efficacy and safety details from each of these studies is presented in the following section. *Efficacy of Sphinkeeper™ Implant in treating faecal incontinence* A recently conducted study that was not considered in the initial Interventional Procedure Guidance (IPG) assessment of the device(s) was work conducted by Litta et al. (2020) focussing on the efficacy of the Sphinkeeper™ (SK) implant in treating faecal incontinence [11]. In this study, forty-two patients with faecal incontinence (14 with sphincter defects) underwent SK	Thank you for your comment. Consultee has presented data from recently published studies that were not included in the original overview. The new studies added to the overview will be considered by the committee. Litta et al. will be added to table 2 of the overview. Brusciano et al. was identified in the updated literature search and will be added to table 2 of the overview.

			implantation and were followed up for a mean (SD) of 15.9 (18.6) months. Patients included in the study were those who had previously experienced faecal incontinence for at least 6 months and had failed conservative treatment, amongst other inclusion criteria. Evaluation of patient outcomes included: assessment of faecal incontinence episodes over 2 weeks; ability to defer defacecation (in minutes); need to wear pads and/or wear constipating drugs; CCFIS; Vaizey score; Quality-of-Life assessed using the FIQL Scale and the Short Form 36 (SF-36). Assessments were carried out at 3, 6 and 12 months following implantation, and annually thereafter. Results of the study, presented in Table 1 below, indicate that faecal incontinence of all types decreased after undergoing the procedure, and the ability of patients to defer defaecation improved significantly. Additionally, in relation to patient quality-of-life, all domains of the FIQL improved after the procedure and the physical functioning domain of the SF-36 was also improved. Finally, and crucially, no intra-operative or perioperative complications associated with the procedure were identified. Although the sample size of the study was relatively small, this finding was in keeping with previous studies of the SK procedure [12, 13, 14, 15], highlighting the safety of the intervention. **Table 1.** Results for soiling episodes per week, and faecal incontinence severity scores *Effectiveness of Polyacrilonitrile Anal Implants in the Treatment of Passive Faecal Incontinence: a Prospective Study* In another recent study, the methods and results of which are currently unpublished but which have been presented at an international conference, Zino and Camilleri-Brennan (2020, poster presentation) carried out a study into the effectiveness of the Gatekeeper™ (GK) implant for the treatment of passive faecal	Grossi et al. was identified in the updated literature search and will be added to table 2 of the overview. Leo et al. was identified in the updated literature search and will be added to table 2 of the overview. Conference abstracts and poster presentations are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview unless they contain important safety data. The table submitted by the consultee is included in the appendix at the end of this document.

incontinence [16]. Included in the study were twenty patients who either had a structurally intact but weak internal anal sphincter (IAS) or had IAS damage due to childbirth, haemorrhoidectomy, anal stretch or sphicterectomy. All patients had undergone previous conservative measures for their condition or had undergone an injection of other bulking agents such as PTQ™ or Permacol which had ultimately failed. 4 to 6 GK prostheses were implanted in each patient under general anaesthesia in a day-case setting (6 implants used in 17 patients and 4 implants used in 3 patients) at the Forth Valley Royal Hospital, Scotland. Continence scores were assessed prior to undergoing the procedure and 6 weeks folllowing the procedure, as well as at 3, 6, 12, 24 and 36 months post-operatively using the Vaizey questionnaire. Quality-of-life was also assessed pre- and post-operatively (6 and 24 months) using the FIQL questionnaire.
Results from the study indicated that there were no post-operative complications associated with the procedure. Significant sustained improvement in median Vaizey scores were recorded, with median (range) scores improved from 16 (12-17) pre-operatively to 5 (3-9), 4 (3-7), 4 (3-5), 5 (3-6) and 5 (3-6) at 6 weeks and at 3, 6, 12, 24 and 36 months respectively (Table 2). Additionally, FIQL scores improved across all four domains (Lifestyle, Coping and Behaviour, Depression and Embarrassment) at 6 and 24 months follow-up, compared to the baseline assessment. Therefore, study results indicated that the GK was safe and effective in improving both continence and quality-of-life in patients with passive faecal incontinence.

Table 2. Vaizey scores

Time of Assessment	**Median Score (Range)**
Pre-operative	16 (12-17)
6 weeks	5 (3-9)

			<table><tr><td>3 months</td><td>4 (3-7)</td></tr><tr><td>6 months</td><td>4 (3-5)</td></tr><tr><td>12 months</td><td>4 (3-5)</td></tr><tr><td>24 months</td><td>5 (3-6)</td></tr><tr><td>36 months</td><td>5 (3-6)</td></tr></table> *Middle-term Outcomes of Gatekeeper Implantation for Faecal Incontinence* A further study that was not considered in the initial assessment was the work conducted by Brusciano et al. (2020) exploring the middle-term outcomes of the GK implantation for the treatment of faecal incontinence [17]. Twenty patients at a large university tertiary care hospital were recruited and followed-up for a period of 36 months in this prospective cohort study. Patients were included if they had experienced faecal incontinence for greater than 6 months prior to their first visit and if their symptoms were refractory to standard conservative measures. All patients (all of whom were female) received 4 to 6 GK prostheses and underwent ultrasonography and manometry pre-operatively and at 2 and 3 months post-operatively. Additionally, the CCFIS was calculated for each patient at baseline and at 1, 3, 12, 24, and 36 months post-operatively. Results from the pre- and post-operative ultrasonography and manometry indicated that normal prosthesis localization was present in 16 patients (80%), and that mean anal resting pressure was significantly improved post-procedure. The mean (SD) pre-operative CCFIS was 12.4 (1.8), and this improved to 4.9 (1.5) at 3 months and was sustained up to 36 months (4.9 (1.7)). In addition, no complications associated with the procedure were identified. Findings of this study highlight the immediate improvements for patient faecal incontinence associated with the GK implantation, and also indicate that these improvements are sustained in the medium-term.	

			Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of Gatekeeper versus SphinKeeper Another study that was not considered in the assessment of the intervention was the work conducted by Grossi et al. (2020), which looked at morphofunctional changes of the sphincter complex in patients receiving GK and SK procedures [18]. In this retrospective cohort analysis, ten female patients undergoing the SK implant (receiving 10 prostheses) were age-matched with ten female patients who previously underwent GK implantation (receiving 6 prostheses). Muscle tension and the CCFIS was assessed at baseline (pre-operatively) and again at 12 months post-operatively. Results from this study indicated that CCFIS was improved in both groups 12 months following implantation, with symptom improvement following SK 33% greater than symptom improvement following GK. A significant improvement in muscle tension was also identified in both groups at 12 months, with muscle tension being significantly higher in those patients who had undergone SK compared to those who had undergone GK, after controlling for baseline values. As in the previous studies presented, results indicate that both GK and SK are safe and effective and that they also have good short-term clinical outcomes. *Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit* The final study of relevance which has been conducted since the initial assessment of the procedure(s) was the work carried out by Leo et al. (2020), which looked at clinical data prospectively collected from patients undergoing a SphinKeeper™ implant in two UK tertiary centres [19]. The study focussed on the technique, safety, feasibility and short-term effectiveness of the procedure. Specifically, information on baseline data, intra-operative and post-operative complications, symptoms (using St Mark's	

			incontinence score [SMIS]) and radiological outcomes were assessed. Twenty-seven patients (18 female, 9 male) in total underwent the procedure. No intra-operative complications were reported, and all patients were discharged on the same or following day. There was a significant improvement in SMIS from baseline (median -6 points [range -12 to +3]; $p < 0.00016$), with approximately 50% of patients achieving a 50% reduction in SMIS score. Clinical success of the procedure was also determined to be unrelated to rate of misplaced/migrated implants. *Summary of new evidence* As detailed above, recently conducted studies would appear to support the argument that both GK and SK procedures are safe and clinically effective. Additionally, limitations originally noted by NICE including the fact that previous studies were not based in the UK and were of limited follow-up duration have been overcome. The studies by Zino and Camilleri-Brennan (2020) and Leo et al. (2020) were conducted in a UK setting [16, 19], while the studies carried out by Brusciano et al. (2020) and Zino and Camilleri-Brennan (2020) included follow-up to 36 months post-procedure [16, 17].	
16	Consultee 7 Company THD UK	**General**	**4. Comparator procedures which have undergone assessment** Comparator procedures to use of GK and SK implants include the use of injectable bulking agents, endoscopic radiofrequency therapy, percutaneous tibial nerve stimulation, sacral nerve stimulation, and alternative surgical treatments including anorectal and trans abdominal artificial anal sphincter implants, gracilopasty and colostomy. Many of these comparator procedures have already been evaluated by NICE as part of their IPG programme, and many received a more favourable outcome than that received for the GK and SK implants. A summary of	Thank you for your comment. The consultee has presented data from relevant IPGs as a comparison to the current guidance, noting that they have all been given recommendations for 'special arrangements' or 'normal arrangements'. IPAC considers efficacy and safety of a procedure and does

			these comparators, their associated IPG evaluations and their clinical efficacy and safety relative to GK and SK has previously been presented in the Structured Information Request that was submitted to NICE. A re-iteration of these findings is presented below to potentially inform a revised outcome for the GK and SK implants. **Relevant Interventional Procedures Guidance** **Table 3.** Summary of efficacy, safety and recommendations for IPGs listed as 'Relevant NICE Guidance' *Summary of relevant Interventional Procedure Guidance* A number of comparators to the GK and SK implants have undergone assessment as part of the NICE IPG programme. Literature reviews were conducted for each evaluation, and in most cases the majority of the studies identified were case series (as in the assessment of the GK and SK procedures). As was the case in most of the studies identified in the GK/SK assessment, many of these case series studies had low patient numbers and limited follow-up durations. Clinical efficacy of the intervention being evaluated was demonstrated for all interventions presented in Table 3. However, results are largely comparable to the demonstrated clinical efficacy of the GK/SK procedures. All comparator interventions had associated complications and some of the interventions presented had arguably higher complication rates than those demonstrated for the GK/SK procedures. All comparator interventions presented above were recommended for use under 'Normal Arrangements' or 'Special Arrangements', which is in contrast to the recommendation made based on the assessment of the GK and SK procedures.	not make a decision on comparative effectiveness. The summary table submitted by the consultee is included in the appendix at the end of this document. The Committee considered this comment but decided not to change the guidance.
17	Consultee 7 Company THD UK	**1.1**	**Conclusion** Concerns were raised in the initial IPG evaluation of the GK and SK procedures that existing studies exploring safety and clinical	Thank you for your comment. Consultee disagrees with main recommendation.

			efficacy of the implants were limited, with small patient numbers, limited duration of follow-up and a lack of studies conducted in a UK setting. Since completion of the initial assessment of the procedures, a number of additional studies have been undertaken which overcome these limitations, whilst highlighting the safety of the implants and their clinical efficacy. Additionally, a number of IPG evaluations of comparator procedures have previously been undertaken by NICE. As presented in this document, as well as in previously submitted documentation (Structured Information Request), many of these comparator procedures received a more favourable outcome from their evaluation than the procedures presented here, despite having comparable or inferior safety and efficacy evidence. On this basis, we would suggest that the GK and SK procedures should receive a recommendation for use under standard arrangements, or special arrangements, rather than in the context of research only.	The Committee considered this comment but decided not to change the guidance.
18	Consultee 7 Company THD UK	**refs**	References 1. THD Gatekeeper® and THD Sphinkeeper® Methods. https://www.thdlab.co.uk/patients/treatments/hot-to-treat-faecal-incontinence/thd-gatekeeper-and-sphinkeeper-methods. [Accessed on 18/07/20]. 2. National Institute for Health and Care Excellence (2019). Interventional procedure overview of self-expanding implant insertion into the intersphincteric space for faecal incontinence. Interventional Procedures Programme. 3. 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. 4. Trenti L, Biondo S, Noguerales F. (2017). Outcomes of GatekeeperTM prosthesis implantation for the treatment of fecal incontinence: a multicenter observational study. Techniques in Coloproctology 21: 963–70.	Thank you for your comment.

			5. Ratto C, Parello A, Donisi L et al. (2011). Novel bulking agent for faecal incontinence. The British Journal of Surgery 98: 1644–52. 6. La Torre M, Lisi G, Milito G et al. (2019). SphinkeeperTM for faecal incontinence: a preliminary report. Colorectal Disease doi: 10.1111/codi.14801. 7. Leo, C.A., Leeuwenburgh, M., Orlando, A., Corr, A., Scott, S.M., Murphy, J., Knowles, C.H., Vaizey, C.J. and Giordano, P. (2020), Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit. Colorectal Dis. Accepted Author Manuscript. doi:10.1111/codi.15277 8. Ratto C, Donisi L, Litta F et al. (2016). Implantation of SphinKeeperTM: a new artificial anal sphincter. Techniques in Coloproctology 20: 59–66. 9. Grossi U, De Simone V, Parello A et al. (2019). Gatekeeper improves voluntary contractility in patients with fecal incontinence. Clinical Innovation 26: 321–7. 10. Grossi U, Brusciano L, Tolone S, Del Genio G, Di Tanna G, Gambardella C, Docimo L. (2020) Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of GateKeeper versus SphinKeeper, Surgical Innovation, 10.1177/1553350620934932, (155335062093493) 11. de la Portilla F, Reyes-Diaz ML, Maestre MV et al. (2017). Ultrasonographic evidence of GatekeeperTM prosthesis migration in patients treated for faecal incontinence: a case series. International Journal of Colorectal Disease 32: 437–40. 12. Al-Ozaibi L, Kazim Y, Hazim W et al. (2014). The GatekeeperTM for fecal incontinence: Another trial and error. International Journal of Surgery Case Reports 5: 936–8. 13. Litta F, Parello A, De Simone V et al. (2020) Efficacy of Sphinkeeper™ implant in treating faecal incontinence. Br J Surg;107(5):484-488. doi:10.1002/bjs.11558. 14. Ratto C, Parello A, Donisi L, Litta F, De Simone V, Spazzafumo L et al. (2011). Novel bulking agent for faecal incontinence. Br J Surg; 98: 1644– 1652.	

			15. Ratto C, Donisi L, Litta F, Campennì P, Parello A. (2016). Implantation of SphinKeeper™: a new artificial anal sphincter. Tech Coloproctol; 20: 59– 66. 16. Ratto C, Buntzen S, Aigner F, Altomare DF, Heydari A, Donisi L et al. (2016). Multicentre observational study of the Gatekeeper™ for faecal incontinence. Br J Surg; 103: 290– 299. 17. de la Portilla F, Reyes-Díaz ML, Maestre MV, Jiménez-Rodríguez RM, García-Cabrera AM, Vázquez-Monchul JM et al. (2017). Ultrasonographic evidence of Gatekeeper™ prosthesis migration in patients treated for faecal incontinence: a case series. Int J Colorectal Dis; 32: 437– 440. 18. Zino S, Camilleri-Brennan J. Effectiveness of Polyacrilonitrile ('Gatekeeper') Anal Implants in the Treatment of Passive Faecal Incontinence: a Prospective Study. Poster presentation. 19. Brusciano, Luigi M.D., Ph.D.1; Tolone, Salvatore M.D., Ph.D.1; Del Genio, Gianmattia M.D., Ph.D.1; Grossi, Ugo M.D.2; Schiattarella, Antonio M.D.1; Piccolo, Francesco Pio M.D.1; Martellucci, Jacopo M.D., Ph.D.3; Schiano di Visconte, Michele M.D.4; Docimo, Ludovico M.D., Ph.D.1. (2020). Middle-term Outcomes of Gatekeeper Implantation for Fecal Incontinence, Diseases of the Colon & Rectum: - Volume 63 - Issue 4 - p 514-519 doi: 10.1097/DCR.0000000000001559. 20. Grossi U, Brusciano L, Tolone S, Del Genio G, Di Tanna GL, Gambardella C, & Docimo L. (2020). Implantable Agents for Fecal Incontinence: An Age-Matched Retrospective Cohort Analysis of GateKeeper versus SphinKeeper. Surgical Innovation. 21. Leo CA, Leeuwenburgh M, Orlando A, Corr A, Scott SM, Murphy J, Knowles CH, Vaizey CJ, Giordano P. (2020). Initial experience with SphinKeeper™ intersphincteric implants for faecal incontinence in the United Kingdom: a two-centre retrospective clinical audit. Colorectal Disease. 22. National Institute for Health and Care Excellence (2007). Interventional procedure overview of injectable buling agents for faecal incontinence. Interventional Procedures Programme 210.	

			23. National Institute for Health and Care Excellence (2011). Interventional procedure overview of Endoscopic radiofrequency therapy of the anal sphincter for faecal incontinence. Interventional Procedures Programme 393. 24. National Institute for Health and Care Excellence (2004). Interventional procedure overview of Sacral nerve stimualtion for faecal incontinence. Interventional Procedures Programme 99. 25. National Institute for Health and Care Excellence (2011). Interventional procedure overview of Percutaneous tibial nerve stimulation for faecal incontinence. Interventional Procedures Programme 395. 26. National Institute for Health and Care Excellence (2004). Interventional procedure overview of Artificial anal sphincter implantation. Interventional Procedures Programme 66. 27. National Institute for Health and Care Excellence (2008). Interventional procedure overview of Transabdominal artificial bowel sphincter implantation for faecal incontinence. Interventional Procedures Programme 276. 28. National Institute for Health and Care Excellence (2006). Interventional procedure overview of Stimulated graciloplasty for faecal incontinence. Interventional Procedures Programme 159. 29. National Institute for Health and Care Excellence (2014). Interventional procedure overview of Insertion of a magnetic bead band for faecal incontinence. Interventional Procedures Programme 483.	
19	Consultee 8 NHS Professional	**1.1**	I feel that the recommendations are well balanced and appropriate. At the present time I am involved in the commissioning of specialist pelvic mesh removal services and would urge extreme caution in the suggestion that such a procedure is rolled out to a wider population where evidence is not yet robust and long term outcomes and adverse events quantified.	Thank you for your comment. Consultee agrees with main recommendation.

Appendix

Comment 14: Safety and efficacy findings detailed in NICE assessment

Study	Study type	Efficacy evidence	Safety evidence
Ratto, C. (2016) [3]	Case series with 54 patients	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. All FIQL questionnaire items (lifestyle, coping and behaviour, depression and self-perception, and embarrassment) were statistically significantly improved at 1 year.	Intra-operative complications • Implant extrusion=6% (3/54) (a single implant was extruded spontaneously immediately after placement, and was replaced). There were no post-operative 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.
Trenti, L. (2017) [4]	Case series with 49 patients	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)	There were no intra-operative 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.

		• Long-term follow-up (mean 2.7 years)=5.7 (SD 5.3)	
Ratto, C. (2011) [5]	Case series with 14 patients	Clinical success=92.9% (13/14). 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 post-evacuation 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 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 embarassment (p=0.001).	There were no intra-operative or post-operative 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.

La Torre, M. (2019) [6]	Case series with 13 patients	Improved CCFIS score at 6 months. Improved FIQL score across all domains at 6 months. Reduced total number of incontinence episodes per week at 6 months.	There were no intra-operative or inhospital 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).
Ratto, C. (2016) [7]	Case series with 10 patients	No efficacy data were reported.	There were no intra-operative complications or early post-operative 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.
Grossi, U. (2019) [8]	Case series with 16 patients	Assessments at baseline and 12 months. Improved mean CCFIS score. Improved FIQL score across all domains.	No safety data were reported.

De la Portilla, F. (2017) [9]	Case series with 7 patients	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 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).	There were no immediate intra-operative or post-operative 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 implant 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
Al-Ozaibi, L. (2014) [10]	Case report with 1 patient	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	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.

		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.	

Comment 15: Results for soiling episodes per week, and faecal incontinence severity scores

	Baseline (n=42)	3 months (n=42)	6 months (n=42)	12 months (n=28)	Last follow-up (n=42)	p-value
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 score	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

Comment 16: Summary of efficacy, safety and recommendations for IPGs listed as 'Relevant NICE Guidance'

Title	ID Number	Date	Recommendation	Relevant Evidence	Summary of Efficacy	Summary of Safety
Injectable bulking agents for faecal incontinence [20]	IPG210	Feb-07	Special Arrangements	7 Case series	Improved continence and quality-of-life (where reported) generally reported across studies.	Approximately 50% of the identified studies report some incidence of adverse events associated with the procedure. Complications reported include: pain at anal injection site, leakage of bulking agent, pain or ulceration over the injection site, passage of bulking agent.
Endoscopic radiofrequency therapy of the anal sphincter for faecal incontinence [21]	IPG393	May-11	Special Arrangements	7 Case series, 1 Case report	Improvements in CCFIS, FIQL and other quality-of-life questionnaires utilised generally reported across studies.	All studies included in the assessment, apart from 1, reported complications associated with the procedure. These complications included: discomfort or pain due to the procedure, anal mucosal ulceration, bleeding, nausea and vomiting, abscess formation, urinary tract infection, constipation, anal mucosal erosion. Complication rates varied across studies.
Sacral nerve stimualtion for faecal incontinence [22]	IPG99	Nov-04	Normal Arrangements	6 Case series, 1 double-blind crossover study, 1 prospective multicentre non-	Improvements in ability to defer defaecation, reduction in faecal episodes per week, improved CCFIS score, and improved quality-of-life generally reported across studies.	In the 6 Case series, lead migration, lead dislodgement, pain, infection, pain from implanted electrode were among the adverse events reported.

				randomised trial		
Percutaneous tibial nerve stimulation for faecal incontinence [23]	IPG395	May-11	Special Arrangements	6 Case series, 1 non-randomised comparative study	Ability to defer defaecation, reduction in faecal episodes per week improved CCFIS score, and improved quality-of-life generally reported across studies.	Approximately 50% of included studies reported adverse events but these were largely minimal. Complications reported included swollen leg (unclear if this was due to procedure), gastrodynia after treatment, numbness in leg after treatment, discomfort or pain at insertion site.
Artificial anal sphincter implantation [24]	IPG66	Jun-04	Special Arrangements	22 Case series, 3 Case reports, 1 non-randomised comparative study	High variability in efficacy reported across studies, with results focussing on a range of aspects including: explants and implants, functional results, manometric results, incontinence score, FIQL, amongst others.	Complications reported for all studies presented in the NICE IPG66 overview. Complications presented included infection, bleeding, perforation, haematoma, wound dehiscence, amongst others.
Transabdominal artificial bowel sphincter implantation for faecal incontinence [25]	IPG276	Nov-08	Special Arrangements	1 Case series	Efficacy data from 1 study (12 patients) indicated that after 1 year, mean continence score based on the CCFIS had reduced from 16 (7-20) to 3 (0-7). Authors indicated that the device was removed in 3 of the first 6 patients after implantation, and that after modification no devices were removed in the next 6 patients.	3 patients underwent removal due to complications. 1 patients was re-admitted to hospital soon after discharge. 1 patient developed a streptococcal infection at the pump site 5 months after implantation. 1 patient developed a disruption of the strap that joined the two components of the sphincter. 2 patients required an admission to hospital for bowel washout.

Stimulated graciloplasty for faecal incontinence [26]	IPG159	Mar-06	Normal Arrangements	11 Case series, 1 non-randomised comparative study, 1 systematic review	Efficacy findings reported for 5 of the included papers. In the first paper, 42%-85% of patients achieved continence with graciloplasty. 0% of patients achieved continence with colostomy. In the second paper, 85% achieved “success” with 1-step graciloplasty. 69% of patients achieved success with 2-step gracilopasty. In the third paper, 76% of patients had a successful outcome. In the fourth paper, no efficacy data were reported. In the fifth paper, overall success was achieved in 62% of non-stoma patients at 12 months.	Complications were reported in 3 out of the 5 papers presented in the NICE IPG159 overview. Complications reported included infection, deep vein thrombosis, pulmonary embolism, thrombophlebitis, urinary retention.
Insertion of a magnetic bead band for faecal incontinence [27]	IPG483	Mar-14	Special Arrangements	2 Case series, 2 non-randomised comparative studies	Median continence scores were reduced and median quality-of-life scores were increased in all studies presented.	Adverse events were reported in all studies presented. Complications presented included anal bleeding, faecal impaction, device separation, pain, infection, swelling and erythema, vaginal bleeding. Complication rates varied across studies.