

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of Barnett Continent Intestinal Reservoir (modified continent ileostomy) to restore continence after colon and rectum removal

When the large intestine (colon) and rectum are surgically removed, waste from the small intestine has to exit the body through an opening (stoma) created in the abdominal wall (an ileostomy). The waste is continuously collected in a bag worn over the stoma. In this procedure, a cut is made in the abdominal wall and a pouch is created on the inside of the wall using the last part of the small intestine (ileum). Waste collects in the pouch and is drained by inserting a tube (catheter) into the stoma, usually 2 or 3 times a day. It avoids the need for a bag on the outside of the abdomen to collect the waste.

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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 specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in August 2018.

Procedure name

Barnett Continent Intestinal Reservoir (modified continent ileostomy) to restore continence after colon and rectum removal.

Specialist societies

- The Association of Coloproctology of Great Britain and Ireland (ACPGBI)
- British Society of Gastroenterology
- Royal College of Surgeons.

Description of the procedure

Indications and current treatment

Various groups of patients may need surgery to remove the colon and sometimes the rectum. They include patients with: ulcerative colitis that is unresponsive to medical treatment or who cannot tolerate the treatment; familial adenomatous polyposis; Crohn's disease; or cancer-related problems. An ileostomy is then needed to allow intestinal contents to exit the body through a stoma on the abdominal wall.

There are different surgical techniques for creating an ileostomy, including: a Brooke ileostomy (this involves creating a standard stoma that empties intestinal contents continuously into an external ileostomy bag); or a Kock continent ileostomy (this involves creating an internal ileal reservoir connected through the abdominal wall that is drained intermittently by the patient). In patients with good

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anal sphincter control, a long-term ileostomy may be avoided by creating an ileal pouch reservoir connected directly to the anus (ileal pouch-anal anastomosis).

The Barnett Continent Intestinal Reservoir (BCIR) is a type of continent ileostomy (CI) and may be considered as an option for some patients.

What the procedure involves

The BCIR procedure is done under general anaesthesia, usually through a midline incision. It may be done as a primary procedure, when the colon and rectum are removed, or to modify a pre-existing ileostomy. A pouch incorporating a collar and an isoperistaltic valve is created using the last 60 cm of the ileum. The valve is made by intussuscepting a segment of small bowel and fixing it to the pouch wall with staples. This valve functions in the opposite direction to that in a Kock pouch, ensuring the bowel's normal peristaltic action keeps intestinal contents in the pouch rather than expelling them. The collar is formed by wrapping a segment of small bowel around the top of the pouch and valve. It holds the valve in place and provides further continence when the pouch is full and under high pressure. The flat stoma opening is located just above the pubic area and covered with a small adhesive dressing.

When there is a sensation of fullness, the patient drains the pouch by inserting a catheter through the stoma and valve into the pouch. This is typically done 2 or 3 times a day, but the patient determines the exact frequency.

Efficacy summary

Procedural outcomes

In a retrospective case series of 510 patients with ulcerative colitis (n=475), familial polyposis (n=26) or conditions other than Crohn's colitis (n=9) who had the BCIR procedure converted from a Brooke ileostomy (n=370), total proctocolectomy (n=92) or failed ileal pouch-anal anastomosis (IPAA) or Kock procedure (n=48), the procedure was successful (with fully functioning pouch) in 92% (470/510) of patients 1 year after surgery. It had failed (pouches excised and replaced with conventional ileostomy) in 7% (33/510) of patients and needed closure and pouch function restored in 1% (7/510) of patients.¹

In a registry analysis of 1,376 patients who had BCIR procedure converted from a failed IPAA (n=42) or other CI procedures (n=1,334), the procedure was successful (with fully functioning pouch) in 93% (40/42) of patients in the failed IPAA group and in 89% (1,184/1,334) of patients in the other CI procedures group at a mean follow-up of 3.4 years. Failures (pouch excision) were reported

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in 5% (2/42) of patients in the failed IPAA group compared with in 9% (116/1334) of patients in the other CI procedures group.²

Reoperation rate

In the retrospective case series of 510 patients, there was major subsequent repair surgery for pouch-related complications other than excision in 13% (60/470) of patients with functioning pouches and minor surgical repair in 8% (38/470) of patients.¹

In the registry analysis of 1,376 patients, reoperation rate was 43% (8/42) in patients who had BCIR procedure converted from a failed IPAA.²

Readmission rates

In the registry analysis of 1,376 patients, patients who had conversion to the BCIR from a failed IPAA had more readmissions than patients who had conversion from other CI procedures (45% versus 40%). There was no statistically significant difference in the mean number of admissions (2.3 versus 2.2 readmissions). Patients in the failed IPAA group had more medical-related readmissions than those in the other CI procedures group (43% versus 22%) and had a higher mean number of readmissions (2.3 versus 1.7 readmissions). The main reasons for readmissions were pouchitis, small bowel obstruction and pouch fistula.²

Quality of life

In the retrospective case series of 510 patients, consistent improvement in quality of life was reported for all the 3 self-assessed questions (which were on quality of life, state of mind and general health status), although different scales were used for those who had a response.¹

In the registry analysis of 1,376 patients, response to a quality-of-life question showed that all patients who had conversion to the BCIR from a failed IPAA rated their quality of life as 'better as' or 'much better than' before compared with 92% (983/1068) of patients who had conversion from other CI procedures. Within 2 years, the patients in the failed IPAA group had either identical or superior quality of life (also measured by the SF-36) compared with those in the other CI procedures group on each of the 8 quality-of-life subscales.²

Safety summary

Pouch excisions

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Pouch excisions were reported in 7% (33/510) of patients in the retrospective case series of 510 patients. These were replaced with conventional ileostomies.¹

Pouch failure leading to removal was reported in 5% (2/42) of patients after conversion to BCIR for failed IPAA and 9% (116/1,334) of patients after conversion from other CI procedures in the registry analysis of 1,376 patients.²

Valve slippage

Valve slippage of the intussuscepted segment occurred in 6% (32/510) of patients in the case series of 510 patients. Twenty three patients had a fully functional pouch after construction of new valves for valve slippage or subsequent surgeries and 9 had pouch excisions.¹

Valve slippage was reported in 10% (4/42) of patients after conversion to BCIR for failed IPAA in the registry analysis of 1,376 patients who had BCIR.²

Fistula formation involving either the valve or pouch

Fistula formation involving either the valve or pouch or both were reported in 10% (52/510) of patients in the case series of 510 patients. Of these, 5% (23/510) had a valve fistula; primary repair or valve replacement was done in 20 patients and 3 patients had their pouches excised. Pouch or collar fistulas occurred in 6% (32/510) of patients; 25 patients needed reoperation for correction (of which 4 had temporary ileostomies and were in the process of treatment) and 7 patients needed pouch excision.¹

Fistula formation involving either the valve or the pouch was reported in 10% (4/42) of patients after conversions for failed IPAA in the registry analysis of 1,376 patients.²

Pouch leak

Pouch leak occurred in 2% (11/510) of patients in the case series of 510 patients. After treatment, 7 patients had functioning pouches, 1 had a temporary ileostomy and 3 had pouches removed.¹

Peristomal hernia

Peristomal hernia that needed surgical repair occurred in 2% (8/510) of patients in the case series of 510 patients.¹

Hernia repair was reported in 1 patient after conversion to BCIR for failed IPAA in the registry analysis of 1,376 patients.²

Stoma stenosis

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Stoma stenosis or redundant mucosa at the skin level needing surgical revision developed in 8% (40/510) of patients in the case series of 510 patients. Revision was done in all cases under local anaesthesia¹.

Stoma revision was reported in 12% (5/42) of patients after conversion to BCIR for failed IPAA in the registry analysis of 1,376 patients.²

Small bowel obstruction

Small bowel obstruction was reported in 10% (50/510) of patients in the case series of 510 patients. Surgical intervention was needed in 4% (20/510) of patients and 6% (30/510) of patients were treated conservatively.¹

Bowel obstruction was reported in 1 patient after conversion to BCIR for failed IPAA in the registry analysis of 1,376 patients.²

Wound infection

Wound infections occurred in 4% (23/510) of patients in the case series of 510 patients. All of them were treated with prophylactic antibiotics.¹

Venous line-related sepsis

Venous line-related sepsis (managed with catheter removal and administration of intravenous antibiotics) was reported in 2% (10/510) of patients in the case series of 510 patients.¹

Ventral hernia

Ventral hernias that were repaired surgically were reported in 1% (6/510) of patients in the case series of 510 patients.¹

Pouchitis

Pouchitis (treated with antibiotics) is the most common complication reported but no pouch has been removed because of this problem in the case series of 510 patients.¹

Laparotomy for strictures

Laparotomy for strictures was reported in 1 patient after conversion to BCIR for failed IPAA in the registry analysis of 1,376 patients.²

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Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers 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, specialist advisers listed no anecdotal adverse events. They considered that the following was a theoretical adverse event: chance of intestinal failure if the surgeon does not check that the patient has sufficient bowel length remaining just in case the procedure needs to be excised or diverted in the future.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to Barnett Continent Intestinal Reservoir (modified continent ileostomy) to restore continence after colon and rectum removal. The following databases were searched, covering the period from their start to 10-07-2018: 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.

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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 continence after removal of the colon and rectum.
Intervention/test	Barnett Continent Intestinal Reservoir (modified continent ileostomy).
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 1,376 patients from 2 retrospective case series.¹⁻²

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](#).

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Table 2 Summary of key efficacy and safety findings on Barnett Continent Intestinal Reservoir (modified continent ileostomy) to restore continence after colon and rectum removal

Study 1 Mullen P (1995)

Details

Study type	Retrospective case series
Country	US
Recruitment period	1988–1991
Study population and number	n=510 patients with ulcerative colitis (n=475), familial polyposis (n=26) or conditions other than Crohn's colitis (n=9)
Age and sex	56% (286/510) female
Patient selection criteria	Patients with diagnosis of ulcerative colitis, familial polyposis or other conditions other than Crohn's colitis; in good health other than primary bowel disorder; and conversions from previous failed surgical procedures (such as Brooke ileostomy, ileal pouch-anal anastomosis (IPAA), or Kock continent pouch procedures) Patients with an initial diagnosis of Crohn's disease were excluded.
Technique	Barnett Continent Intestinal Reservoir (BCIR) – includes modifications to the original Kock pouch, designed to reduce the incidence of valve slippage and fistula formation. Principle modifications include an intestinal collar, an isoperistaltic valve, and a lateral pouch design. <ul style="list-style-type: none"> • 72% (370/510) were conversions from conventional (Brooke) ileostomy • 9% (48/510) were conversions from a previously failed alternative procedures (IPAA or Kock procedure) and • 18% (92/510) were conversions from primary total proctocolectomy. Preoperative evaluation and postoperative care were similar in all centres.
Follow-up	mean 2.2 years (range 0.8 to 4.8 years)
Conflict of interest/source of funding	Not declared

Analysis

Follow-up issues: 86.7% patients were followed until end of study or excision of the pouch. 13.3% of patients were lost to follow-up but were included in the analysis assuming they have had no further pouch-related surgeries. They were excluded from the quality-of-life analysis. Each centre had different follow-up intervals because surgeons at each centre had been trained at different times.

Study design issues: large retrospective analysis of surgical records and data collection (using a questionnaire) from 5 hospitals that collaborated for this study. Surgeons developed expertise in a structured program also involving direct observation. Complication rates were examined only for 4 of 5 centres as the fifth centre did not accumulate sufficient patients at the time of study. Quality of life was assessed using a questionnaire that involved post BCIR quality of life, state of mind and general health issues.

Other issues: there is an overlap of patients between the 2 studies in table 2.

Authors indicate that those with Crohn's disease or a colostomy are usually not candidates for a BCIR.

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Key efficacy and safety findings

Efficacy				Safety	
Number of patients analysed: 510				Adverse events	
BCIR surgery outcomes after 1 year					
				% (n)	
Fully functional pouches 1 year after surgery	92 (470/510)				
Failures (Pouch excision and replacement with conventional Brooke ileostomy)*	6.5 (33/510)				
Intact pouch with temporary ileostomies awaiting closure and restoration of pouch function	1.4 (7/510)				
Post-pouch surgery in patients with functioning pouches					
No subsequent pouch-related surgery	79.1 (372/470)				
Major subsequent repair surgery (reoperation rate)	12.8 (60/470)				
Minor surgery only	8.1 (38/470)				
*63.6% of these occurred within 1 year.					
Quality of life pre and post BCIR procedure (self-assessment, n=423)					
Quality of life	Failed Kock pouch, IPAA	Primary surgery	Brooke conversion		
Much better	76%	76%	72%		
Better	16%	11%	19%		
Same	8%	5%	3%		
Worse	0	4%	4%		
Much worse	0	4%	2%		
Questionnaire responses revealed a consistent statistically significant improvement in general quality of life, state of mind, and overall health despite different scales used to record them. Mucus secretions from pouch access were excessive in 22% patients and the median number of intubations is 4 in 24 hours in 32.5% (138/424) patients.					
Abbreviations used: BCIR, Barnett Continent Intestinal Reservoir; IPAA, ileal pouch-anal anastomosis.					
				Pouch-related complications	
				Slipped valve*	
				6.3 (32/510)	
				Valve fistula^	
				4.5 (23/510)	
				Pouch and collar fistula^	
				6.3 (32/510)	
				Pouch leak+	
				2.1 (11/510)	
				Peristomal hernia (repaired surgically)	
				1.6 (8/510)	
				Stoma stenosis/redundant mucosa at the skin needing surgical revision	
				7.8 (40/510)	
				Non-pouch-related complications	
				Small bowel obstruction needing surgical intervention	
				3.9 (20/510)	
				Small bowel obstruction treated conservatively	
				5.9 (30/510)	
				Wound infection (treated with antibiotics)	
				4.3 (22/510)	
				Venous line-related sepsis (managed with intravenous antibiotics)	
				2.0 (10/510)	
				Ventral hernia (repaired surgically)	
				1.2 (6/510)	
				Pouchitis	
				*23 patients had a fully functional pouch and 9 had pouch excisions.	
				^39 had successful results, 9 had pouch excisions and 4 had temporary ileostomies.	
				+7 had functioning pouches, 1 temporary ileostomy and 3 had pouches excised.	

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Study 2 Behrens DT (1999)

Details

Study type	Retrospective case series (registry data)
Country	US (5 centres)
Recruitment period	1989–1996
Study population and number	n=1,376 (42 patients with failed ileal pouch-anal anastomosis [IPAA] procedures versus 1,334 patients with other continent ileostomy [CI] procedures) (Brooke CI: n=1,038, failed Kock pouch: n=62, CI with simultaneous total proctocolectomy: n=192)
Age and sex	IPAA group: mean age 34 years, 62% (26/42) female ; other CI procedures group: mean age 40 years, 55% (730/1334) female
Patient selection criteria	Patients having continent ostomy procedure to replace a failed IPAA and a much larger population having CI procedures for other reasons were included in the study.
Technique	Barnett Continent Intestinal Reservoir (BCIR) – includes modifications to the original Kock pouch. Procedure uses a collar of ileum, continuous with the pouch, wrapped round the access segment at the base of the valve and an isoperistaltic access segment both intended to reduce valve slippage. In failed IPAA group: the original pouch was retained and a new valve, access segment and collar were constructed in 4 patients and a new pouch was constructed in 38 patients.
Follow-up	Failed IPAA group: average 3.6 years, other CI procedures group: 3.4 years.
Conflict of interest/source of funding	Not declared

Analysis

Follow-up issues: 95.2% patients in whom IPAA failed and 89.7% of the other CI procedure group were followed until end of study.

Study design issues: data analysis of registry data of CI procedures done in 5 centres by 12 surgeons. Results of patients who had BCIR for failed IPAA were compared with patients who had BCIR after other CI procedures such as Brooke ileostomies, failed Kock pouches and those who had primary proctocolectomies. Quality of life was assessed using SF-36 since 1991 and is only available in a small group of patients. All patients were mailed follow-up questionnaires annually for a minimum of 5 years after surgery and efforts were made for regular follow-up.

Study population issues: the difference between patient populations between the 2 groups were not statistically significant. Preoperative diagnosis of Crohn's disease was 6% (83/1334) in the other CI procedures group compared with only 5% (2/42) in IPAA group; postoperatively, an additional 1% patients were diagnosed with Crohn's disease in both the groups.

Other issues: there is an overlap of patients between the 2 studies in table 2.

Reasons for conversion to BCIR were incontinence, associated skin excoriation, pain and frequent bowel movements.

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Key efficacy and safety findings

Efficacy			Safety	
Number of patients analysed: 1,376 (42 failed IPAA versus 1,334 other CI procedures)			Adverse events in BCIR patients for failed IPAA conversions	
BCIR surgery outcomes after 1 year			Complications	% (n)
	Failed IPAA group % (n)	Other CI group % (n)	Slipped valve	9.5 (4/42)
Pouch status			Fistula formation (1 pouch vesical fistula)	9.5 (4/42)
Fully functional pouches 1 year after surgery	93 (40/42)	89 (1,184/1,334)	Bowel obstruction	2.4 (1/42)
Failures (pouch excision)*	4.7 (2/42)	8.7 (116/1,334)	Pouch removal	4.8 (2/42)
Intact pouch with temporary ileostomies awaiting closure and restoration of pouch function	0	0.7 (9/1,334)	Laparotomy for strictures	2.4 (1/42)
Subsequent surgical repair (reoperation rate)	43 (18/41)	NR	Hernia repair	2.4 (1/42)
Readmission rates (for both medical and surgical reasons)	45 (19/42)	40 (536/1,334)	Stoma revision	11.9 (5/42)
Mean number of readmissions	2.3	2.2	Death because of unrelated causes (90 days follow-up)	1
Medical readmission rates	43 (18/42)	22 (300/1,334)	Pouchitis (needed antibiotic treatment, 3 hospitalised)	26 (11/42)
Mean medical readmission rate	2.3	1.7		
*1 after developing a pouch vesical fistula and the other after Crohn's disease.				
Quality of life				
Response	Failed IPAA group % (n)	Other CI group % (n)		
Much better	85 (34/42)	75.8 (810/1,068)		
Better	15 (6/42)	16.2 (173/1,068)		
Same	0	3.1 (33/1,068)		
Worse	0	2.7 (29/1,068)		
Much worse	0	2.2 (23/1,068)		
Quality of life measured by the SF-36 shows that within 2 years, the patients in the failed IPAA group had either identical or superior outcomes compared with the general CI population on each quality life subscale.				
Abbreviations used: BCIR, Barnett Continent Intestinal Reservoir; CI, continent ileostomy, IPAA, ileal pouch-anal anastomosis; NR, not reported				

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Validity and generalisability of the studies

- There are no randomised controlled studies.
- There is very little published literature on this procedure (only 2 retrospective case series).
- There are no comparative data of BCIR procedure over standard procedures.

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.

Technology appraisals

- Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy. NICE technology appraisal guidance 329 (2015). Available from <http://www.nice.org.uk/guidance/TA329>
- Vedolizumab for treating moderately to severely active ulcerative colitis. (2015) NICE technology appraisal guidance 342 (2015). Available from <http://www.nice.org.uk/guidance/TA342>

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist 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 specialist advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public

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consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Specialist Adviser Questionnaires for Barnett Continent Intestinal Reservoir (modified continent ileostomy) to restore continence after colon and rectum removal were submitted and can be found on the [NICE website](#)

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

There is no specific device used for this procedure. Therefore, no structured information requests were sent to companies.

Issues for consideration by IPAC

- There are many modifications to the Kock abdominal continent pouch procedure and BCIR is 1 modified approach that uses the isoperistaltic valve and intestinal collar with the aim to achieve the same outcome as the Kock pouch.
- Recent valve modifications such as stapling the valve to the reservoir wall have limited BCIR necessity (Beck 2008).

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References

1. Mullen P, Behrens D, Chalmers T et al (1995). Barnett continent intestinal reservoir. Multicenter experience with an alternative to the Brooke ileostomy. *Diseases of the Colon & Rectum* 6(38): 573-82.
2. Behrens DT, Paris M, Luttrell J (1999). Conversion of failed ileal pouch-anal anastomosis to continent ileostomy. *Diseases of the Colon & Rectum* 42(4): 490-6.

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Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	26/10/2018	Issue 10 of 12, October 2018
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	26/10/2018	Issue 9 of 12, September 2018
HTA database (CRD website)	26/10/2018	n/a
MEDLINE (Ovid)	26/10/2018	1946 to October 23, 2018
MEDLINE In-Process (Ovid) & Medline ePub ahead (Ovid)	26/10/2018	October 23, 2018
EMBASE (Ovid)	26/10/2018	October 25, 2018

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

- 1 *colonic pouches/
- 2 ((modif* or customi* or adapt* or internal* or abdom* or external* or intra-abdom*) adj4 (kock or ileal or ileum or ileo* or colon*) adj4 (pouch or pouches or reservoir*)).tw.
- 3 ((modif* or customi* or adapt* or internal* or abdom* or external* or intra-abdom*) adj4 ("k-pouch*" or "j-pouch*" or "s-pouch*" or "w-pouch*" or "h-pouch*")).tw.
- 4 ((modif* or customi* or adapt* or internal* or abdom* or external* or intra-abdom*) adj4 IPAA).tw
- 5 (modif* adj4 (continen* adj4 ileostom*)).tw.
- 6 ((nipple* or collar* or isoperist* or lateral*) adj4 (pouch or pouches or reservoir* or valve* or intestin*)).tw.
- 7 or/1-6
- 8 Proctocolectomy, Restorative/
- 9 ((anal or anus or rectal* or rectum* or colorectal* or colon* or bowel* or coloanal* or colo-anal*) adj4 (dissect* or excis* or close* or remov* or surg* or resect*)).tw.
- 10 ileostomy/
- 11 (ileostom* or proctocolectom* or ostom* or coloproctectom*).tw.
- 12 or/8-11
- 13 ("Barnett Continent Intestinal Reservoir" or BCIR).tw.
- 14 (barnett adj4 (reservoir* or pouch*)).tw.
- 15 13 or 14
- 16 7 and 12
- 17 15 or 16
- 18 animals/ not humans/

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19 17 not 18
20 limit 19 to english language
21 limit 20 to ed=20180710-20181026

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Appendix

There were no additional papers identified.

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