NICE National Institute for Health and Care Excellence

External Assessment Centre correspondence log: instructions for EAC

Please use this table to record any questions or clarifications sent to the company, expert advisers and organisations/individuals outside of NICE.

Example:

#	Date	Who / Purpose	Question/request	Response received
1.	12/04/2018	**Manufacturer** Initial questions	Can you explain the origin of the included studies i.e. in which database were they found?	The origin of the included studies was pubmed.
2.	12/04/2018	**Manufacturer** Initial questions	Can you provide a rationale for the date limits used?	A 10-year range was decided upon to capture evidence related to the field of cardiology rather than the intervention itself.
3.	12/04/2018	**Manufacturer** Initial questions	Can you explain how the pubmed database was searched i.e. which limits were applied?	This search was completed in January 2018 and was restricted to titles and abstracts. For please see the export files, and the xls export sheet used to select the studies. **Files included in Appendix 1**.
4.	05/05/2018	**Expert – Dr C Smith (consultant cardiologist)** Surgical questions	What are the risks of Transcathetar Aortic Value replacement (TAVR)?	Some of the main risks of an aortic valve replacement include wound, lung, bladder or heart valve infections, blood clots, strokes, arrhythmia and reduced kidney function for a few days.

NICE National Institute for Health and Care Excellence

External Assessment Centre correspondence log

MT461 Endo-sponge for treating colorectal anastomotic leakage

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
X.	*XX/XX/XXXX*	*Who was contacted? (if an expert, include clinical area of expertise)* *Why were they contacted? (keep this brief)*	*Insert question here. If multiple questions, please break these down and enter them as new rows*	*Only include significant correspondence and attach additional documents/graphics/tables in Appendix 1, citing question number*
1.	15/01/2020	BBraun	Telephone call with Company and NICE to discuss get clarity on some issues, primarily related to the technology, how it works, and suitable populations.	Detailed notes attached (See appendix 1: File attachments/additional information from question 1:

2.	27/01/2020	BBraun	E-mail to confirm the CE marking of Endo-SPONGE due to a discrepancy between the scope, MIB and company submission	It was an error on the original submission, Endo-SPONGE is class IIb device
3.	29/01/2020	BBraun	Follow up e-mail on CE marking as company response was different to their submission	It is a class IIa as the DoC says, when you asked previously I looked at the CE cert which covers all our Wound Closure portfolio and mistakenly read is as IIb
4.	06/03/2020	BBraun	E-mail to company regarding two references used in the economic submission. The reference links don't work, can we check the source please?	Reply received 11/03/2020 Company provided the reference links.
5.	17/01/2020	Clinical Experts	A number of additional questions covering clinical pathways, pain relief (the use of anaesthetics), the comparator, the use of the technology in clinical practice)were sent to clinical experts and responses received from 3 experts (These are attached below).	Files 3 to 5 attached
6.	17/02/2020	Clinical Expert	Telephone call with a clinical expert to discuss Endo-SPONGE in more detail including clinical pathway, indication, contraindication, the length of the procedure, long-term survival, and the clarity of the difference between stoma/ileostomy reversal and restoration of bowel continuity).	Notes from call attached
7.	27/02/2020	Clinical Expert	Telephone call with a clinical expert to discuss Endo-SPONGE in more detail including the grading system for anastomotic leak, the definition of chronic and acute leakage, contraindication, clinical parameters for the economic modelling such as the length of the procedure, the use of anaesthetics and staff level	Notes from call attached – please not these notes have **NOT** been verified by the clinical expert as accurate.

8.	12/03/2020	Clinical Expert	A telephone call was originally arranged for 20/02/2020 however there were problems with the call. A follow-up list of questions was sent to this expert.	Response received 12/03/2020 which was after the submission date for the final report. These responses are included below but have not been included in the EAC report.

Insert more rows as necessary

Appendix 1.

During correspondence with the company and experts, additional information is sometimes included as file attachments, graphics and tables. Any questions that included additional information of this kind is added below in relation to the relevant question/answer:

File attachments/additional information from question 1:

Questions for Company Meeting M

File attachments/additional information from question 5:

3. MT461 NICE Expert Adviser Respo

4. MT461 NICE Expert Adviser Respo

5. MT461 NICE Expert Advisor Respo

File attachments/additional information from question 6:

11. CedarinterviewEndo

File attachments/additional information from question 7:

11. Endo-SPONGE telephone call.docx

File attachments/additional information from question 8:

Follow-up questions for econc

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Questions for Company (B Braun)

Topic	Endo-SPONGE for treating colorectal anastomotic leakage (MT461)
Date sent	13th January 2020

	Company Submission Page Number (section)	EAC Question	Company Response
1	3 (decision problem)	Antibiotics are listed as both a comparator and an outcome. Could the company clarify whether this is because patients may be initially treated with endo-sponge and antibiotics?	Use of antibiotics will be an individual clinician decision and largely dependent on the patient and severity of condition Treatment options: • Antibiotics alone • Antibiotics + conservative management (inc. endo-sponge) • Antibiotics + surgical management
2		In the event that a patient required antibiotics, would patients initially managed using endo-sponge have antibiotics added to their treatment (endo-sponge + antibiotics) or would treatment be sequential (endo-sponge followed by antibiotics) **EAC Note:** This appears to be addressed on page 12 (Non-surgical intervention) where it states that antibiotics may be used alone or in combination with percutaneous drainage) suggesting possible treatment combinations of: • Antibiotics alone • Percutaneous drainage alone • Antibiotics + percutaneous drainage • Percutaneous drainage followed by antibiotics if required	As above. Endo-sponge is considered to be a non-surgical intervention by the company. The majority of patients do not require sedation, some will require mild sedation. The company opinion is that a very small number of patients would undergo an operative procedure in a theatre setting with general anaesthetic. Majority of patients can be seen in the endoscopy suite or as outpatients. The company acknowledges that the literature does include patients who have endo-sponge operatively.

	Company Submission Page Number (section)	EAC Question	Company Response
3	4 (the technology)	Could the company give a brief overview of how the technology works in practice? For example, would a pack of 10 or 5 be required for each patient?	Average of 7-10 sponges per patient depending on cavity size Sponge inserted and attached to an external vacuum bottle (2 settings on the bottle, company state (IFU) that the second setting should not be used. Each individual kit in a pack is wrapped and sterile with a 5 year shelf life Patients can be either inpatient or outpatient and this will largely be dependent on the severity of the patient condition and clinical decision on the best way to manage the anastomotic leak. Some patients may be kept in for long enough for treatment to be confirmed working then treated as outpatients. The company states that a pack of 10 or 5 contains each individual wrapped kit. One kit contains one sponge, a pack of 5 kits would have 5 separate sponges. There is pressure button on the top of vacuum bottle, including on and off, and option 1 and 2 (applying different pressure). Only option 1 should be used, option 2 is too strong a vacuum.
		Are any parts of the system reusable?	None of the kit is re-useable. The components in the kit are single use.
		How is the sponge resized through the course of treatment or are sponges available in different sizes separately?	Endoscopist/Surgeon will check the cavity size to determine what size sponge is required When previously used sponge is removed, its size can be used as a reference for the next sponge. Sponge can be cut (sides, top or both) to size
		How are multiple sponges placed within the cavity?	Large cavities, up to 3 sponges can be used. 2 sponges can be attached to one bottle but 3rd sponge will require an additional vacuum bottle

	Company Submission Page Number (section)	EAC Question	Company Response
4	10	Point of clarity This section states the sponge system is changed every 48-72 hours. The EAC note that the MIB states every 24 to 72 hours. Could the company clarify which timings are accurate?	Clinicians often remove the initial sponge after 24 hours to check if treatment is working. They will inspect the cavity after the sponge is removed. After 72 hours the sponge can become difficult to remove as it promotes healing and can begin to 'grow' around the sponge. Also, effectiveness of the sponge is reduced. It is likely that different clinical teams will see the same patient for insertion/change of sponge(s).
5	14 & 15	Could the company clarify that Endo-sponge would replace current non-operative methods? **EAC note:** This goes back to the query about antibiotics? Are antibiotics considered a non-operative intervention or are they used in addition to other non-operative methods (endoscopic clips, fibrin glue etc)?	The company consider that endo-sponge would be a viable alternative to all non-operative and operative interventions apart from antibiotics. I believe we mentioned that in the literature we used, we saw that Endo-SPONGE was being used successfully in anastomotic leaks that were up to 270 degrees around, which is extremely severe. The intention is for endo-sponge to come in early in the clinical pathway to prevent/reduce antibiotic use.
6	18 (Training)	Could the company indicate whether they consider there to be any risks associated with not routinely providing training in clinical practice?	• The company deliver group presentations/demonstrations to MDTs/clinicians • Additional training can be provided if necessary on a request basis • Product can be purchased without training but any new customers are contacted by the company • Procedure would always be performed by an endoscopist/surgeon • The team from company is assisting during the first procedure performed by the new client.

	Company Submission Page Number (section)	EAC Question	Company Response
		Is there an additional cost for hands on training?	No additional training costs
		Does the company have any details on the number of users who request more hand on training?	Minimal to zero
7	19-22	Please confirm the number of included studies (Table on p19 states 20, Table 1 includes 21 studies)	Company state 20 however acknowledge there are some errors in the data and requested to send an updated version. This has been agreed by NICE and EAC provided the content/conclusions do not change and that all corrections are clearly marked (tracked changes/comments box) for comparison against original submission
8	67 (Complaints)	% complaints for 9 months of 2019 is higher than in previous years. Could the company comment on this/provide some detail?	Complaints consisted of • Internal complaints (about the product such as package and labelling) • Some customer complaints Overall rate of complaint is still very low but company consider the increase in 2019 due to wider reach/use of product and resulting increase in production.
		Could the company comment on the nature of complaints? Do they relate to the same issue?	Most related to packaging, contents of package/kits Not related to the use of endo-sponge clinically
		Could the company comment on whether complaints are impacted by whether users undergo hands on training or not?	Not considered an issue

Cedar
Healthcare Technology Research Centre

Questions for NICE Expert Advisers

Topic	Endo-SPONGE for treating colorectal anastomotic leakage (MT461)
Date sent	17 January 2020
Please respond by	5.00 pm (UTC/GMT) on Friday 24th January

Cedar has been commissioned by the National Institute for Health and Care Excellence (NICE) to carry out external assessments of clinical and economic evidence on behalf of the Medical Technologies Evaluation Programme.

The purpose of this document is:

- to facilitate researchers' understanding of the clinical topic
- to clarify technical information about a device, procedure, intervention or standard care comparator
- to check whether assumptions made in the literature or economic model reflect "real world" context and practices (with particular emphasis on the UK NHS).

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Instructions:
Please complete the final column of the following table with your response to each question.
The completed form should be returned by **5.00 pm (UTC/GMT) on Friday 24th January.**
In the subject line, please write "MT461 Endo-SPONGE: Expert responses".

No.	EAC Question	Expert Adviser response
Clinical Pathway		
1	What is the pathway of care for a patient with anastomotic leak?	Large anastomotic leak with significant par anal discharge or chronic low grade pelvic sepsis provided no contraindications such as Crohns fistula
2	Would you typically treat patients in an inpatient or outpatient setting or a combination of both?	Both
3	Do you consider vacuum assisted therapy (specifically endo-sponge) to be an operative or non-operative procedure	Non-operative procedure
4	Do you anticipate that Endo-SPONGE would replace current treatments or be an addition to current treatment options?	Not replace but be a very good alternative or in addition
5	For patients with anastomotic leak, would there be multiple attempts at conservative management using different treatment options before turning to surgical options?	Yes. Endo-sponge is labour intensive for both surgeon and patient. Even then, the concept is much safer and better for patients compared with major surgery
6	Could you provide an estimate of the number of patients in the UK who • Undergo low anterior resection/anastomosis • Experience anastomotic leak following surgery • Persistent leak following treatment (e.g. suture repair, fibrin glue, Endo-Sponge etc)	I do not know how many patients undergo anterior resection. Risk of leak in low anastomosis is circa 10-12%. Persistent leak following treatment over is rare given most leaks are not large cavity
7	Would antibiotics be given alone or in combination with other treatments?	It needs to be in combination
Pain Relief		
8	In your experience do patients require some form of pain relief before endo-sponge can be placed?	Yes
9	Would patients treated typically receive • Mild pain relief (gas&air) • General anaesthetic	Depends, I have experienced both depends on pain threshold and how deep the cavity is.
10	Would many patients (if any) receive mild pain relief and be proceed to general anaesthesia?	About half and half

No.	EAC Question	Expert Adviser response
11	How does this compare with other forms of treatment for anastomotic leak?	Fibrin glue does not really work. Suture is not applicable unless re-laparoscoped
Clinical Experience		
12	Did you encounter any problems while using Endo-SPONGE in practice?	Yes, labour intensive. We all have to be around for it. Not the best for patients in terms of attendance
13	What is the furthest segment of the intestines that can be reached and treated with EndoSPONGE?	8cm from verge
14	Following the removal of Endo-SPONGE and during an endoscopic exploration of the cavity, is perforation likely to occur? Are there any adverse events associated with repeated endoscopic explorations?	It's a sinus by then so perforation is unlikely to occur. I am not aware of issues with repeated endoscopic explorations.
15	Are you aware of any high-quality published evidence or any ongoing studies specifically relating to Endo-sponge, other than: • Popivanov (2019) • Shalaby (2019) **If yes, please provide the full reference(s).**	No
16	What are the most important potential study confounders to account for when assessing the effectiveness of vacuum-assisted therapy for anastomotic leak?	Width and depth of cavity. If small already then healing may have occurred as quick without Endosponge
17	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	Mindful of contraindications of its usage

Thank you very much for providing your expert input into this assessment.
All responses will be taken into consideration.

Cedar
Healthcare Technology Research Centre

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No.	EAC Question	Expert Adviser response
Clinical Pathway		
1	What is the pathway of care for a patient with anastomotic leak?	Once the index of suspicion has been raised they require admission, IV fluids and IV antibiotics. Then investigation by CT with IV and preferably rectal contrast. Once confirmed the patient requires either drainage via IR or theatre and a defunctioning ileostomy if they do not have one already.
2	Would you typically treat patients in an inpatient or outpatient setting or a combination of both?	Inpatient setting
3	Do you consider vacuum assisted therapy (specifically endo-sponge) to be an operative or non-operative procedure	Non-operative procedure
4	Do you anticipate that Endo-SPONGE would replace current treatments or be an addition to current treatment options?	Addition
5	For patients with anastomotic leak, would there be multiple attempts at conservative management using different treatment options before turning to surgical options?	No
6	Could you provide an estimate of the number of patients in the UK who • Undergo low anterior resection/anastomosis • Experience anastomotic leak following surgery • Persistent leak following treatment (e.g. suture repair, fibrin glue, Endo-Sponge etc)	Reviewing the recent NBOCA annual report approximately 2760 patients have an anterior resection in Wales and England. The quoted leak rate is variable from 4-10%. Therefore the number experiencing a leak could range from 110 to 276 It is difficult to quantify the persistent leak rate, but a third of patients do not have their ileostomy reversed. One reason being a persistent leak, although there are concerns such as function.
7	Would antibiotics be given alone or in combination with other treatments?	In combination
Pain Relief		

No.	EAC Question	Expert Adviser response
8	In your experience do patients require some form of pain relief before endo-sponge can be placed?	I have no direct experience with sndo-sponge, but would imagine the first few changes would require a sedative such as midazolam or possibly a GA for the first procedure.
9	Would patients treated typically receive • Mild pain relief (gas&air) • General anaesthetic	Probably a GA for the first insertion, then midazolam thereafter for changes
10	Would many patients (if any) receive mild pain relief and be proceed to general anaesthesia?	See above
11	How does this compare with other forms of treatment for anastomotic leak?	This is a new technique, an addition to the armoury
Clinical Experience		
12	Did you encounter any problems while using Endo-SPONGE in practice?	I have no direct experience
13	What is the furthest segment of the intestines that can be reached and treated with EndoSPONGE?	I would expect it to be only used for low rectal anastomotic leaks in colorectal surgery
14	Following the removal of Endo-SPONGE and during an endoscopic exploration of the cavity, is perforation likely to occur? Are there any adverse events associated with repeated endoscopic explorations?	Unlikely due to the fibrosis, but always a possibilty
15	Are you aware of any high-quality published evidence or any ongoing studies specifically relating to Endo-sponge, other than: • Popivanov (2019) • Shalaby (2019) **If yes, please provide the full reference(s).**	No
16	What are the most important potential study confounders to account for when assessing the effectiveness of vacuum-assisted therapy for anastomotic leak?	Patient variability, patient factors vary widely and given the low numbers of leaks in a single institution creating a study design that mitigates these confounding variables would be tricky.

No.	EAC Question	Expert Adviser response
17	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	I have no clinical experience of using endo-sponge.

Thank you very much for providing your expert input into this assessment.
All responses will be taken into consideration.

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PLEASE SEE TEXT BELOW FOR ANSWERS

No.	EAC Question	Expert Adviser response
Clinical Pathway		
1	What is the pathway of care for a patient with anastomotic leak?	
2	Would you typically treat patients in an inpatient or outpatient setting or a combination of both?	
3	Do you consider vacuum assisted therapy (specifically endo-sponge) to be an operative or non-operative procedure	
4	Do you anticipate that Endo-SPONGE would replace current treatments or be an addition to current treatment options?	
5	For patients with anastomotic leak, would there be multiple attempts at conservative management using different treatment options before turning to surgical options?	
6	Could you provide an estimate of the number of patients in the UK who • Undergo low anterior resection/anastomosis • Experience anastomotic leak following surgery • Persistent leak following treatment (e.g. suture repair, fibrin glue, Endo-Sponge etc)	
7	Would antibiotics be given alone or in combination with other treatments?	
Pain Relief		
8	In your experience do patients require some form of pain relief before endo-sponge can be placed?	
9	Would patients treated typically receive • Mild pain relief (gas&air) • General anaesthetic	
10	Would many patients (if any) receive mild pain relief and be proceed to general anaesthesia?	

No.	EAC Question	Expert Adviser response
11	How does this compare with other forms of treatment for anastomotic leak?	
Clinical Experience		
12	Did you encounter any problems while using Endo-SPONGE in practice?	
13	What is the furthest segment of the intestines that can be reached and treated with EndoSPONGE?	
14	Following the removal of Endo-SPONGE and during an endoscopic exploration of the cavity, is perforation likely to occur? Are there any adverse events associated with repeated endoscopic explorations?	
15	Are you aware of any high-quality published evidence or any ongoing studies specifically relating to Endo-sponge, other than: • Popivanov (2019) • Shalaby (2019) **If yes, please provide the full reference(s).**	
16	What are the most important potential study confounders to account for when assessing the effectiveness of vacuum-assisted therapy for anastomotic leak?	
17	Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?	

Thank you very much for providing your expert input into this assessment.
All responses will be taken into consideration.

1. **What is the pathway of care for a patient with anastomotic leak?**

(Refer to Issues in professional practice, prevention, diagnosis and management of colorectal anastomotic leakage March 2016, ACPGBI)

Diagnosis of leakage

1. Clinician suspicion
2. Clinical evidence of sepsis, non-progression after surgery and or peritonitis
3. Raised serum markers of inflammation and sepsis
4. Radiological investigations
5. Treatment
    a. Sepsis 6
    b. Organ support if required
    c. Source control
        i. Conservative
        ii. Radiological drainage
        iii. EndoSPONGE
        iv. Laparoscopy/Laparotomy
        v. Diversion stoma or resect anastomosis and end stoma

2. **Would you typically treat patients in an inpatient or outpatient setting or a combination of both?**

Most patients are in sepsis which will require inpatient care.

In the context of role of EndoSPONGE, this could be initiated as an inpatient and may be followed up as an outpatient.

3. **Do you consider vacuum assisted therapy (specifically endo-sponge) to be an operative or non-operative procedure**

Any invasive procedure could be considered as an operative procedure from the patient perspective.

I would class it is as 'minimally' invasive as the cavity are accessible transanally quiet often and the EndoSPONGE can be deployed in my experience either without any adjuncts or with minimal pain killers. In one case we required sedation.

4. **Do you anticipate that Endo-SPONGE would replace current treatments or be an addition to current treatment options?**

Endosponge will remain an adjunct as it is a subgroup of colorectal anastomotic leakages (see later for more details).

I have recently read that it is considered for use in oesophageal leakage, which I do not have any first-hand knowledge.

5. **For patients with anastomotic leak, would there be multiple attempts at conservative management using different treatment options before turning to surgical options?**

It is not desirable to have prolonged attempt to manage an anastomotic leakages conservatively as there is usually underlying sepsis which precludes such an option. In the context of EndoSPONGE, it is important that the sepsis is controlled before the patient can be expected to be maintained on this device. If the sepsis is not controlled with the EndoSPONGE alone, it may require an operative intervention including proximal diversion of bowel which the managing surgeon has to consider.

6. **Could you provide an estimate of the number of patients in the UK who**
    a. Undergo low anterior resection/anastomosis

As per latest NBOCAP data, there were 4516 resections for rectal cancer in the year 2016-17

    b. Experience anastomotic leak following surgery

Reported leakage rate of around 11% after rectal surgery in systematic review

(Ann Surg. 2010 May;251(5):807-18. doi: 10.1097/SLA.0b013e3181dae4ed.Postoperative complications following surgery for rectal cancer)(Paun BC[1], Cassie S, MacLean AR, Dixon E, Buie WD. http://dx.doi.org/10.1136/gutjnl-2015-309861.786)

    c. Persistent leak following treatment (e.g. suture repair, fibrin glue, Endo-Sponge etc)

I apologise for not able to get a data for this. I do not have experience with suture repair or fibrin glue.

7. **Would antibiotics be given alone or in combination with other treatments?**

Antibiotic alone may not be adequate as more than often it will require source control.

8. **In your experience do patients require some form of pain relief before endo-sponge can be placed?**

Explained below

9. **Would patients treated typically receive**
    a. Mild pain relief (gas&air)
    b. general anaesthetic

The first placement of EndoSPONGE will require a General anaesthetic assessment of cavity deep in the pelvis by an experience surgeon and the suitability for placement of EndoSponge placement.

Subsequent placements/changes, as I mentioned previously, there were occasions where I have changed without any adjuncts in well-conditioned patients who is independent as an outpatient. In other occasions, I required sedation with the help of an anaesthetist for each change. It depends very much on the patient's tolerance and how close it is to the index operation.

10. Would many patients (if any) receive mild pain relief and be proceed to general anaesthesia?

Not in my experience as it will depend on the judgement made by the surgeon. After explaining to the patient what it entails, depending on the height of the cavity from the anal opening, patients tolerance and difficulty of endoscopic access an appropriate decision has to be made by the surgeon.

11. How does this compare with other forms of treatment for anastomotic leak?

As I mentioned previously, Endosponge is ideal for a subgroup of patients who had a low colorectal anastomotic leakage with an extra-peritoneal collection.

This low extraperitoneal anastomosis is usually protected by a proximal diversion ileostomy at primary surgery, which is a common practise by most colorectal surgeons considering the higher risk of anastomotic leakage in such cases.

In case of leakage, the proximal ileostomy tends to be protective and reduce the contamination (also dependent on prior bowel preparation preoperatively). However the local pus and leakage may still require source control.

We follow this algorithm as in the ACPGBI guidance referenced before.

In this algorithm pg 22 the case scenario 1, 2a and 2b could be managed using Endosponge instead of the Interventional radiology transperineal/ transanal drainage. Endosponge in these situations give a much better control over the effluent, ease of deployment and more efficient considering the larger calibre of draining tubes as against the small calibre of radiological drains.

12. Did you encounter any problems while using Endo-SPONGE in practice?

There is a very short and steep learning curve with the equipment. I had one occasion where a small ring from the neck of the lubricating gel was accidentally introduced into the cavity.

This was not identified until surgery was performed for completion resection of rectal stump.

I have raised it with the MHRA and the company, B Braun. To my understanding the company has since changed the design of the gel tube without the free plastic ring at the neck.

13. What is the furthest segment of the intestines that can be reached and treated with EndoSPONGE?

As mentioned above, this is clinically useful tool for extraperitoneal low colorectal anastomotic leakage.

To my understanding, EndoSPONGE is designed to be in the peritoneal cavity for drainage of any further proximal anastomosis. From my clinical experience I will not suggest its use for any proximal leakages.

This is because the access transanally by open or endoscopic method will be difficult. Higher anastomotic leakage will also be open to the peritoneal cavity with associated extensive contamination, requiring laparotomy.

I am aware EndoSPONGE is now been trialled with results for Oesophageal anastomotic leakage. However, I do not have experience with this to give any further comments.

14. **Following the removal of Endo-SPONGE and during an endoscopic exploration of the cavity, is perforation likely to occur? Are there any adverse events associated with repeated endoscopic explorations**

The endosponge is introduced into the cavity of collection through a perforation in the bowel (ie, the dehiscence of anastomosis). The aim of the treatment with the Endosponge is also to maintain the perforation until the cavity heals completely following which the perforation is allowed to heal over.

I haven't had any adverse impact from the repeated procedure. The mental health of the patient through the process is important as it can be prolonged and repeated visits to the hospital may be required.

In one case, the anaesthetist raised the risk of neurological impact in older individuals who have repeated GA. We changed to sedation which worked well as short GA.

15. **Are you aware of any high-quality published evidence or any ongoing studies specifically relating to Endo-sponge, other than:**

- Popivanov (2019)
- Shalaby (2019)

If yes, please provide the full reference(s).

None I could reference, however I cannot claim to have done an extensive search from time constraints.

16. **What are the most important potential study confounders to account for when assessing the effectiveness of vacuum-assisted therapy for anastomotic leak**?

If a study has to be set up to study this, the most important factors to consider will be

a. The lack of uniformity of intervention among surgeons for anastomotic leakage
b. The lack of clear radiological criteria for extraperitoneal leakage
c. Lack of knowledge of Endosponge among surgeons
d. No clear clinical criteria for the 2 different settings on the EndoSPONGE suction bottle
e. Differing pain control requirements of patients requiring different setups.
f. Different healing rates of cavity dependent on patient's co morbidity.

g. Difficulty in referencing the size of the sponge introduced as they require trimming as the cavity gets smaller.

17. Are there any other important issues directly related to this assessment which you would like to bring to the attention of Cedar/NICE?

I do not have any concerns except that the table form do not give enough space for description and very short time line initially provided.

Telephone Call with clinical expert (17/02/2020), notes have been verified by clinical expert.

Query	Comment
Can you provide some oversight on the clinical pathway and where Endo-SPONGE is likely to fit?	Endo-SPONGE is not a replacement, it is an additional treatment option. The decision to use endo-SPONGE will be based on a number of factors including patient condition, location and size of leak, why the leak occurred. Left for the clinical judgment. Most of these patients have already had a de-functioning stoma Intervention (with Endo-SPONGE or other) may not be required. Treatment involves management of initial sepsis symptoms and once patient is stable, further treatment may be considered (e.g. Endo-SPONGE)
Are there any contra-indications	Yes J pouch (IPAA) Low coloanal anastomosis generally although might be possible in some cases
Is there a particular grading system for AL that is used in the UK?	I'm not that familiar. It's a guide, very much dependent on patient's situation.
Can you comment on the use of the terms acute/chronic leak in relation to endo-sponge?	I wouldn't use endo-sponge immediately. I'm unsure what's meant by acute/chronic in this context. Clinical (as opposed to subclinical AL) AL not a common but significant problem and consider how bothersome clinically to a patient before treating
Would the majority of patients having colorectal surgery be for colorectal cancer?	Yes, likely to be mostly rectal cancer patients but there will be other indications, especially in teaching centres where it will be done for other conditions. E.g. endometriosis, mesh erosions from rectopexy etc
Can you comment on the long term survival of the patient group (patients undergoing colorectal surgery) regardless of whether they have an anastomotic leak or not?	Patients with AL are likely to have lower survival than patients with no AL. Ann Surg. 2011 May;253(5):890-9. **Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. Having said that, a paper this year (level 3) suggested the contrary.** Dis Colon Rectum. 2019 Mar;62(3):286-293. **Influence of Anastomotic Leak After Elective Colorectal Cancer Resection on Survival and Local Recurrence: A Propensity Score Analysis. As I said on the phone, one needs to view the 2011 paper with care given the heterogeneity of the study**
Could you comment on the length of time is takes to apply Endo-SPONGE. Literature suggests 15 minutes	15 minutes just to apply Endo-SPONGE seems reasonable however there are a number of other factors which need to be considered when determining the full time it takes to complete an appointment such as need for anaesthetic (GA or local), theatre time. Organising the procedure takes a lot of work. These are not emergency patients so they go to the bottom of the list. Total time could easily be 2 hours but this may include time making arrangements. For the ones needing sedation or GA, a district hospital under

	emergency pressures can take hours for the patient hanging around in recovery. I would not underestimate the 2 hours.In my very few experience, a range of 30 mins and 1 hour from entering to leaving theatre would not be too inaccurate. Patient needing to go to theatre has added time of sending, WHO checklist, sedation or GA time, washout if indicated etc so there is always additional time. Not all go to theatre and then it could be quicker. I've never done this as an outpatient procedure.
Can you comment on the staff that may be required for an Endo-SPONGE application?	In my experience (primarily inpatients) Consultants or registrars to apply Endo-SPONGE Anaesthetist if GA or sedation (not always with sedation) is required Other members of clinical team to arrange treatment/theatre etc.
Can you comment on any additional length of stay associated with Endo-SPONGE?	No, my patients are already inpatients. No obvious additional length of stay with Endo-SPONGE The use of endosponge means that the patient is in hospital longer with such symptomatic leak
Can you clarify the difference between stoma/ileostomy reversal and restoration of bowel continuity?	Protective stoma is given as the risk of AL is higher in low colorectal anastomosis than high anastomosis unless there are additional risk factors for a leak such as patients on immunosuppressants etc. Stoma/ileostomy reversal is done with the intention of restoring bowel continuity. I would consider these to be indicative of the same thing.

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The notes from this call have been sent to the clinical expert for verification but we have not had a response as of 10/03/2020

Please note:

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1. Is there a standard grading system in use in the UK for grading anastomotic leaks?

Yes, but this is largely used for presentations/publications etc. In clinical terms, a patients either has a leak or doesn't.

2. Could you provide some clinical insight into the difference between a chronic and acute leak (we have seen literature referring to this but no clear definition)

An acute leak is generally one diagnosed in the first few days post-surgery. A chronic leak however is a leak that is likely to have occurred in the first few days post-surgery but did not get picked up until later. Generally hasn't healed because the patient has been defunctioned during primary surgery.

3. Are there any specific contraindications for Endo-SPONGE treatment

Use for low or rectal anastomosis

Patients with IAAP not contraindicated

Largely dependent on patient condition and location of anastomotic leak

4. Is the primary indication for colorectal surgery colorectal cancer or would the patient group comprise a number of different indications for surgery?

70-75% of patients will be having primary surgery for rectal cancer.

5. Without an anastomotic leak, what would the expected/anticipated survival rate for a group of patients undergoing colorectal surgery be? (If it is predominantly colorectal patients, what would 5 and 10 year survival be)

Approximately 65% (5 year survival) – a 10 year time horizon in the model would be appropriate.

6. In your experience, does treatment with Endo-SPONGE result in a change in length of hospital stay (increased/decreased) compared with other options for managing leak?

Not necessarily, patients are likely to already be in hospital when their leak is diagnosed so managing and treating the leak will not necessarily add any extra length to their stay. It may be that endo-SPONGE treatment can continue treatment in an outpatient setting.

7. Literature suggests that Endo-SPONGE application takes approximately 15 minutes however we are concerned this does not reflect the totality of treatment time for a patient. In your experience;
    a. is 15 minutes a reasonable estimate for application of Endo-SPONGE

Yes, 15 minutes to apply Endo-SPONGE seems sensible.

    b. approximately how long would the total treatment time take for a patient requiring theatre (inpatient, general anaesthetic)

Depends on what the patient requires and when the Endo-SPONGE treatment happens. On diagnosis of anastomotic leak most patients will have a laparoscopy and ileostomy (defunctioning) and it would be feasible to do the first Endo-SPONGE treatment at this time. In this case, Endo-SPONGE treatment would only add an extra few minutes to the process.

    c. approximately how long with total treatment time take in the outpatient setting?

In an outpatient setting, Endo-SPONGE applications/changes would take approximately 20-25 mins.

8. What staff would be involved in an appointment/treatment with Endo-SPONGE?

Consultant (surgeon who performed the primary surgery).

9. In your experience, what proportion of patients need a GA?

Usually the first placement however this may not be an additional general anaesthetic if the Endo-SPONGE application is being done as part of the leak diagnosis and management.

10. Is there a standard definition for what qualifies as an early leak (we have seen some literature suggesting 60 days post op).

Early versus late leak is related to when the leak is diagnosed by the clinical team rather than when the leak actually occurs as most leaks will have occurred quite soon following initial surgery but just not been picked up.

11. Would most patients have a protective stoma following a leak diagnosis
    All patients will have a protective stoma if they haven't already had one as part of primary surgery.

    General Comments
    Overall, Endo-SPONGE would not replace anything in the current clinical pathway. It would be an adjunct to current treatment options including antibiotics and percutaneous abdominal drainage.
    In general patients with leak will go back to theatre for laparoscopy, drain insertion to drain the abscess, defunctioning stoma and washout of the area. During this procedure it may be appropriate to begin Endo-SPONGE treatment as well.
    - ***Antibiotics will be given to all patients with a leak as they will have symptoms (infection, sepsis) to manage/prevent so antibiotics would not be an appropriate comparator to Endo-SPONGE.***
    - ***Percutaneous drainage would not be an appropriate comparator as all patients with leak will have drains inserted and Endo-SPONGE would be an add-on.***

    The main benefit with Endo-SPONGE is likely to be in the fact that is can reduce the amount of time a patient will have a stoma by a significant amount of time compared with not using Endo-SPONGE (can reduce the time to stoma reversal by weeks or months) this will

    - ***Improve patient quality of life***
    - ***reduce the costs associated with stoma management/stoma care***

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1. Is there a standard grading system in use in the UK for grading anastomotic leaks?

As per the ACPGBI document, it can be classed as intra peritoneal leakage and extra-peritoneal leakage broadly. Also there is a classification of severity of intra-peritoneal leakage in the same document (Page 22-23, Prevention, diagnosis and management of colorectal anastomotic leakage, March 2016).

The endosponge is ideal for extra-peritoneal leakage of a low colorectal anastomosis, with level 2 or 3 severity), for the reason that the patient has localised sepsis in the pelvis.

2. Could you provide some clinical insight into the difference between a chronic and acute leak (we have seen literature referring to this but no clear definition)

Chronic sinuses from the anastomosis tend to be radiological finding and usually does not present clinically as acute sepsis. Endo Sponge is not suitable for those scenarios.

3. Are there any specific contraindications for Endo-SPONGE treatment

Absolute CI will be allergy to the material used.

Relative CI would be the following:

a. site of the anastomotic leakage: it is not suitable for intraperitoneal perforation of colonic anastomosis with or without sepsis. It is ideal for a extraperitoneal colorectal anastomosis with localised sepsis.
b. If the patient has grade 4 or 5 sepsis, it may require a laparotomy and resection of anastomosis, than a endosponge alone.
c. Lack of proximal diversion, as in a de-functioning proximal stoma, is detrimental in its success.
d. Patient factors including mental health as this will require repeated procedures.

4. Is the primary indication for colorectal surgery colorectal cancer or would the patient group comprise a number of different indications for surgery?

Surgery resulting in a low colorectal anastomosis (in the context of Endo Sponge) can be varied. However, on a national context, the commonest indication for an operation with a low anastomosis will invariably be colorectal cancer.

Other indications will include Ulcerative colitis, where following total colon resection and a pouch could be formed from small bowel and anastomosed to low rectum. Other rarer possibilities are for resection of large polyps in rectum and surgery for rectal trauma.

5. Without an anastomotic leak, what would the expected/anticipated survival rate for a group of patients undergoing colorectal surgery be? (If it is predominantly colorectal patients, what would 5 and 10 year survival be)

There is extensive data regarding this particular question about risk of local recurrence and long term survival after an anastomotic leakage in colorectal cancer resection.

The guidance from ASGBI had clearly stated that there is a higher risk of local recurrence, and reduction in the overall survival and disease free survival and this is the general opinion held in colorectal discussions and meetings (pg 11, Issues in clinical practice, Prevention, diagnosis and management of Colorectal anastomotic leakage, March 2016).There are studies which has shown no significant impact following rectal surgery in particular, however these are isolated reports and to my knowledge not the accepted wisdom.

As regarding Endo Sponge, it may be difficult to compare a cohort of patients who had Endo Sponge treatment for anastomotic leakage versus none. Moreover, the risk is the leakage itself in my opinion, than the treatment they may receive for leakage.

6. In your experience, does treatment with Endo-SPONGE result in a change in length of hospital stay (increased/decreased) compared with other options for managing leak?

In my opinion, Endo-Sponge gives better control of the site of leakage which reduces the requirement for major surgical intervention, reduce impact of sepsis by giving source control in appropriate cases and thus reduce hospital stay overall. In these patients, they will be able to leave in-patient care much earlier as was the case with the 3 of my patients and be managed as outpatients with Endo-Sponge. This made a significant reduction in morbidity and improvement in their mental health.

7. Literature suggests that Endo-SPONGE application takes approximately 15 minutes however we are concerned this does not reflect the totality of treatment time for a patient. In your experience;

I assume that this is regarding patients who already had an Endo-Sponge placed and requiring change.

   a. is 15 minutes a reasonable estimate for application of Endo-SPONGE

The actual procedure to change an Endo-sponge may take only 15 minutes, however there are logistics involved in setting up, including endoscopy, sedation or even in OPD. So I agree it is an underestimate of the actual time it may be required.

The analogy will be with an inguinal hernia operation in theatre, where the operation itself may take 45minutes, but the bringing the patient to theatre, anaesthetising, check list, operation itself and waking them up and out of theatre will all together take up to 60-75 minutes!

b. approximately how long would the total treatment time take for a patient requiring theatre (inpatient, general anaesthetic)

If under GA (or deep sedation) as in one of my patients, the anaesthetic time to find an IV access and then to sedate them will take up to 15minutes anaesthetic time in my recall.
In outpatient settings, it will be upto 15 min to set up the required equipment, position patient on left lateral, analgesic administration if required and proceed to change an Endo-Sponge.
I have not had a patient who required change by endoscopy, hence cannot comment of the time required with this setup.

c. Approximately how long with total treatment time take in the outpatient setting?

As above

In my opinion, it is not appropriate to compare procedure depending on time it may take. I have patients who need reassuring and discussion before we proceed.

I believe we should be comparing the ease of procedure, reproducibility of efficacy by different teams and how the patients cope.

8. What staff would be involved in an appointment/treatment with Endo-SPONGE?

Again, I assume we are discussing patients who had an Endo-Sponge placed already by a Colorectal Consultant and requiring change.

In majority of the episodes, as a Colorectal Consultant, I was directly involved in the procedure.

I had Higher Surgcial trainees who were able to change them under guidance.

I also have a Surgical care practitioner (SCP) who has changed them very effectively even in my absence.

It is a reflection of the ease with which it can be placed once the patient and the operator knows the routine. However, it will require experience and the confidence form the patient to get to that place and also will require the guidance of a colorectal Consultant to assess the progression of healing.

In short it has to be Consultant delivered or led at all times.

9. In your experience, what proportion of patients need a GA?

One of the 3 patients had GA initially and then we changed to deep sedation for changes. The other 2 were managed without GA or sedation in OPD, for changes of Endo-Sponge.

Please note that the initial assessment and decision of placement required GA for all 3 of my patients.

10. You mention in you initial information that the time from index operation would have an impact on need for GA. Would patients who have a leak sooner be more likely to need GA?

    Although, I do not remember making that statement, as mentioned above, all 3 of my patients required GA for assessment of the cavity and decision on Endo-Sponge management initially.

    The patient, who required a GA initially for further changes, had a more extensive sepsis of her perineum involving a rectovaginal fistula. She then settled to have sedation to have them changed. I can only extrapolate from the limited number of cases, that if the sepsis is significant, the patients are likely to need GA.

11. Is there a standard definition for what qualifies as an early leak (we have seen some literature suggesting 60 days post op).

All cases which are likely to be managed in a hospital with Endo-Sponge are acute conditions with leakage from colorectal anastomosis with associated sepsis. Endo-Sponge is a form of source control for such situations.

In leaks picked up by radiological investigations with none or minimal symptoms to the patient, will not warrant management with Endo-Sponge. In my experience they are managed by conservative measures (watch and wait).