NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endoscopic full thickness removal of non-lifting colonic polyps

Colonic polyps are small growths in the wall of the large bowel. Non-lifting polyps are deep in the wall, so are difficult to remove, and are also more likely to become cancerous if left untreated. In endoscopic full thickness removal, a special device is passed through a colonoscope (a thin, flexible tube with a camera on the end that is inserted through the anus into the large bowel) and used to remove the polyp and seal the bowel wall closed afterwards. The aim is to remove polyps in deeper layers of the bowel without causing bowel damage.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) 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 IP overview was prepared in September 2016.

Procedure name

- Endoscopic full thickness removal of non-lifting colonic polyps

Specialist societies

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

Description

Indications and current treatment

Colonic polyps are mucosal lesions that project into the lumen of the large bowel. Most colonic polyps cause no symptoms, but they may cause rectal bleeding, mucus in stools, abdominal pain and, rarely, diarrhoea or constipation. There is a small risk that, after several years, polyps may develop into bowel cancer if left untreated.

Benign polyps and those with very early signs of malignancy can often be successfully removed by endoscopic polypectomy, or endoscopic mucosal or submucosal resection. However, polyps that are non-lifting usually involve deeper layers of the bowel wall as a result of either invasion by malignant cells or scaring from previous attempts at removal. Trying to remove these polyps by standard techniques risks incomplete resection of invasive disease and bowel perforation.

What the procedure involves

Full thickness endoscopic bowel excision uses a full thickness resection device. This comprises a modified snare to remove the adenoma and deeper layers of the bowel wall, and a clasp device that closes the full thickness of the bowel wall to prevent perforation. The device is attached to the end of a standard endoscope and advanced through the colon until the adenoma is identified. The adenoma is grasped at its centre and slowly pulled into the cap of the device. An ‘over-the-scope’ clip is released closing the site of a potential defect in the bowel wall. A snare is simultaneously placed around the adenoma, which is retrieved for histological analysis after the clip is deployed. The surgical site is examined for signs of haemorrhage and to check that the clip has closed the bowel wall.

The procedure is usually done with the patient under sedation but sometimes general anaesthesia is needed.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endoscopic full thickness removal of non-lifting colonic polyps. The following databases were searched, covering the period from their start to 22 September 2016: 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 appendix C for details of search

strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

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

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with colonic polyps.
Intervention/test	Endoscopic full thickness removal of non-lifting colonic polyps.
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 308 patients from 4 case series[1-3,] (1 of which unpublished)[6], 2 case reports[4, 5] and 1 unpublished registry[7].

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

Table 2 Summary of key efficacy and safety findings on endoscopic full thickness removal of non-lifting colonic polyps

Study 1 Schmidt A (2015)

Details

Study type	Retrospective case series
Country	Germany and Switzerland
Recruitment period	2012 to 2014
Study population and number	n=**25**
Age and sex	70 years (range 43 to 84 years)
Patient selection criteria	Patients included had non-lifting adenomas (13/25), recurrent adenomas (9/25), incompletely resected adenomas (2/25), and previously untreated adenomas (2/25).
Technique	Endoscopic full-thickness resection using an over-the-scope clip. All procedures were performed under deep sedation without endotracheal intubation. All patients had intravenous prophylactic antibiotic therapy for 3 days before procedure. All procedures were performed by experienced endoscopists. Patients were started on clear fluids 3-6 hours after the procedure and on normal diet on the following day.
Follow-up	**3 to 6 months**
Conflict of interest/source of funding	The department of gastroenterology and oncology has received financial support from Ovesco Endoscopy for the coordination and performance of a multicentre trial investigating treatment of recurrent peptic ulcer bleeding using over-the-scope clips. Prof. Caca and Dr Schmidt have received lecture frees from Ovesco Endoscopy for FTRD training course. The resection device and technical support were provided by Ovesco Endoscopy.

Analysis

Follow-up issues: All patients were monitored in hospital for at least 48 hours. First endoscopic follow-up was scheduled to 3-6 months post procedure and was obtained in 76% (19/25) of patients. In 6 patients lost to follow-up was not possible because: deaths by liver failure in 1 patient with known cirrhosis, 2 patients with adenocarcinoma were treated with hemicolectomy, 1 patient refused and 2 patients missed the appointment

Study design issues: Multicentre design.

Study population issues: None.

Other issues: None.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>

n=25

Median procedure time = 50 min (10 to 177 minutes)

Mean size of the specimens = 24mm (12 to 40mm)

Mean hospital stay = 4 days (1 to 12 days)

<table>
<tr><td>Target lesion reached with FTRD</td><td>96% (24/25)</td></tr>
<tr><td>Technical success (macroscopic)[1]</td><td>83% (20/24)</td></tr>
<tr><td>Complete resection (R0)</td><td>75% (18/24)</td></tr>
<tr><td>Full-thickness resection (histology)</td><td>88% (21/24)</td></tr>
<tr><td>Residual adenoma[2]</td><td>16% (4/25)</td></tr>
<tr><td>Local recurrence</td><td>4% (1/25)</td></tr>
<tr><td>Reoperation rate[3]</td><td>8% (2/24)</td></tr>
<tr><td>Development of colorectal cancer</td><td>8% (2/24)</td></tr>
</table>

In 1 patient with history of diverticulitis, target lesion couldn't be reached because of sigmoid stenosis. This patient was excluded from the resection efficacy calculations.

[1]In 2 patients the adenomas were at the appendix, which prevented the complete en bloc resection. In 2 other patients the FTRD was retrieved and the adenomas were removed with a normal monofilament snare.

[2]In 4 patients with incomplete removal, histology identified adenoma cells in 1 case, adenocarcinoma in another, leiomyoma in a third patient and hamartoma in the fourth.

[3]The reason reoperation was a positive cancer histology from the resected specimen. Analysis from the surgical specimen determined initial endoscopic full thickness resection had completely removed the tumour.

Clip removal

In 37% (7/19) patients the OTSC was still in place at the first follow-up but in 63% (12/19) the clip had dislodged spontaneously.

</td><td>

<table>
<tr><td>Minor bleeding*</td><td>4% (1/25)</td></tr>
<tr><td>Postpolypectomy syndrome**</td><td>8% (2/25)</td></tr>
<tr><td>Infection</td><td>8% (2/25)</td></tr>
</table>

*Haemostasis was achieved using local epinephrine.

**Abdominal pain, fever, leukocytosis, and peritoneal inflammation in the absence of perforation after polypectomy with electrocoagulation

</td></tr>
<tr><td colspan="2">Abbreviations used: FTRD, full-thickness resection device, OTSC, over-the-scope clip; R0, no microscopic residual tumour.</td></tr>
</table>

Study 2 Fähndrich M (2014)

Details

Study type	**Retrospective case series**
Country	Germany
Recruitment period	2010 to 2014
Study population and number	n=**17**
Age and sex	Median 58 years (21-85 years); 47% (8/17) males.
Patient selection criteria	Patients with indication for endoscopic resection. Exclusion criteria were: gastric lesions <30 mm, age <18 years, failure to provide informed consent and coagulopathy (INR>1.5, thrombocytes <50,000/µL).
Technique	All cases performed using a combination of the OTSC system and Inoue Cap for EFTR. In 1 case the new FTRD-OTSC was used.
Follow-up	**Perioperative**
Conflict of interest/source of funding	None declared.

Analysis

Follow-up issues: Patients were monitored during the perioperative period only. No recurrence of polyps or progression to malignancy was reported.

Study design issues: Recruitment happened in a consecutive group of patients.

Study population issues: Not all patients were treated for endoscopic full-thickness resection of colonic adenoma: 6 carcinoids (1 stomach, 1 duodenum, 4 rectum), 7 R1 situations after conventional endoscopic polypectomy with low risk for colorectal cancer (2 ascending colon, 1 descending colon, 4 sigmoid colon), 3 adenoma relapses (1 each in the ascending, descending and sigmoid colon) and 1 submucosal lesion of the stomach.

Other issues: None.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>n=17
Outcomes in patients with colonic lesions (n=10)
<table>
<tr><td>Target lesion reached with FTRD</td><td>100% (10/10)</td></tr>
<tr><td>Technical success (macroscopic)</td><td>90% (9/10)</td></tr>
<tr><td>Complete resection (R0)</td><td>100% (9/9)</td></tr>
<tr><td>Full-thickness resection (histology)</td><td>100% (9/9)</td></tr>
</table>
Outcomes in all patients (n=17)
<table>
<tr><td>Target lesion reached with FTRD</td><td>100% (17/17)</td></tr>
<tr><td>Technical success[1]</td><td>94% (16/17)</td></tr>
<tr><td>Complete resection (R0)</td><td>100% (16/16)</td></tr>
<tr><td>Full-thickness resection (histology)[2]</td><td>69% (11/16)</td></tr>
</table>
[1]In 1 patient the OTSC didn’t deploy correctly.
[2]In 5 patients deep muscle margin was present at the vertical margin of the resected specimen.

Clip removal
In 9 patients the OTSC was removed using the Nd-YAG laser, in 3 patients the clip fell off spontaneously, in 3 patients it remained attached (2 patients were booked a removal session and 1 patient died of another illness). In 1 patient the OTSC was resected during surgery for diverticulitis in a different location.</td><td>Scattered spleen tissue was present at histology in 1 patient treated for gastric lesion.</td></tr>
<tr><td colspan="2">Abbreviations used: INR, international normalised ratio; EFTR, endoscopic full-thickness resection; FTRD, full-thickness resection device; Nd-YAG laser, Neodymium: yttrium-aluminium-garne laser; OTSC, over-the-scope clip; R0, no microscopic residual tumour.</td></tr>
</table>

Study 3 Schmidt A (2014)

Details

Study type	**Case series**
Country	Germany
Recruitment period	Not reported.
Study population and number	n=**3**
Age and sex	81, 72 and 70 years old, gender not stated
Patient selection criteria	Patients referred for resection of recurrent non-pedunculated adenomas with a negative lifting sign.
Technique	The procedure was done using an OTSC.
Follow-up	**6 months**
Conflict of interest/source of funding	The department of gastroenterology in Ludwigsburg does get financial support for coordinating and conducting a multicentre study investigating OTSC in recurrent peptic ulcer bleeding. The authors disclose no conflicts. The resection device was provided by Ovesco Endoscopy, Tübingen, Germany.

Analysis
Follow-up issues: All 3 patients completed 6-months follow-up.
Study design issues: None.
Study population issues: Two patients had adenomas located in the rectosigmoid transition; in the remaining patient the adenoma was located in the descending colon.
Other issues: None

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>n=3
Lesions were 20, 20 and 25 mm.
<table>
<tr><td>Target lesion reached with FTRD</td><td>100% (3/3)</td></tr>
<tr><td>Technical success</td><td>100% (3/3)</td></tr>
<tr><td>Full-thickness resection (histology) (R0)</td><td>100% (3/3)</td></tr>
</table>
In 2 cases the clip was still in place after 6 months. To exclude recurrence the clip was removed using a novel cutting device (DC clip cutter, Ovesco Endoscopy).
There was no adenoma recurrence at 6 months follow-up.</td><td>None reported.</td></tr>
<tr><td colspan="2">Abbreviations used: OTSC, over-the-scope clip; R0, no microscopic residual tumour.</td></tr>
</table>

Study 4 Valli PV (2014)

Details

Study type	**Case report**
Country	Switzerland
Recruitment period	Not reported
Study population and number	n=**1**
Age and sex	66 years, female
Patient selection criteria	Patient diagnosed with a pathologic size polyp within a diverticulum.
Technique	The procedure was done under conscious sedation. The polyp was identified using a standard colonoscope and India ink injection. The resection used a FTRD with and mounted OTSC. Peri-interventional antibiotic prophylaxis was administered as a single shot of piperacillin/tazobactam. The patient was discharged on the day following the procedure.
Follow-up	**3 months**
Conflict of interest/source of funding	None.

Analysis
Follow-up issues: None.
Study design issues: None
Study population issues: The lesion was located in the ascending colon.
Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
The polyp had a pathologic size of 13 mm. Technical success 100% (1/1) Full-thickness removal (histologic R0) = 100% (1/1).	None reported.
Abbreviations used: FTRD, full-thickness removal device; OTSC, over-the-scope clip; R0, no microscopic residual tumour.	

Study 5 Probst A (2015)

Details

Study type	**Case report**
Country	Germany
Recruitment period	Not reported
Study population and number	n=**1**
Age and sex	51 years, male
Patient selection criteria	Patient diagnosed with a submucosal tumour.
Technique	Full-thickness resection was done under conscious sedation using the FTRD, Ovesco Endoscopy.
Follow-up	**Not stated.**
Conflict of interest/source of funding	None.

Analysis
Follow-up issues: period of follow-up wasn't specified.
Study design issues: None
Study population issues: The lesion was located in the sigmoid colon.
Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
The lesion had a pathologic size of 15 mm. Procedure time was 25 minutes. Technical success 100% (1/1) Full-thickness removal (histologic R0) = 100% (1/1)	None reported.
Abbreviations used: FTRD, full-thickness removal device; R0, no microscopic residual tumour.	

Study 6 Schmidt A (2016) – Unpublished data from WALL resect (NCT02362126)

Details

Study type	**Prospective multicentre case series**
Country	Germany
Recruitment period	2015 to 2016
Study population and number	n=**180**
Age and sex	Mean 65.9 years (29 to 88)
Patient selection criteria	Patients suitable for endoscopic full-thickness resection of low gastro-intestinal adenoma Inclusion criteria: adenoma with negative lifting sign (recurrent, incompletely resected or untreated), adenoma at difficult anatomic location (with involvement of a diverticulum or of the appendiceal orifice), T1-carcinoma with indication for endoscopic (re-) resection and subepithelial tumours. Exclusion criteria: lesion size greater than 3 cm, lesions located in the upper GI-tract, T1 carcinoma with known high-risk features (submucosal infiltration depth greater than 1000 um, invasion of lymphatic vessels, G3), suspected colorectal stenosis, dual platelet inhibition therapy, inability to sign informed consent, pregnancy.
Technique	Full-thickness resection was done under conscious sedation using the FTRD, Ovesco Endoscopy.
Follow-up	**Not stated.**
Conflict of interest/source of funding	The preliminary data was reported by the manufacturer.

Analysis
Follow-up issues: period of follow-up wasn't specified.
Study design issues: None
Study population issues: It is not possible to determine the number of adverse events resulting from interventions in the colon.

Lesion location, n (%)	
- caecum	55 (30.6 %)
- ascending colon	35 (19.4 %)
- transverse colon	22 (12.2 %)
- descending colon	8 (4.4 %)
- sigmoid	20 (11.1 %)
- rectosigmoid transition	10 (5.6 %)
- rectum	30 (16.6 %)
• lower rectum (0-5 cm)	9 (5.0 %)
• upper rectum (6-12 cm)	21 (11.7 %)

Other issues: None.

Key safety findings

Safety

n=180

Mean size of lesion 17.6 mm (8 to 30mm)

Adverse events	**9% (17/180)**
- Bleeding	3% (5/180)
- Perforation	3% (5/180)
• immediate	2% (4/180)
• secondary	1/180
- Appendicitis	1% (2/180)
• Mild/conservative treatment	1/180
• Appendectomy	1/180
- Postpolypectomy syndrome	2% (4/180)
- Recurrent abdominal pain for several weeks	1/180
Need for surgery	**7% (13/180)**
- High-risk situation after resection of T1-carcinoma	5% (9/180)
- Due to incomplete resection	1/180
- Emergency surgery due to perforation	1% (2/180)
- Emergency surgery due to appendicitis	1/180

Study 7 Ovesco registry (2016) unpublished data

Details

Study type	**Registry**
Country	Germany
Recruitment period	2015 to 2016
Study population and number	n=87
Age and sex	Not stated
Patient selection criteria	Not stated
Technique	Not stated
Follow-up	**Not stated**
Conflict of interest/source of funding	Manufacturer's registry

Analysis
Follow-up issues: Period of follow-up wasn't specified.
Study design issues: None
Study population issues: Lesion location wasn't reported by the manufacturer.
Other issues: None.

Key efficacy and safety findings

Efficacy

n=87

Mean specimen size 21×20mm.

Complications	
Perforations	6% (5/87)
• Perforation during procedure[1]	5% (4/87)
• Perforation post-procedure	1/87
Bleeding[2]	5% (4/87)
Sepsis	1/87
Anastomotic leak[3]	1/87

[1]One caused by the full-thickness resection device.

[2]All treated endoscopically

[3]Required surgical treatment

Efficacy

Technical success

In a retrospective case series of 25 patients with non-lifting colonic lesions treated by endoscopic full-thickness removal (EFTR), there was technical success in 83% (20/24).[1]

In a retrospective case series of 17 patients (10 with colonic lesion) treated by EFTR, there was technical success in 90% (9/10).[2]

In a case series of 3 patients with non-lifting adenomas treated by EFTR, there was technical success in 100% (3/3).[3]

In a case report of 1 patient diagnosed with a polyp within a diverticulum and treated by FTRD, technical success was 100%.[4]

In a case report of 1 patient diagnosed with a submucosal tumour and treated by FTRD, technical success was 100%.[5]

Complete resection

In the retrospective case series of 25 patients treated by EFTR, there was complete resection (no microscopic residual tumour) in 75% (18/24). In the same study, residual adenomas were present in 16% (4/25) of patients.[1]

In the retrospective case series of 17 patients treated by EFTR, there was compete resection in 100% (9/9) of those with colonic lesions.[2]

In the case report of 1 patient diagnosed with a polyp within a diverticulum and treated by FTRD, complete resection (R0) was achieved and confirmed by histology.[4]

In the case report of 1 patient diagnosed with a submucosal tumour and treated by FTRD, complete resection was accomplished and confirmed by histology.[5]

Full thickness resection

In the retrospective case series of 25 patients treated by EFTR, there was full-thickness resection in 88% (21/24).[1]

In the retrospective case series of 17 patients treated by EFTR, there was full-thickness resection in 100% (9/9) of those with colonic lesions. [2]

In a case series of 3 patients treated by EFTR, full thickness resection was 100% (3/3).[3]

Recurrence rate

In the retrospective case series of 25 patients treated by EFTR, local recurrence was reported in 4% (1/25).[1]

Clip displacement

In the retrospective case series of 25 patients treated by EFTR, the over-the-scope clip (OTSC) was still in place at first follow-up (3 to 6 months) in 37% (7/19) but has dislodged spontaneously in 63% (12/19) patients.[1]

Safety

Haemorrhage

Minor bleeding was reported in 4% (1/25) of patients treated by endoscopic full-thickness resection (EFTR) for colonic polyps in a case series of 25 patients.[1]

Bleeding was reported in 3% (5/180) of patients treated by EFTR in an unpublished case series of 180 patients with low gastro-intestinal tract polyps.[6]

Bleeding was reported in 5% (4/87) of patients treated by EFTR whose data was recorded in an unpublished registry of 87.[7]

Perforation

Immediate perforation was reported in 2% (4/180) of patients in the unpublished case series of 180 patients treated by EFTR. Secondary perforation was reported in 1/180 patient of the same unpublished study.[6]

Perforation during procedure was reported in 5% (4/87) of patients in the unpublished case series of 180 patients treated by EFTR. Perforation post-procedure was reported in 1/87patient treated by EFTR in the unpublished registry of 87 patients.[7]

Anastomotic leak requiring surgery was reported in 1/87 patient in the unpublished registry of 87 patients treated by EFTR.[7]

Further surgery after EFTR

In the case series of 25 patients, 8% (2/24) patients had subsequent surgical resection after the diagnosis of high risk adenocarcinoma. However, histology of the surgical specimen revealed EFTR had completely removed the tumour in the initial resection.[1]

Further surgery after EFTR of lesions in the lower gastro-intestinal tract was done in 7% (13/180) of patients in the unpublished case series of 180 patients. The reasons for surgery included the diagnosis after resection of high-risk T1 carcinoma in 5% (9/180) of patients, incomplete resection in less than 1% (1/180), perforation in 1% (2/180) and appendicitis in less than 1% (1/180).[6]

Postpolypectomy syndrome

Postpolypectomy syndrome was reported in 8% (2/25) of patients in the retrospective case series of 25 patients.[1]

Postpolypectomy syndrome was reported in 2% (4/180) of patients treated by EFTR in low gastro-intestinal (GI) lesions of the unpublished case series of 180 patients.[6]

Infection

Infection was reported in 8% (2/25) of patients in the retrospective case series of 25 patients.[1]

Appendicitis was reported in 1% (2/180) of patients treated by EFTR for low gastro-intestinal tract lesions in the unpublished case series of 180 patients.[6]

Pain

Recurrent abdominal pain for several weeks was reported in 1/180 patient treated by EFTR in low gastro-intestinal (GI) lesions of the unpublished case series of 180 patients.[6]

Validity and generalisability of the studies

- Endoscopic full-thickness removal of colonic polyps is novel and therefore the available evidence is limited.
- Limitations of the evidence are: no medium to long follow-up data, small number of patient data, no comparative or randomised data, limited efficacy and safety reporting.

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. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Combined endoscopic and laparoscopic removal of colonic polyps. NICE interventional procedure guidance 503 (2014). Available from https://www.nice.org.uk/guidance/ipg503

NICE guidelines

- Colorectal cancer: diagnosis and management. NICE clinical guideline 131 (2011, updated in 2014).). Available from https://www.nice.org.uk/guidance/cg131
- Colonoscopic surveillance for preventing colorectal cancer in adults with ulcerative colitis, Crohn's disease or adenomas. NICE clinical guideline 118 (2011). Available from https://www.nice.org.uk/guidance/cg118

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 consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Tree Specialist Advisor Questionnaires for endoscopic full-thickness removal of colonic polyps were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent xxx questionnaires to xxx NHS trusts for distribution to patients who had the procedure (or their carers). NICE received xxx completed questionnaires.

Section to be inserted if there is no patient commentary

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

Section to be inserted if patient commentators raised no new issues

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Section to be inserted if patient commentators raised new issues

The patient commentators raised the following issues about the safety/efficacy of the procedure, which did not feature in the published evidence or the opinions of specialist advisers, and which the committee considered to be particularly relevant:

- [insert additional efficacy and safety issues raised by patient commentators and highlighted by IPAC, add extra rows as necessary].
- [Last item in list].

Company engagement

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

Issues for consideration by IPAC

- None.
- Ongoing studies:

- NCT02673983 Safety and Efficacy Study of the FTRD System for Obtaining Full-thickness Intestinal Biopsies. Location Skane, Sweden. RCT. Recruiting. Estimated enrolment 40 patients. Estimated completion date: December 2017.
- NCT02353533 Endoscopic Full-thickness Resection of Residual Colorectal Lesions - The FiRE Study (FiRE) Location: Munich, Germany. RCT. Recruiting. Estimated enrolment 40 patients. Estimated completion date: January 2017.
- NCT02362126 Endoscopic Full Thickness Resection in the Lower GI Tract With the "Full Thickness Resection Device". Location: Germany. Multicentre prospective cohort (WALL-RESECT). Estimated enrolment 80 patients. Estimated completion date: February 2017.

References

1. Schmidt A, Bauerfeind P, Gubler C et al. (2015) Endoscopic full-thickness resection in the colorectum with a novel over-the-scope device: first experience. Endoscopy 47:719-725.
2. Fähndrich M, Sandmann M (2015) Endoscopic full-thickness resection for gastrointestinal lesions using the over-the-scope clip system: a case series. Endoscopy 47: 76-79.
3. Schmidt A, Damm M, Caca K (2014) Endoscopic full thickness resection using a novel over-the-scope device. Gastroenterology 147: 740-742.
4. Valli M, Vrugt B, Bauerfeind P (2014) Endoscopic Resection of a Diverticulum-Arisen Colonic Adenoma Using a Full-Thickness Resection Device. Gastroenterology 147:969-971.
5. Probst A, Schaller T, Messmann H (2015) Gastrointestinal stromal tumor of the colon - endoscopic treatment by full-thickness resection. Endoscopy 47: 460-461.
6. Schmidt A, Meining A, Birk M et al. Endoscopic full-thickness resection in the lower gastrointestinal tract using an over-the-scope device - Interim results of a prospective multicenter trial (WALL RESECT) unpublished, made available by the manufacturer – (NCT02362126).
7. Ovesco ® FTRD System registry Germany, Unpublished, made available by the manufacturer.

Appendix A: Additional papers on endoscopic full thickness removal of non-lifting colonic polyps

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

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Damm M, Schmidt A, Gubler C et al. (2015) Endoscopic full thickness resection in the lower gastrointestinal tract using a novel over-the-scope device. Gastrointestinal endoscopy 81:248.	Case series n=32 patients FU - perioperative	Full-thickness resection is feasible and effective in low gastrointestinal lesions. Prospective studies are necessary to further evaluate the technique.	It is not possible to determine from the abstract the degree of overlap with paper 1, table 2. Conference abstract, not yet published.

Appendix B: Related NICE guidance for endoscopic full thickness removal of non-lifting colonic polyps

Guidance	Recommendations
Interventional procedures	**Combined endoscopic and laparoscopic removal of colonic polyps. NICE interventional procedure guidance 503 (2014).** 1.1 Current evidence on the safety and efficacy of combined endoscopic and laparoscopic removal of colonic polyps is adequate. Therefore this procedure may be used with normal arrangements for clinical governance, consent and audit. 1.2 This procedure should be done only by teams experienced in laparoscopic colonic surgery and complex interventional endoscopy.

NICE guidelines	**Colorectal cancer: diagnosis and management. NICE clinical guideline 131 (2011, updated in 2014).** 1.1 Investigation, diagnosis and staging The recommendations in section 1.1 refer to people whose condition is being managed in secondary care. For recommendations for urgent referral from primary care for patients with suspected colorectal cancer see referral for suspected cancer (NICE guideline CG27). 1.1.1 Diagnostic investigations 1.1.1.1 Advise the patient that more than one investigation may be necessary to confirm or exclude a diagnosis of colorectal cancer. [2011] 1.1.1.2 Offer colonoscopy to patients without major comorbidity, to confirm a diagnosis of colorectal cancer. If a lesion suspicious of cancer is detected, perform a biopsy to obtain histological proof of diagnosis, unless it is contraindicated (for example, patients with a blood clotting disorder). [2011] 1.1.1.3 Offer flexible sigmoidoscopy then barium enema for patients with major comorbidity. If a lesion suspicious of cancer is detected perform a biopsy unless it is contraindicated. [2011] 1.1.1.4 Consider computed tomographic (CT) colonography as an alternative to colonoscopy or flexible sigmoidoscopy then barium enema, if the local radiology service can demonstrate competency in this technique. If a lesion suspicious of cancer is detected on CT colonography, offer a colonoscopy with biopsy to confirm the diagnosis, unless it is contraindicated. [2011] 1.1.1.5 Offer patients who have had an incomplete colonoscopy: • repeat colonoscopy or • CT colonography, if the local radiology service can demonstrate competency in this technique or • barium enema. [2011] 1.1.2 Staging of colorectal cancer 1.1.2.1 Offer contrast-enhanced CT of the chest, abdomen and pelvis, to estimate the stage of disease, to all patients diagnosed with colorectal cancer unless it is contraindicated. No further routine imaging is needed for patients with colon cancer. [2011]

1.1.2.2 Offer magnetic resonance imaging (MRI) to assess the risk of local recurrence, as determined by anticipated resection margin, tumour and lymph node staging, to all patients with rectal cancer unless it is contraindicated. [2011]

1.1.2.3 Offer endorectal ultrasound to patients with rectal cancer if MRI shows disease amenable to local excision or if MRI is contraindicated. [2011]

1.1.2.4 Do not use the findings of a digital rectal examination as part of the staging assessment. [2011]

1.2 Management of local disease

1.2.1 Preoperative management of the primary tumour

For the purposes of this guideline we have defined three different risk groups of patients with rectal cancer, according to the risk of local recurrence. These groups are defined in table 1.

Table 1 Risk of local recurrence for rectal tumours as predicted by MRI

Risk of local recurrence	Characteristics of rectal tumours predicted by MRI
High	A threatened (<1 mm) or breached resection margin or Low tumours encroaching onto the inter-sphincteric plane or with levator involvement
Moderate	Any cT3b or greater, in which the potential surgical margin is not threatened or Any suspicious lymph node not threatening the surgical resection margin or The presence of extramural vascular invasion[a]
Low	cT1 or cT2 or cT3a and No lymph node involvement
[a] This feature is also associated with high risk of systemic recurrence.	

Patients whose primary rectal tumour appears resectable at presentation

1.2.1.1 Discuss the risk of local recurrence, short-term and long-term morbidity and late effects with the patient after discussion in the multidisciplinary team (MDT). [2011]

	1.2.1.2 Do not offer short-course preoperative radiotherapy (SCPRT) or chemoradiotherapy to patients with low-risk operable rectal cancer (see table 1 for risk groups), unless as part of a clinical trial. [2011] 1.2.1.3 Consider SCPRT then immediate surgery for patients with moderate-risk operable rectal cancer (see table 1 for risk groups). Consider preoperative chemoradiotherapy with an interval to allow tumour response and shrinkage before surgery for patients with tumours that are borderline between moderate and high risk. [2011] 1.2.1.4 Offer preoperative chemoradiotherapy with an interval before surgery to allow tumour response and shrinkage (rather than SCPRT), to patients with high-risk operable rectal cancer (see table 1 for risk groups). [2011] Patients whose primary colon or rectal tumour appears unresectable or borderline resectable 1.2.1.5 Discuss the risk of local recurrence and late toxicity with patients with rectal cancer after discussion in the MDT. [2011] 1.2.1.6 Offer preoperative chemoradiotherapy with an interval before surgery, to allow tumour response and shrinkage, to patients with high-risk locally advanced rectal cancer. [2011] 1.2.1.7 Do not offer preoperative chemoradiotherapy solely to facilitate sphincter-sparing surgery to patients with rectal cancer. [2011] 1.2.1.8 Do not routinely offer preoperative chemotherapy alone for patients with locally advanced colon or rectal cancer unless as part of a clinical trial. [2011] 1.2.2 Colonic stents in acute large bowel obstruction 1.2.2.1 If considering the use of a colonic stent in patients presenting with acute large bowel obstruction, offer CT of the chest, abdomen and pelvis to confirm the diagnosis of mechanical obstruction, and to determine whether the patient has metastatic disease or colonic perforation. [2011] 1.2.2.2 Do not use contrast enema studies as the only imaging modality in patients presenting with acute large bowel obstruction. [2011]

	1.2.2.3 For patients with acute left-sided large bowel obstruction caused by colorectal cancer that is potentially curable, and for whom surgery is suitable: • Resuscitate patients and explain to them and their family members or carers (as appropriate) that acute bowel obstruction can initially be managed either with emergency surgery or a colonic stent, and that there is no clear evidence that one treatment is better than the other. [new 2014] • Offer patients the chance to take part in a randomised controlled trial [2] (if available) that compares emergency surgery with colonic stent insertion to initially manage acute bowel obstruction. [new 2014] 1.2.2.4 For patients with acute left-sided large bowel obstruction caused by colorectal cancer that is not potentially curable, or for whom surgery is unsuitable: [new 2014] Resuscitate patients with acute large bowel obstruction, then consider placing a self-expanding metallic stent to initially manage a left-sided complete or near-complete colonic obstruction. [2011] A consultant colorectal surgeon should consider inserting a colonic stent in patients presenting with acute large bowel obstruction. They should do this together with an endoscopist or a radiologist (or both) who is experienced in using colonic stents. [2011] 1.2.2.5 Do not place self-expanding metallic stents: • in low rectal lesions or • to relieve right-sided colonic obstruction or • if there is clinical or radiological evidence of colonic perforation or peritonitis. [2011] 1.2.2.6 Do not dilate the tumour before inserting the self-expanding metallic stent. [2011] 1.2.2.7 Only a healthcare professional experienced in placing colonic stents who has access to fluoroscopic equipment and trained support staff should insert colonic stents. [2011] 1.2.3 Stage I colorectal cancer

	1.2.3.1 The colorectal MDT should consider further treatment for patients with locally excised, pathologically confirmed stage I cancer, taking into account pathological characteristics of the lesion, imaging results and previous treatments. [2011] 1.2.3.2 Offer further treatment to patients whose tumour had involved resection margins (less than 1 mm). [2011] 1.2.4 Stage I rectal cancer 1.2.4.1 An early rectal cancer MDT[3] should decide which treatment to offer to patients with stage I rectal cancer, taking into account previous treatments, such as radiotherapy. [2011] 1.2.4.2 After discussion in the MDT responsible for the management of stage I rectal cancer, discuss uncertainties about the potential risks and benefits of all treatment options with patients and their family members and carers (as appropriate), taking into account each patient's circumstances. [new 2014] 1.2.4.3 Explain to patients and their family members or carers (as appropriate) that there is very little good-quality evidence comparing treatment options for stage I rectal cancer. [new 2014] 1.2.4.4 Offer patients the chance to take part in a randomised controlled trial (if available) that compares treatment options for stage I rectal cancer. [new 2014] 1.2.5 Laparoscopic surgery The recommendations in this section are from laparoscopic surgery for colorectal cancer (NICE technology appraisal guidance 105). 1.2.5.1 Laparoscopic (including laparoscopically assisted) resection is recommended as an alternative to open resection for individuals with colorectal cancer in whom both laparoscopic and open surgery are considered suitable. [2006] 1.2.5.2 Laparoscopic colorectal surgery should be performed only by surgeons who have completed appropriate training in the technique and who perform this procedure often enough to maintain competence. The exact criteria to be used should be determined by the relevant national professional bodies. Cancer networks and constituent trusts should ensure that any local laparoscopic colorectal surgical practice

	meets these criteria as part of their clinical governance arrangements. [2006] 1.2.5.3 The decision about which of the procedures (open or laparoscopic) is undertaken should be made after informed discussion between the patient and the surgeon. In particular, they should consider: • the suitability of the lesion for laparoscopic resection • the risks and benefits of the two procedures • the experience of the surgeon in both procedures. [2006] 1.2.6 Adjuvant chemotherapy in rectal cancer 1.2.6.1 Assess pathological staging after surgery, before deciding whether to offer adjuvant chemotherapy. [2011] 1.2.6.2 Consider adjuvant chemotherapy for patients with high-risk stage II and all stage III rectal cancer to reduce the risk of local and systemic recurrence. [2011] 1.2.7 Adjuvant chemotherapy for high-risk stage II colon cancer 1.2.7.1 Consider adjuvant chemotherapy after surgery for patients with high-risk stage II colon cancer. Fully discuss the risks and benefits with the patient. [2011] 1.2.8 Adjuvant chemotherapy for stage III colon cancer The recommendations in this section are from capecitabine and oxaliplatin in the adjuvant treatment of stage III (Dukes' C) colon cancer (NICE technology appraisal guidance 100). 1.2.8.1 The following are recommended as options for the adjuvant treatment of patients with stage III (Dukes' C) colon cancer following surgery for the condition: • capecitabine as monotherapy • oxaliplatin in combination with 5-fluorouracil and folinic acid. [2006] 1.2.8.2 The choice of adjuvant treatment should be made jointly by the individual and the clinicians responsible for treatment. The decision should be made after an informed discussion between the clinicians and the patient; this discussion should take into account contraindications and the side-effect profile of the agent(s) and the method of administration as well as

the clinical condition and preferences of the individual. [2006]

Colonoscopic surveillance for preventing colorectal cancer in adults with ulcerative colitis, Crohn's disease or adenomas. NICE clinical guideline 118 (2011).

1.1 List of all recommendations
People with inflammatory bowel disease

1.1.1 Offer colonoscopic surveillance to people with inflammatory bowel disease (IBD) whose symptoms started 10 years ago and who have:

- ulcerative colitis (but not proctitis alone) or
- Crohn's colitis involving more than one segment of colon.

1.1.2 Offer a baseline colonoscopy with chromoscopy and targeted biopsy of any abnormal areas to people with IBD who are being considered for colonoscopic surveillance to determine their risk of developing colorectal cancer (see table 1).

Table 1 Risk of developing colorectal cancer in people with IBD

Low risk:

- extensive but quiescent ulcerative colitis or
- extensive but quiescent Crohn's colitis or
- left-sided ulcerative colitis (but not proctitis alone) or Crohn's colitis of a similar extent.

Intermediate risk:

- extensive ulcerative or Crohn's colitis with mild active inflammation that has been confirmed endoscopically or histologically or
- post-inflammatory polyps or
- family history of colorectal cancer in a first-degree relative aged 50 years or over.

High risk:

- extensive ulcerative or Crohn's colitis with moderate or severe active inflammation that has been confirmed endoscopically or histologically or
- primary sclerosing cholangitis (including after liver transplant) or
- colonic stricture in the past 5 years or
- any grade of dysplasia in the past 5 years or
- family history of colorectal cancer in a first-degree relative aged under 50 years.

1.1.3 Offer colonoscopic surveillance to people with IBD as defined in 1.1.1 based on their risk of developing colorectal cancer (see table 1), determined at the last complete colonoscopy:

- Low risk: offer colonoscopy at 5 years.
- Intermediate risk: offer colonoscopy at 3 years.
- High risk: offer colonoscopy at 1 year.

1.1.4 For people with IBD who have been offered colonoscopic surveillance, continue to use colonoscopy with chromoscopy as the method of surveillance.

1.1.5 Offer a repeat colonoscopy with chromoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed.

People with adenomas

1.1.6 Consider colonoscopic surveillance for people who have had adenomas removed and are at low risk of developing colorectal cancer (see table 2).

1.1.7 Offer colonoscopic surveillance to people who have had adenomas removed and are at intermediate or high risk of developing colorectal cancer (see table 2).

1.1.8 Use the findings at adenoma removal to determine people's risk of developing colorectal cancer (see table 2).

Table 2 Risk of developing colorectal cancer in people with adenomas

Low risk: • one or two adenomas smaller than 10 mm. Intermediate risk: • three or four adenomas smaller than 10 mm or • one or two adenomas if one is 10 mm or larger. High risk: • five or more adenomas smaller than 10 mm or • three or more adenomas if one is 10 mm or larger.

1.1.9 Offer the appropriate colonoscopic surveillance strategy to people with adenomas based on their risk of developing colorectal cancer as determined at initial adenoma removal (see table 2).

Low risk: consider colonoscopy at 5 years:

- if the colonoscopy is negative (that is, no adenomas are found) stop surveillance
- if low risk, consider the next colonoscopy at 5 years (with follow-up surveillance as for low risk)

	• if intermediate risk, offer the next colonoscopy at 3 years (with follow-up surveillance as for intermediate risk) • if high risk, offer the next colonoscopy at 1 year (with follow-up surveillance as for high risk). Intermediate risk: offer colonoscopy at 3 years: • if the colonoscopy is negative, offer the next colonoscopy at 3 years. Stop surveillance if there is a further negative result • if low or intermediate risk, offer the next colonoscopy at 3 years (with follow-up surveillance as for intermediate risk) • if high risk, offer the next colonoscopy at 1 year (with follow-up surveillance as for high risk). • High risk: offer colonoscopy at 1 year. • if the colonoscopy is negative, or low or intermediate risk, offer the next colonoscopy at 3 years (with follow-up surveillance as for intermediate risk) • if high risk, offer the next colonoscopy at 1 year (with follow-up surveillance as for high risk). 1.1.10 Offer a repeat colonoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed. 1.1.11 Consider computed tomographic colonography[1] (CTC) as a single examination if colonoscopy is not clinically appropriate (for example, because of comorbidity or because colonoscopy cannot be tolerated). 1.1.12 Consider double contrast barium enema as a single examination if CTC is not available or not appropriate. 1.1.13 Consider CTC or double contrast barium enema for ongoing surveillance if colonoscopy remains clinically inappropriate, but discuss the risks and benefits with the person and their family or carers. Providing information and support 1.1.14 Discuss the potential benefits, limitations and risks with people who are considering colonoscopic surveillance including: • early detection and prevention of colorectal cancer and • quality of life and psychological outcomes. 1.1.15 Inform people who have been offered colonoscopy, CTC, or barium enema about the procedure, including:

	• bowel preparation • impact on everyday activities • sedation • potential discomfort • risk of perforation and bleeding. 1.1.16 After receiving the results of each surveillance test, discuss the potential benefits, limitations and risks of ongoing surveillance. Base a decision to stop surveillance on potential benefits for the person, their preferences and any comorbidities. Make the decision jointly with the person, and if appropriate, their family or carers. 1.1.17 If there are any findings at surveillance that need treatment or referral, discuss the options with the person, and if appropriate, their family or carers. 1.1.18 Throughout the surveillance programme, give the person and their family or carers the opportunity to discuss any issues with a healthcare professional. Information should be provided in a variety of formats tailored to the person's needs and should include illustrations.

Appendix C: Literature search for endoscopic full thickness removal of non-lifting colonic polyps

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	22/09/2016	Issue 9 of 12, September 2016
HTA database (Cochrane Library)	22/09/2016	Issue 3 of 4, July 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	22/09/2016	Issue 8 of 12, August 2016
MEDLINE (Ovid)	22/09/2016	1946 to September Week 2 2016
MEDLINE In-Process (Ovid)	22/09/2016	September 21, 2016
EMBASE (Ovid)	22/09/2016	1974 to 2016 Week 38
PubMed	22/09/2016	n/a
BLIC	22/09/2016	n/a

Trial sources searched on 05 07 2016
- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 05 07 2016
- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

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

The MEDLINE search strategy was adapted for use in the other sources.

1 Endoscopy, Gastrointestinal/ or Endoscopes, Gastrointestinal/
2 Colonoscopes/ or Colonoscopy/
3 1 and 2

4	((endoscop* or endo or colonoscop*) adj2 (full thick* or full-thick* or total wall or total-wall) adj2 (remov* or resect* or excis* or surger* or procedure* or polypectom* or treat* or therap* or device* or probe*)).tw.
5	(full* adj2 thick* adj2 (resect* or excis* or remov* or device* or probe*)).tw.
6	FTRD.tw.
7	EFTR.tw.
8	OTSC.tw.
9	(over-the-scope or "over the scope" or (over adj2 scope*)).tw.
10	((endoscop* or endo) adj4 clip*).tw.
11	or/3-10
12	Colonic Polyps/
13	((transanal* or anal* or anus* or colon* or colorect* or rectal* or rectum* or bowel* or hyperplastic* or neoplastic* or ademomat* or homartomat* or subepithelial or gastro*) adj4 (polyp* or lesion* or growth* or tumour* or tumor*)).tw.
14	((transanal* or anal* or anus* or colon* or colorect* or rectal* or rectum* or bowel* or hyperplastic* or neoplastic* or ademomat* or homartomat* or subepithelial or gastro* or non-lift*) adj4 (adenom* or cancer* or carcinoma* or neoplasm*)).tw.
15	or/12-14
16	11 and 15
17	ovesco.tw.
18	16 or 17
19	animals/ not humans/
20	18 not 19