
1190

Final Decision Analytic
Protocol to guide the
assessment of
Magnetic Resonance
Imaging (MRI) for:

- a) Small bowel
Crohn's disease
- b) Fistulising perianal
Crohn's disease

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MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Minister for Health and Ageing (the Minister) to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

Purpose of this document

This document is intended to provide a draft decision analytic protocol that will be used to guide the assessment of an intervention for a particular population of patients. The draft protocol that will be finalised after inviting relevant stakeholders to provide input to the protocol. The final protocol will provide the basis for the assessment of the intervention.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

Patients – specification of the characteristics of the patients in whom the intervention is to be considered for use;

Intervention – specification of the proposed intervention

Comparator – specification of the therapy most likely to be replaced by the proposed intervention

Outcomes – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention

Purpose of application

A proposal for an application requesting MBS listing of MRI for patients with Crohn's disease was received from the Gastroenterology Society of Australia by the Department of Health and Ageing in July 2011. This Decision Analytic Protocol specifically looks at two populations:

- MRI small bowel in patients with small bowel Crohn's disease and
- MRI pelvis for patients with fistulising perianal Crohn's disease

The applicant notes that in the future it is intended that a separate application be made seeking MBS listing for MRI pelvis in patients with non-Crohn's disease related perianal fistulae.

Background

Current arrangements for public reimbursement

MRI for Crohn's disease is not currently funded under the MBS. For patients to access MRI for this condition it would have to be on a self-pay basis. While the cost of MRI pelvis should be similar to other MBS MRI items (around \$400), the long patient preparation, scan duration and specialist expertise required to perform an MRI small bowel means that an MRI in this patient population is likely to cost more than an MRI for other conditions.

Regulatory status

MRI is currently available in public and private facilities in major centres in each state and territory. One hundred and thirty sites have been licensed by the Department of Health and Ageing to provide services that are eligible for funding under the MBS. From 1 November 2012 a further thirty sites will be fully licensed to provide eligible services in rural areas and 161 will have partial licenses.

Intervention

Description of patient population

Crohn's Disease

Crohn's disease is a chronic inflammatory disorder that can affect any part of the gastrointestinal tract from the mouth to the anus, but most commonly causes inflammation and ulceration of the ileum and the colon. It may cause the intestine to develop fistulae to the bowel or skin, or strictures causing narrowing of the bowel. Symptoms of Crohn's disease include diarrhoea, weight loss, rectal bleeding and fever. Complications may include rectal abscesses and fistulisation. Perianal fistulas are a frequent manifestation of Crohn's disease and may arise from inflamed or infected anal glands and/or penetration of fissures or ulcers of the rectum or anal canal (Schwartz & Herdman 2004). Consequences of perianal fistulas include perianal drainage, pain, dyspareunia and faecal incontinence.

Crohn's disease is most common in adolescents and young adults, but can occur at any age. Diagnosis is based on a composite of endoscopy, radiography and pathological findings. Management depends on the disease location, disease severity, and disease-associated complications (Lichtenstein et al 2008). Since there is no cure for Crohn's disease, the goals of treatment are to induce remissions, maintain remissions, minimise side effects of treatment, and improve quality of life. Non-surgical treatment for Crohn's disease includes dietary measures and drug therapy. Corticosteroids, antibiotics and anti TNF agents are used to induce remission, and immunosuppressive agents or maintenance anti TNF therapy to maintain remission. Surgical removal of the affected bowel is sometimes necessary but this is not curative as the disease can recur in other sites. Some people with Crohn's disease however have long periods of symptom-free remission.

Description of technology

MRI

MRI is an imaging technique that allows accurate visualisation of the entire gastrointestinal tract through the acquisition of multiplanar images with high-contrast resolution of the tissue. Bowel distension is needed to obtain optimal visualisation and is achieved through the use of an enteric contrast material. This may be administered orally (enterography) or through an enteric (nasojejunal tube). These techniques are referred to as MR enterography and MR enteroclysis respectively, with the term 'MRE' representing an abbreviation used to describe all small bowel MR techniques.

Improvements in MRI technology such as fast scanning techniques and the use of bowel antiperistaltic agents have permitted more accurate diagnosis of complications of Crohn's disease, including abscess, fistula and stenosis. MRI is also useful when ionising radiation is contraindicated such as in children and pregnant women or when patients are at risk of accumulating significant exposure from multiple diagnostic procedures, such as may occur in chronic, remitting and relapsing condition such as Crohn's disease.

Crohn's disease is a lifelong condition which often requires repeat diagnostic investigations to evaluate and assess disease; patients may undergo MRI as frequently as several times a year or not at all depending on their progress and disease severity.

Small bowel MRI is used in conjunction with enteric contrast material to achieve bowel distention (the exception to this is in pregnant women where the use of the contrast agent may not be used). As such small bowel MRI may involve preparatory drinking or enteral tube intubation about one hour before the test as well as insertion of an intravenous cannula for intravenous contrast. Similarly an MRI of the pelvis generally requires insertion of intravenous cannula and IV contrast. The actual MRI takes around 30 to 40 minutes depending on whether it is for the small bowel or for pelvis.

To perform a MRI in patients with Crohn's disease, a specialist radiologist with expertise in interpreting MRI scanning and familiarity with Crohn's disease would be needed. The scan, in order to attract a rebate, must also be requested by a specialist medical practitioner or consultant physician and be performed on a Medicare-eligible MRI unit by a Medicare-eligible provider, and be an MRI service listed in the MBS.

Co-administered interventions

There is no single diagnostic test in the evaluation of patients with Crohn's disease. As such patients undergo a combination of clinical, laboratory, histological, endoscopic and imaging assessments including colonoscopy (MBS item 32090), gastroscopy (MBS item 30473), CT with or without enterography (MBS item 56507), small bowel radiology (MBS item 58915) and blood tests (MBS 66512). For patients with perianal disease surgical examination may also be undertaken (G44C – ARTG)

Other related procedures

Capsule endoscopy may also be used for the diagnosis of suspected uncomplicated small bowel Crohn's disease. It is however contraindicated in patients with complicated small bowel disease since the capsule may become lodged thereby requiring surgical removal. It is also contraindicated in pregnant women. Capsule endoscopy is therefore not listed as a comparator in this review since its application is in relation to different circumstances from which this submission is based.

Listing proposed and options for MSAC consideration

Proposed MBS listing

MRI is proposed for patients with small bowel Crohn's and fistulising perianal disease in the following indications:

- Evaluation of disease extent at time of initial diagnosis of Crohn's disease
- Evaluation of exacerbation/suspected complications of known Crohn's disease
- Evaluation of known or suspected Crohn's disease in pregnancy
- Assessment of change to therapy in patients with Crohn's disease

At the April PSAC meeting it was noted that the descriptor and the fee would need further discussion and that separate descriptors and fees would be needed to distinguish between MR enterography and MR enteroclysis. In response to these comments the RANZCR recommended that a separate fee of \$265.25 be established for the MRI enteroclysis procedure; comprising \$130 for the naso-jejunal tube and \$135.25 for the procedure (which is the same procedure fee that applies to the Double Contrast Barium Enema procedure item 58921). These comments were presented at the August PASC meeting and are reflected in Table 1.

A fee of \$627.50 was suggested for the MRI small bowel procedure which is considered equivalent in complexity to MRI item 63473 (staging of cervical cancer).

It was also noted in the RANZCR response that the current MRI Schedule includes a separate modifying item (MBS item 63491) to be claimed when contrast is used which attracts a fee of \$44.80.

Table 1: Proposed MBS item descriptor for MRI for small bowel Crohn's disease with and without contrast agent

Category 5 – Diagnostic Imaging Services
<p>MRI to evaluate small bowel Crohn's disease. Medicare benefits are only payable for this item if the service is provided to patients for :</p> <ul style="list-style-type: none"> (a) Evaluation of disease extent at time of initial diagnosis of Crohn's disease (b) Evaluation of exacerbation/suspected complications of known Crohn's disease (c) Evaluation of known or suspected Crohn's disease in pregnancy (d) Assessment of change to therapy in patients with small bowel Crohn's disease <p>NOTE 1: Assessment of change to therapy can only be claimed once in a 12 month period.</p> <p>Fee: \$627.50 Benefit: 75% = \$470.63 85% = \$533.38</p>
<p>MRI enteroclysis for Crohn's disease. Medicare benefits are only payable for this item if the service is related to item XXXX :</p> <p>Fee: \$265.25 Benefit: 75% = \$198.94 85% = \$225.46</p>

For patients with fistulising perianal Crohn's disease the following indications are proposed:

- Evaluation of pelvic sepsis and fistulas associated with established or suspected Crohn's disease
- Assessment of change to therapy to treatment of pelvis sepsis and fistulas from Crohn's disease

A scheduled fee of \$403.20 has been proposed by the applicant given that MRI Pelvis is similar in complexity and time to MBS item 63482 MRI of pancreas and biliary tree. Similarly to the above item(s) the MRI Schedule includes a separate modifying item to be claimed when contrast is used (MBS item 63491), rather than having separate items with and without contrast agent.

Table 2 Proposed MBS item descriptor for MRI for fistulising perianal Crohn's disease

Category 5 – Diagnostic Imaging Services
<p>MRI for fistulising perianal Crohn's disease. Medicare benefits are only payable for this item if the service is provided to patients for:</p> <ul style="list-style-type: none"> • Evaluation of pelvic sepsis and fistulas associated with established or suspected Crohn's disease • Assessment of change to therapy of pelvis sepsis and fistulas from Crohn's disease <p>NOTE 1: Assessment of change to therapy can only be claimed once in a 12 month period.</p> <p>Fee: \$403.20 75% = \$302.40 85% = \$342.72</p>

Clinical place for proposed intervention

Most cases of Crohn's disease can be diagnosed by ileocolonoscopy which permits examination of the inner lining of the anus, rectum, large bowel and terminal ileum. However ileocolonoscopy cannot always be completed and there are several disadvantages including the invasiveness of the test, the risk of bowel perforation as well as the relative poor patient acceptance of the test. It also cannot effectively assess perianal fistulae and cannot examine the small bowel apart from the last few centimetres.

Consequently ileocolonoscopy is largely used to make a diagnosis of Crohn's disease, but not often utilised in assessing patients or evaluating for complications of Crohn's disease. As such other imaging techniques including CT, ultrasonography and MRI have been increasingly used for evaluation of patients with Crohn's disease. The choice between imaging techniques is usually determined by local preference and patient's preparedness to pay for MRI.

MRI for patients with small bowel Crohn's disease

Currently CT scan or small bowel barium follow through (SBFT) are performed to evaluate small bowel Crohn's disease, usually in the clinical context where there is a suspicion of complicated small bowel Crohn's disease (e.g. intestinal stricture or obstruction; intra-abdominal perforation, abscess or fistula). The use of SBFT is now mostly used when CT or MRI services are not available.

Evaluation of disease extent at time of initial diagnosis of Crohn's diagnosis

In this indication MRI is proposed as a **replacement** to CT and SBFT in patients with newly diagnosed Crohn's disease (e.g. on the basis of endoscopy or surgery) and where small bowel involvement is clinically suspected. The main purpose is to inform clinicians about the extent of disease, and whether intestinal complications are already present.

Evaluation of exacerbation/suspected complications of known Crohn's disease

In this indication MRI is proposed as a **replacement** to abdominal CT and SBFT that are currently used to investigate patients with suspected complications from small bowel Crohn's disease. MRI is reported to be much more accurate than SBFT but similar in sensitivity and specificity to CT and avoids the radiation risk associated with these tests (American College of Radiology 2011). A further advantage of MRI over CT is that it can distinguish inflammatory Crohn's disease of the small bowel from complicated small bowel Crohn's disease (fibrotic or fistulising disease). This distinction is clinically important since treatment options differ for the two circumstances (medical treatment for inflammatory disease; surgery for some intestinal complications) and the findings could help determine which therapeutic approach is taken or lead clinicians to an early surgical approach if medical management fails. According to the applicant however there will still be a requirement for abdominal CT scanning to be listed for this indication. This is because in a significant minority of cases (approx 10%) patients present in emergency circumstances and CT scanning is more readily available at most centres when imaging is required emergently. For the remainder of patients in whom the semi-elective evaluation of suspected complications is required, MRI would be a replacement to abdominal CT or small bowel follow through.

Evaluation of known or suspected Crohn's disease in pregnancy

In this indication however MRI is proposed as a **replacement** to ultrasound since alternative radiological options such as CT scan or SBFT are generally avoided due to the foetal radiation risk. Endoscopy which is invasive and associated with a need for vigorous bowel preparation and intravenous sedation is also generally contra-indicated. Abdominal ultrasound is the current comparator that is used in clinical practice for this indication, but its sensitivity is low. In this population MRI is expected to be able to provide information on confirmation on diagnosis, assessment of extent of small bowel involvement and identification of the presence of small bowel complications. It would be anticipated that a requirement for MRI small bowel investigation would be highly exceptional.

Assessment of change to therapy in patients with Crohn's disease

In clinical practice, assessing therapeutic response is generally done by measuring change in symptoms or blood or faecal markers of inflammation. Endoscopic or imaging (CT or SBFT) is indicated when patients symptoms have not resolved or getting worse in spite of treatment; there is a discrepancy between symptoms and blood or faecal tests (or a decision has to be made as to whether to proceed with different medical management or to pursue surgery. This type of investigation may be required on more than one occasion during a patient's life, and MRI offers a non-invasive accurate alternative without the risk of ionising radiation

MRI for patients with fistulising perianal Crohn's disease

Currently there is no satisfactory non-invasive radiological option for evaluating perianal fistulising Crohn's disease. Surgical examination is considered the gold standard in acute deterioration of perianal sepsis, but is invasive. Expertise with endoscopic (endoanal) ultrasound in Australia is limited, and CT scanning is not sufficiently sensitive for this purpose(Horsthuis et al 2005).

Evaluation of pelvis sepsis and fistulas associated with established or suspected Crohn's disease

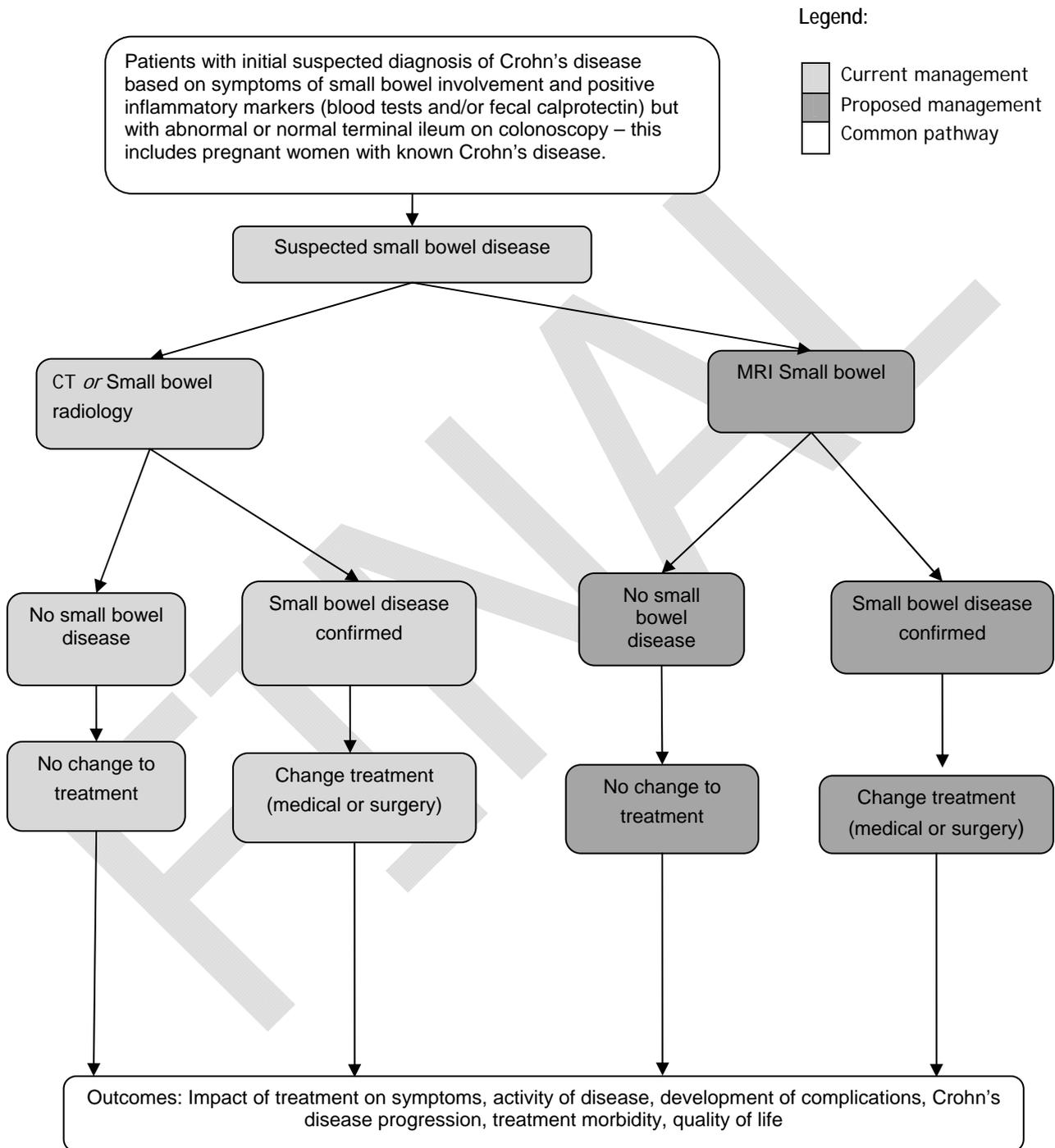
In this indication MRI is proposed as a **replacement** to surgical assessment or endoanal ultrasound. MRI pelvis is able to define the anatomical configuration of a fistulous track thereby providing information to determine whether or not surgery is necessary and to assist with surgical planning. Knowing in advance the anatomy of a complex fistula greatly assists the surgeons make informed decisions. In current practice, surgical assessment [examination under anaesthesia (EUA)] and exploration is often undertaken to evaluate pelvic fistulising Crohn's disease. However surgical assessment is expensive, limited in availability, and carries the risk of damaging the anal sphincter leading to incontinence. Definitive surgery is required in certain circumstances when a perianal abscess or fistula track needs to be drained. Endoanal ultrasound is operator dependent, and expertise with this investigation in Australia is very limited. In any case it has limited capacity to examine distances beyond the bowel wall, and cannot delineate major complex fistulas that run several centimetres away from the intestinal lumen (e.g. ischiorectal abscesses). This is a crucial deficiency of endoanal ultrasound, since exclusion of a pelvic collection is mandatory before intensive medical therapy can be started. MRI is the only non-invasive means able to accurately direct treatment.

Assessment of change to treatment in patients with pelvis sepsis and fistulas from Crohn's disease

Assessment of treatment response is based currently on clinical groups (mainly symptoms including pain and draining), and if indicated, EUA. MRI pelvis will assist in deciding whether or not medical treatment should be continued, including alternative medical treatment and whether or not surgery is an option (Gligorijevic et al 2010).

MRI for patients with small bowel Crohn's disease

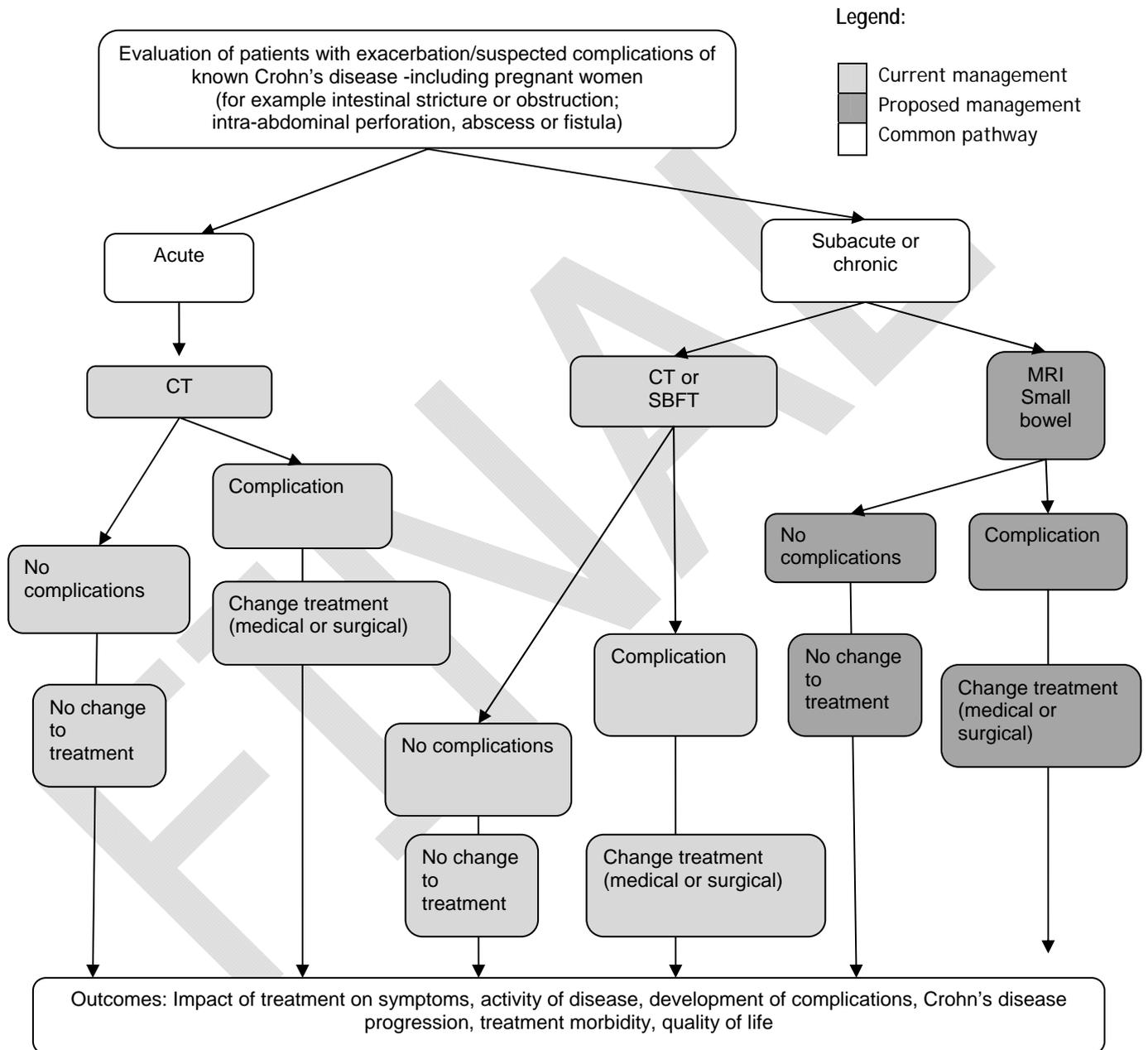
Figure 1 *Evaluation of disease extent at time of initial diagnosis of Crohn's diagnosis**



*Medical treatment may include corticosteroids, anti-inflammatories and biological agents or nutritional therapy. For patients undergoing medical treatment, response to treatment would be evaluated (see Figure 4)

MRI for patients with small bowel Crohn's disease

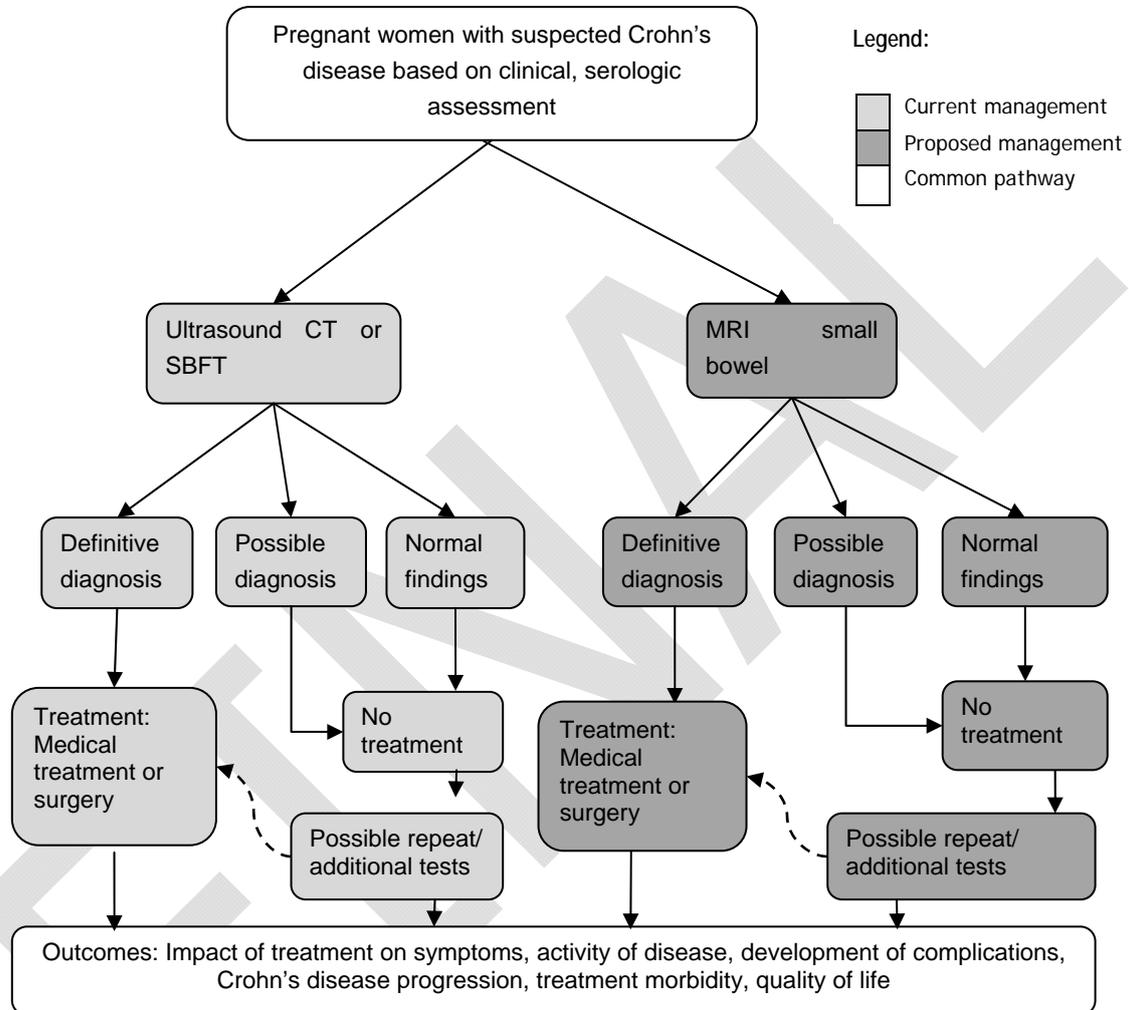
Figure 2 Evaluation of exacerbation/suspected complications of known Crohn's disease*



*Medical treatment may include corticosteroids, anti-inflammatories and biological agents. For patients undergoing medical treatment, response to treatment would be evaluated (see Figure 4)

MRI for patients with small bowel Crohn's disease

Figure 3 Evaluation of suspected Crohn's disease in pregnancy

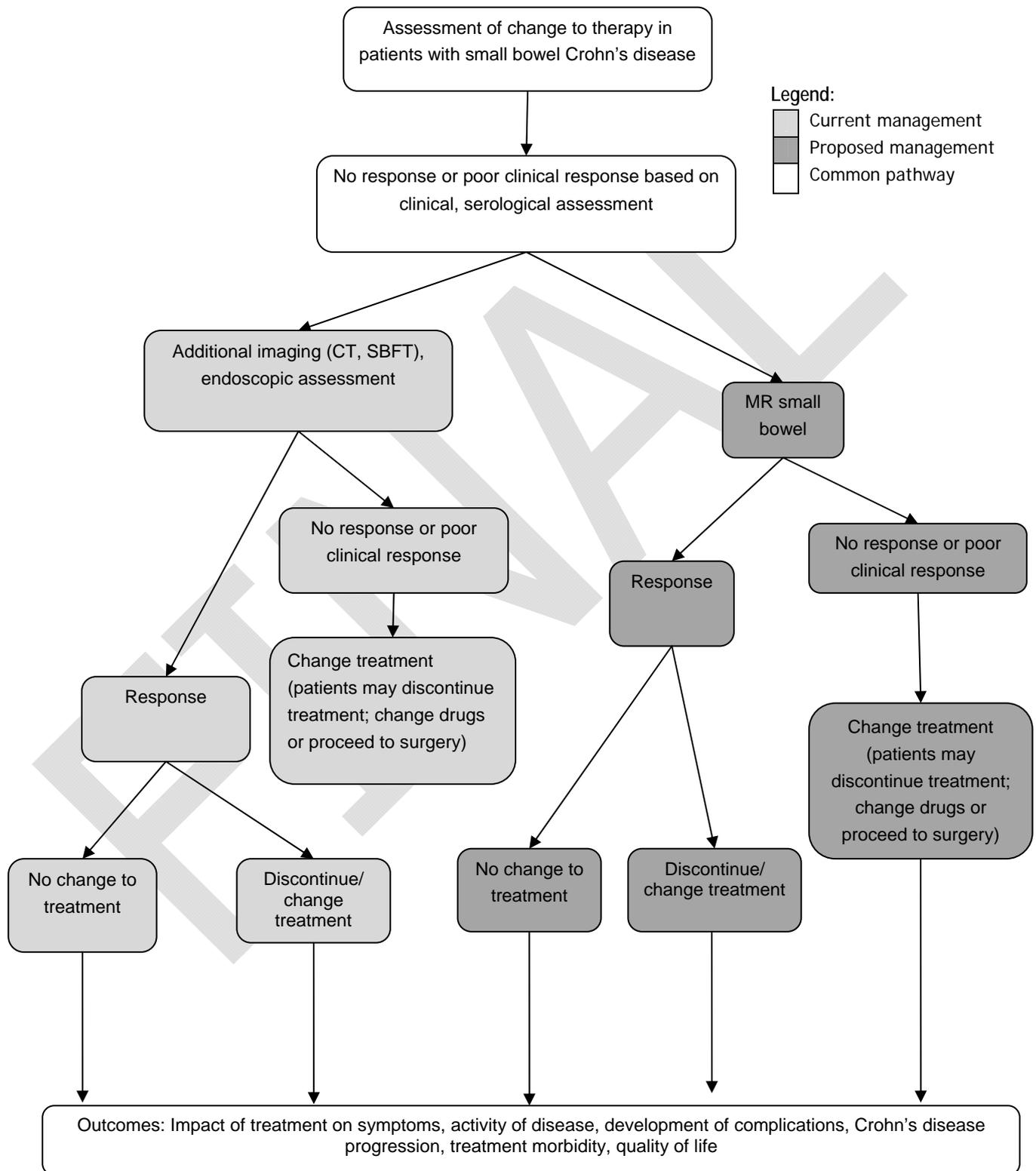


This flowchart is adapted from the MSAC review of Capsule endoscopy for the diagnosis of suspected small bowel Crohn's disease MSAC Application 1146 (MSAC 2011) where MRI was considered as a comparator. The assumption is that the clinical management of pregnant women should be the same as for all symptomatic patients but the choice of test is guided by safety concerns.

It should be noted that this algorithm only addresses suspected disease – the populations in Figure 1 and 2 incorporate pregnant women and address issues around known disease.

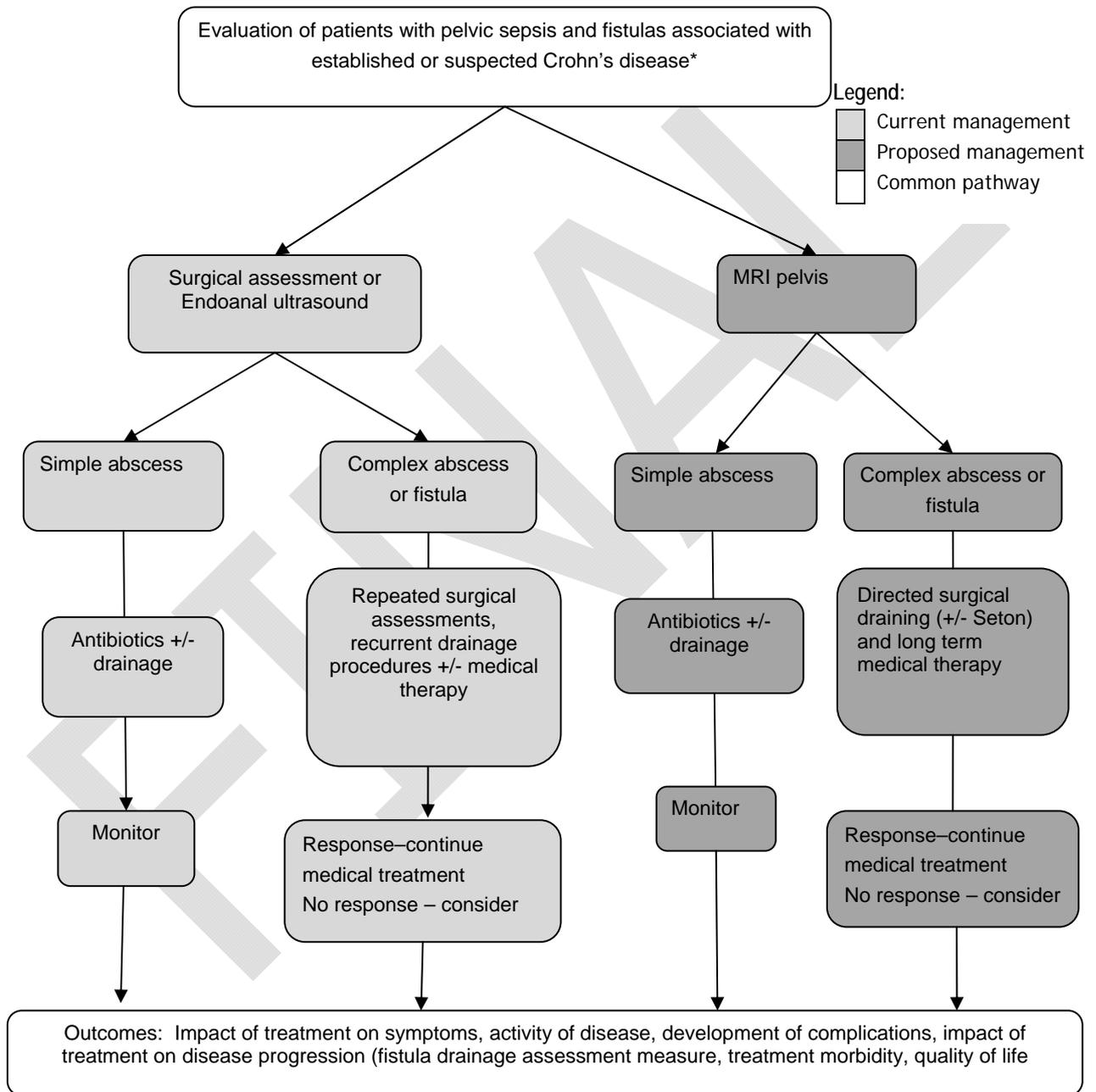
MRI for patients with small bowel Crohn's disease

Figure 4 Assessment of change to therapy in patients with Crohn's disease



MRI for patients with fistulising perianal Crohn's disease

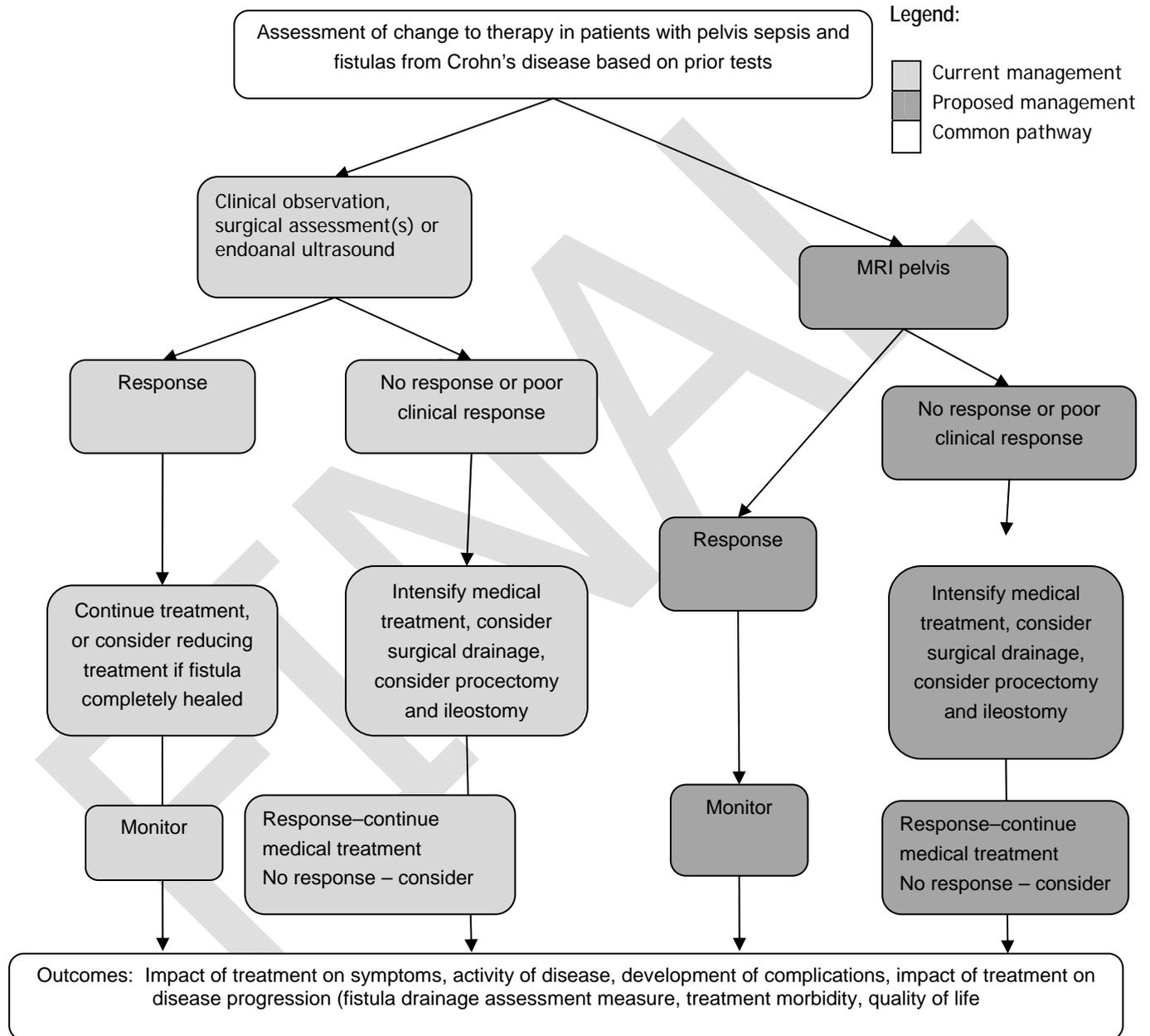
Figure 5 Evaluation of pelvic sepsis and fistulas associated with established or suspected Crohn's disease*



* This excludes emergency/urgent circumstances where MRI would not be considered. Medical therapy includes immunosuppressive biological therapy. CT is not included in the above algorithm as it is insensitive for fistulising perianal disease and not used in clinical practice

MRI for patients with fistulising perianal Crohn's disease -

Figure 6 Assessment of change to therapy in patients with pelvis sepsis and fistulas from Crohn's disease



Endoanal ultrasound is not really an available option in Australia. Surgical assessment cannot accurately define fistula anatomy, and is not useful to assess treatment. Clinical observation provides directive information to the surgeon, thereby limiting extent of surgery. Medical options depend in MRI findings.

Comparator

CT

Abdominal CT is a radiological technique used in the diagnosis of small bowel Crohn's disease. This test provides multiplanar images of the lumen, wall and mesentery of the small bowel. These images have a high degree of spatial resolution and are generated via the use of multidetector CT technology following intravenous contrast and the ingestion of a contrast agent by the patient either orally or via a naso-jejunal tube (CT enteroclysis CTE).

Small bowel follow through (SBFT)

SBFT is a radiological technique for imaging the small bowel. Barium is either ingested by the patient or administered by enteroclysis and then x-ray images are taken of the abdomen. In some Australia settings, SBFT has been superseded by abdomen CT/CTE however clinical practice varies across settings. Moreover, its use is limited by high radiation exposure.

Endoanal Ultrasound

To perform endoanal ultrasound a dedicated probe is required, which can be attached to some standard ultrasound machines. Endoanal ultrasound is only used for perianal disease, as opposed to standard ultrasound which is used for gynaecological evaluation of the pelvis, renal tract or hepatobiliary-pancreatic tree. Expertise in Australia with endoanal ultrasound is limited as there is no formal training and the investigation is usually carried out by interested clinicians who may not have specific radiological training in ultrasound (Rieger et al 2004). The main disadvantage with this endoanal ultrasound is its ability to assess deep, complex fistulas accurately.

Surgical Examination

In practice, surgical assessment [examination under anaesthesia (EUA)] and exploration is undertaken to evaluate fistulising Crohn's disease. This consists of visual inspection, palpation and the passage of metal probes into fistula tracks under general anaesthesia. EUA is the gold standard in the evaluation and classification of acute deterioration of perianal sepsis in Crohn's disease. It is expensive however and carries the risk of damage to the anal sphincter during the procedure leading to incontinence.

Clinical claim

The clinical claims for MRI (small bowel and pelvis) relative to its comparator(s) are listed below:

Potential benefits:

MRI has advantages over other radiological imaging techniques and methods of examination such as EUA in terms of both safety and effectiveness.

In terms of safety the main benefit of MRI is the lack of ionising radiation particularly given that many patients are young and may have multiple follow-up scans to assess disease activity.

It also offers a non-invasive method of evaluating perianal disease, (in comparison to surgical examination) reducing the risk of complications associated with anaesthesia and surgical evaluation.

In terms of effectiveness it is claimed that MRI may have similar sensitivity and specificity to CT in adults with known Crohn's disease (American College of Radiology 2011; Panes et al 2011) and may in fact be more accurate in areas such as

- distinguishing between inflammation and fibrosis
- demonstrating the transmural nature and severity of bowel wall inflammation,

Potential harms (disadvantages):

The main disadvantages in the literature relate to the availability of MRI, the cost of the test and the acceptance by patients (due to the length of time to undertake the test)(Zimmermann & Al-Hawary 2011).

MRI is contraindicated in a small proportion of patients, such as those with pacemakers, internal defibrillators and aneurysm clips. These circumstances are most unusual in the patient population with Crohn's disease who are usually young.

On the basis of this, the clinical claim for MRI in small bowel and pelvis is that it has both superior (or at the very least, comparable) effectiveness and superior safety compared to other options including CT, SBFT, endoanal ultrasound and EUA. As such on the basis of Table 3 below a cost effectiveness or cost utility analysis would seem to be most appropriate. This however is dependent on the evidence; other approaches may be considered once the evidence has been reviewed however these would need to be justified in the report.

Table 3: Classification of an intervention for determination of economic evaluation to be presented

		Comparative effectiveness versus comparator								
		Superior		Non-inferior	Inferior					
Comparative safety versus comparator	Superior	CEA/CUA		CEA/CUA		Net clinical benefit	CEA/CUA			
						Neutral benefit	CEA/CUA*			
						Net harms	None^			
	Non-inferior	CEA/CUA		CEA/CUA*		None^				
								Inferior	Net clinical benefit	CEA/CUA
									Neutral benefit	CEA/CUA*
Net harms	None^									
		None^		None^						

Abbreviations: CEA = cost-effectiveness analysis; CUA = cost-utility analysis

* May be reduced to cost-minimisation analysis. Cost-minimisation analysis should only be presented when the proposed service has been indisputably demonstrated to be no worse than its main comparator(s) in terms of both effectiveness and safety, so the difference between the service and the appropriate comparator can be reduced to a comparison of costs. In most cases, there will be some uncertainty around such a conclusion (i.e., the conclusion is often not in disputable). Therefore, when an assessment concludes that an intervention was no worse than a comparator, an assessment of the uncertainty around this conclusion should be provided by presentation of cost-effectiveness and/or cost-utility analyses.

^ No economic evaluation needs to be presented; MSAC is unlikely to recommend government subsidy of this intervention

The key uncertainties surrounding the selection and implementation of the economic analysis include the following:

- **Obtaining comparative effectiveness data to populate a CEA/CUA model.** The use of MRI in Crohn's disease is relatively new and there is likely to be limited evidence relating to its comparative effectiveness particularly in relation to the evaluation of response. While accuracy information may be available, data on change of management and impact on health outcomes may be limited.
- **Sub group analysis of use of MRI in the evaluation of known or suspected Crohn's disease in pregnancy.** The lower radiation dose of MRI relative to CT, and hence its superior safety, is the key clinical claim of MRI in this population. The proposed population is also likely to be very small and it is possible that a discussion of the costs and consequences of funding MRI in this group may be more appropriate than a decision analytic model aimed at estimating cost effectiveness.

Outcomes and health care resources affected by introduction of proposed intervention

Outcomes

MRI for patients with small bowel Crohn's disease

Diagnostic performance

Sensitivity
Specificity
Additional TP and FP
Diagnostic yield

Therapeutic impact

% change in management plans (e.g. avoidance of surgical procedures)

Patient outcomes

Impact of treatment on symptoms
Activity of disease
Development of complications
Crohn's disease progression
Treatment morbidity
Quality of life

MRI for patients with fistulising perianal Crohn's disease

Diagnostic performance

Sensitivity
Specificity
Additional TP and FP
Diagnostic yield

Therapeutic impact

% change in management plans (e.g. avoidance of surgical procedures)

Patient outcomes

Impact of treatment on symptoms
Activity of disease
Development of complications
Fistula Drainage Assessment Measure
Treatment morbidity
Quality of life

Health care resources

Consequences:

The main potential consequence of using MRI in the clinical management of patients with Crohn's disease is a reduced risk to the patient by avoiding ionising radiation associated with alternative imaging tests. Given that it may be a more accurate diagnostic test in terms of assessing the location, extent and severity of disease it may also lead to changes in patient management such as avoidance of surgery, and may ultimately result in improved patient outcomes.

Costs:

Small bowel: If publically funded MRI will replace CT or SBFT (which is no longer used regularly in the investigation of Crohn's patients) currently performed in the patient population. Therefore some of the costs of MRI will be offset by a reduction in reimbursement costs for these tests. Costs associated with treatment (or delayed treatment) may also be reduced should MRI result in earlier or more appropriate treatment, particularly in the setting of proposed assessment of treatment response in patients with Crohn's disease.

In terms of perianal disease MRI would reduce the need for repeated surgical examinations. MRI is less costly than surgical examination. Costs associated with treatment may also be reduced should MRI result in more appropriate interventions or cessation of expensive drug treatment in the situation where assessing treatment with MRI shows no improvement or conversely where MRI should the fistula has fully healed.

Estimating utilisation

The applicant provides an estimation of potential utilisation of MRI in small bowel Crohn's disease based on published data regarding the natural history of Crohn's disease. Using a cohort of 100 newly diagnosed patients with Crohn's disease, it is estimated that the requirement for MRI small bowel would be 20 in the first year, and 3 per annum thereafter. Repeat investigations may also be required. This figure does not take into account patients with known disease (prevalence) which is the target population for this test. It is estimated that in Australia the prevalence of Crohn's disease is about 50 per 100 000 population.

MRI of the pelvis is required for most patients with perianal fistulas. Using a cohort of 100 newly diagnosed patients with Crohn's disease, - the applicant estimates that 5% may have a perianal fistula at presentation and another 7% by the end of the year (12% in total). The rate of new fistulas thereafter is about 1% per annum and patients would probably require repeat investigations. The demand for MRI in patients with perianal fistulas would be higher once taking into account prevalent cases, it is estimated that around 20% of all Crohn's disease patients will experience a fistula at some stage.

Table 4: List of resources to be considered in the economic analysis (not exhaustive)

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
<u>Resources provided to identify eligible population (comparators)</u>										
- MRI	Radiologists	Outpatient								
- CT/CTE	Radiologist	Outpatient								
- SBFT	Radiologist	Outpatient								
- Surgical Examination	Specialist	Outpatient/ Inpatient								
<u>Resources provided to prior or in conjunction with comparators</u>										
- Colonoscopy	Specialist	Outpatient/ Inpatient								
- Consultant/ - Specialist	Specialist	Outpatient/ Inpatient								
-	Specialist	Outpatient/ Inpatient								
<u>Resources provided in association with medical therapy</u>										
- Prednisone	Specialist	Outpatient/ Inpatient								
- Azathioprine	Specialist	Outpatient/ Inpatient								
- Mesalazine	Specialist	Outpatient/ Inpatient								
- Infliximab	Specialist	Outpatient/ Inpatient								
- Administration costs	Specialist	Outpatient/ Inpatient								
- Adalimumab	Specialist	Outpatient/ Inpatient								
-										
<u>Resources provided to deliver surgery therapy</u>										
- Consultant surgeon	Specialist	Outpatient/ Inpatient								
- Hospitalisation	Specialist	Inpatient								
- General practitioner	GP	Outpatient/ Inpatient								
-										

- MRI costs for contrast agent and nasogastric tube also need to be taken into account.

Proposed structure of economic evaluation (decision-analytic)

For patients with small bowel Crohn's the following indications are proposed:

- Evaluation of disease extent at the time of initial diagnosis of Crohn's disease (including pregnant women)
- Evaluation of exacerbation/suspected complications of known Crohn's disease (including pregnant women)
- Evaluation of suspected Crohn's disease in pregnancy
- Assessment of change to therapy in patients with Crohn's disease

For patients with fistulising perianal Crohn's disease the following indications are proposed:

- Evaluation of pelvic sepsis and fistulas associated with established or suspected Crohn's disease
- Assessment of change to therapy in patients with pelvic sepsis and fistulas from Crohn's disease

Table 5 PICO to define the research question for the evaluation of disease extent at time of initial diagnosis of Crohn's disease

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Patients with initial suspected diagnosis of Crohn's disease with symptoms of small bowel involvement but abnormal or normal terminal ileum on colonoscopy	MRI small bowel	CT SBFT	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans (for example from medical to surgery) Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Crohn's disease progression Treatment morbidity Quality of life	See table 4
What is the safety and effectiveness and cost-effectiveness of MRI small bowel in comparison to CT and SBFT for the evaluation of disease extent in patients initially diagnosed with Crohn's disease with suspected small bowel involvement?				

Figure 7 Simplified decision tree structure for the evaluation of disease extent at the time of initial diagnosis of Crohn's disease

The difference in health resources (surgery vs. medical treatment) will be determined by the proportions in each branch – which will be driven by the discordant results between the imaging tests. While the below tree does not outline paths for true/false negative and true/false positive results this will be incorporated in the cost-effectiveness model for the final assessment.

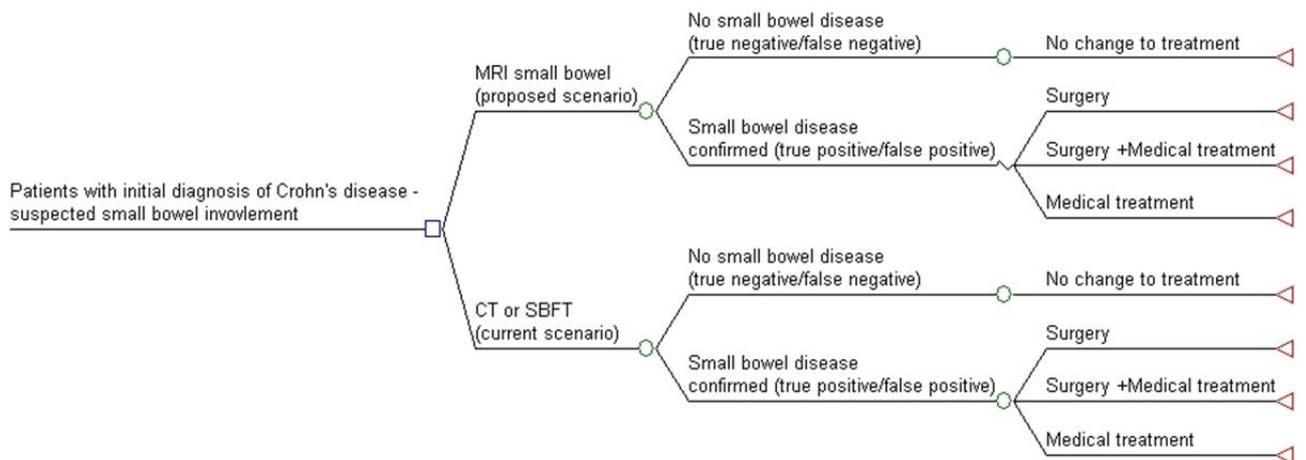


Table 6: PICO to define the research question for the evaluation of patients with exacerbation/suspected complications of known Crohn's disease

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Patients with exacerbation/suspected complications of known Crohn's disease	MRI small bowel	CT SBFT	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans (for example from medical to surgery) Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Crohn's disease progression Treatment morbidity Quality of life	See Table 4
What is the safety and effectiveness and cost-effectiveness of MRI small bowel in comparison to CT and SBFT for the evaluation of patients with exacerbation/suspected complications of known Crohn's disease?				

Figure 8 Simplified decision tree structure for the evaluation of patients with exacerbation/suspected complications of known Crohn's disease

The difference in health resources will be determined by the proportions in each branch – which will be driven by the discordant results between the imaging tests. While the below tree does not outline paths for true/false negative and true/false positive results this will be incorporated in the cost-effectiveness model for the final assessment.

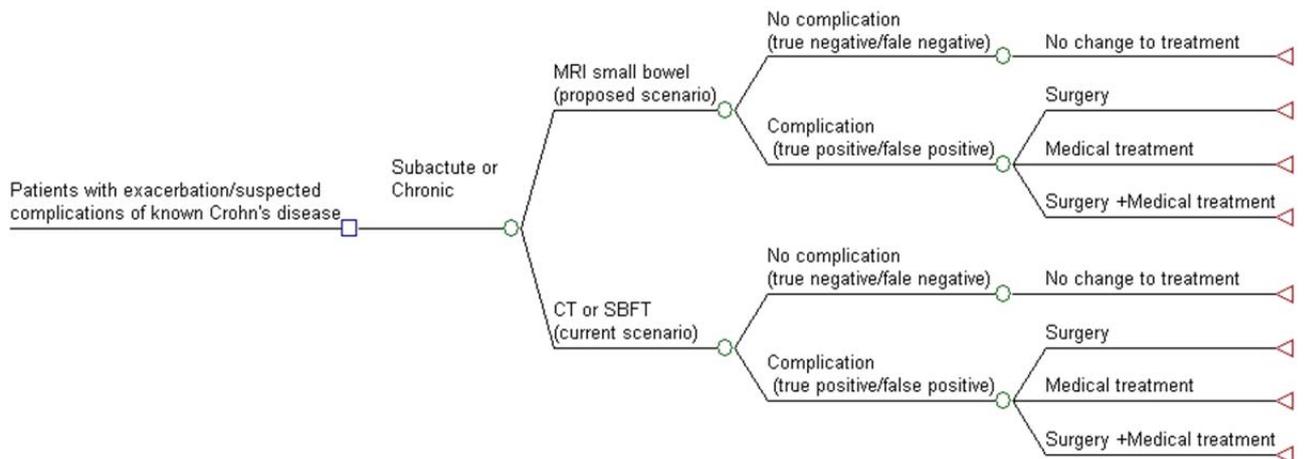


Table 7 PICO to define the research question for the evaluation of pregnant women with suspected small bowel Crohn's disease based on positive

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Pregnant women with suspected small bowel Crohn's disease based on clinical assessment	MRI small bowel	Abdominal Ultrasound (US)	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Crohn's disease progression Treatment morbidity Quality of life	See Table 4
What is the safety and effectiveness and cost-effectiveness of MRI in comparison to US in pregnant women with suspected small bowel Crohn's disease?				

Figure 9 Simplified decision tree structure for the evaluation of patients with exacerbation/suspected complications of known Crohn's disease

The difference in health resources will be determined by the proportions in each branch – which will be driven by the discordant results between the imaging tests.

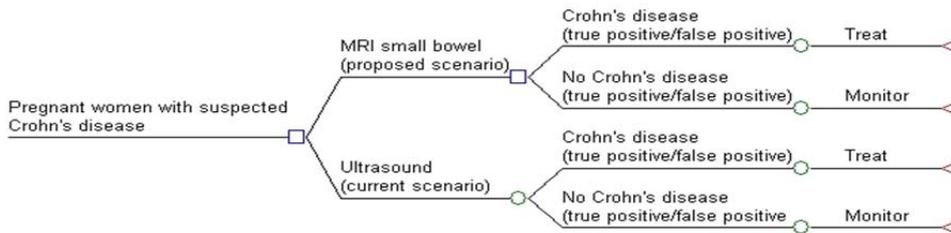


Table 8 PICO to define the research question for the assessment of change to therapy in patients with small bowel Crohn's disease

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Assessment of change to therapy in patients with small bowel Crohn's disease	MRI small bowel	CT SBFT Endoscopic assessment	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Crohn's disease progression Treatment morbidity Quality of life	See Table 4
What is the safety and effectiveness and cost-effectiveness of MRI in comparison to CT, SBFT or endoscopic assessment in the assessment of change to therapy in patients with small bowel Crohn's disease?				

Figure 10 Simplified decision tree structure for the assessment of change to therapy in patients with small bowel Crohn's disease

The difference in health resources will be determined by the proportions in each branch – which will be driven by the discordant results between the imaging tests.

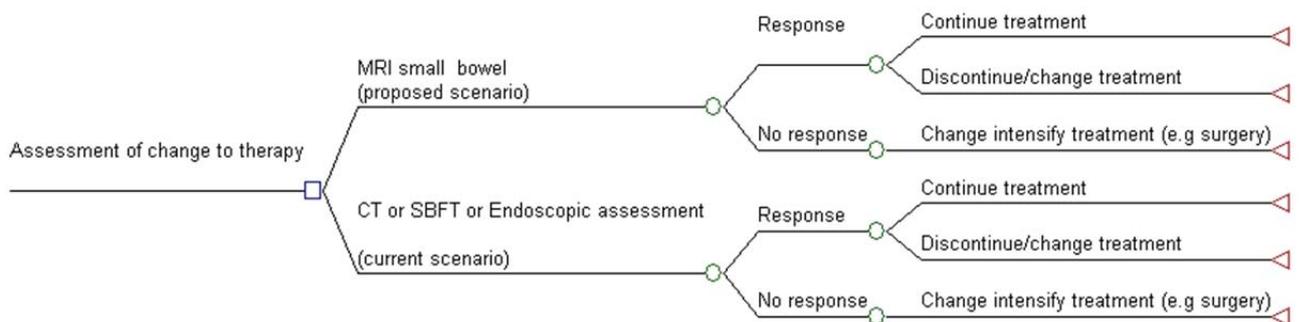


Table 9 PICO to define the research question for the evaluation of patients with pelvic sepsis and fistulas associated with established or suspected Crohn's disease

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Patients with pelvic sepsis and fistulas associated with established or suspected Crohn's disease	MRI pelvis	Surgical assessment or Endoanal ultrasound (EUS)	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Fistula Drainage Assessment Measure Treatment morbidity Quality of life	
What is the safety and effectiveness and cost-effectiveness of MRI in comparison to CT, surgical assessment and endoanal ultrasound in patients with pelvic sepsis and fistulas associated with established or suspected Crohn's disease?				

Figure 11 Simplified decision tree structure for the evaluation of patients with pelvic sepsis and fistulas associated with established or suspected Crohn's disease

The difference in health resources will be determined by the proportions in each branch – which will be driven by the discordant results between the imaging tests.

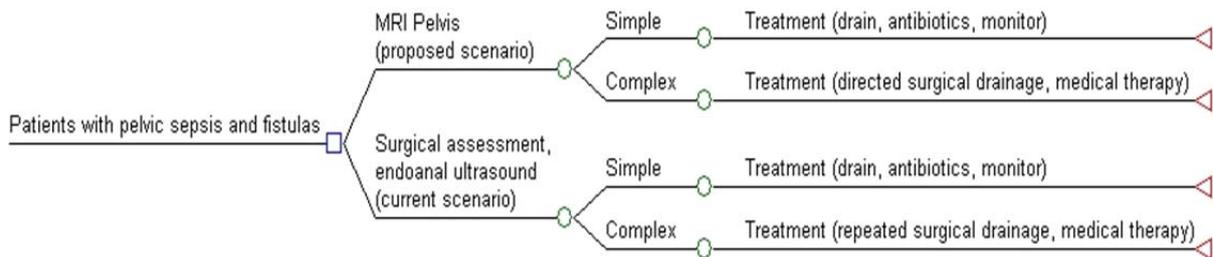
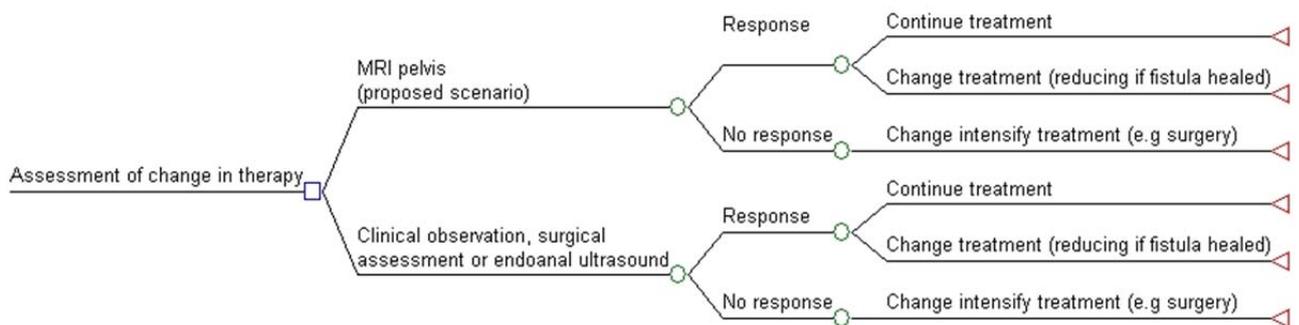


Table 10 PICO to define the research question for the assessment of change to therapy in patients with pelvic sepsis and fistulas from Crohn's disease

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Assessment of change to therapy in patients with pelvic sepsis and fistulas from Crohn's disease	MRI pelvis	Clinical observation, surgical assessment(s) Endoanal ultrasound (EUS)	Diagnostic performance Sensitivity Specificity Additional TP and FP Diagnostic yield Therapeutic impact % change in management plans Patient outcomes Impact of treatment on symptoms Activity of disease Development of complications Fistula Drainage Assessment Measure Treatment morbidity Quality of life	See Table 4
What is the safety and effectiveness and cost-effectiveness of MRI in comparison to CT, surgical assessment and endoanal ultrasound in assessment of change to therapy in patients with pelvis sepsis and fistulas from Crohn's disease?				

Figure 12 Simplified decision tree structure for the assessment of change to therapy in patients with pelvic sepsis and fistulas from Crohn's disease

The difference in health resources between the intervention and the comparator will be determined by the proportions in each branch – which will be driven by the true/false positive and true/false negative results.



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