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GUIDELINES

# European Society of Coloproctology: Guidelines for diagnosis and treatment of cryptoglandular anal fistula

Lillian Reza[1] | Kevin Gottgens[2] | Jos Kleijnen[3] | Stephanie Breukink[4] | Peter C. Ambe[5] | Felix Aigner[6] | Erman Aytac[7] | Gabriele Bislenghi[8] | Andreas Nordholm-Carstensen[9] | Hossam Elfeki[10] | Gaetano Gallo[11] | Ugo Grossi[12] | Baris Gulcu[13] | Nusrat Iqbal[14] | Rosa Jimenez-Rodriguez[15] | Sezai Leventoglu[16] | Giorgio Lisi[17] | Francesco Litta[18] | Philip Lung[19] | Monica Millan[20] | Ersin Ozturk[21] | Charlene Sackitey[22] | Mostafa Shalaby[23] | Jasper Stijns[24] | Phil Tozer[25] | David Zimmerman[26]

**Correspondence**
Lillian Reza, St Mark's The National Bowel Hospital, Central Middlesex, Acton Lane, London NW10 7NS, UK.
Email: l.reza@nhs.net

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European Society of Coloproctology

## Abstract

**Aim:** The primary aim of the European Society of Coloproctology (ESCP) Guideline Development Group (GDG) was to produce high-quality, evidence-based guidelines for the management of cryptoglandular anal fistula with input from a multidisciplinary group and using transparent, reproducible methodology.

**Methods:** Previously published methodology in guideline development by the ESCP has been replicated in this project. The guideline development process followed the requirements of the AGREE-S tool kit. Six phases can be identified in the methodology. Phase one sets the scope of the guideline, which addresses the diagnostic and therapeutic management of perianal abscess and cryptoglandular anal fistula in adult patients presenting to secondary care. The target population for this guideline are healthcare practitioners in secondary care and patients interested in understanding the clinical evidence available for various surgical interventions for anal fistula. Phase two involved formulation of the GDG. The GDG consisted of 21 coloproctologists, three research fellows, a radiologist and a methodologist. Stakeholders were chosen for their clinical and academic involvement in the management of anal fistula as well as being representative of the geographical variation among the ESCP membership. Five patients were recruited from patient groups to review the draft guideline. These patients attended two virtual meetings to discuss the evidence and suggest amendments. In phase three, patient/population, intervention, comparison and outcomes questions were formulated by the GDG. The GDG ratified 250 questions and chose 45 for inclusion in the guideline. In phase four, critical and important outcomes were confirmed for inclusion. Important outcomes were pain and wound healing. Critical outcomes were fistula healing, fistula recurrence

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Dr Zimmerman and Dr Tozer are joint last authors.

and incontinence. These outcomes formed part of the inclusion criteria for the literature search. In phase five, a literature search was performed of MEDLINE (Ovid), PubMed, Embase (Ovid) and the Cochrane Database of Systematic Reviews by eight teams of the GDG. Data were extracted and submitted for review by the GDG in a draft guideline. The most recent systematic reviews were prioritized for inclusion. Studies published since the most recent systematic review were included in our analysis by conducting a new meta-analysis using Review manager. In phase six, recommendations were formulated, using grading of recommendations, assessment, development, and evaluations, in three virtual meetings of the GDG.

**Results:** In seven sections covering the diagnostic and therapeutic management of perianal abscess and cryptoglandular anal fistula, there are 42 recommendations.

**Conclusion:** This is an up-to-date international guideline on the management of cryptoglandular anal fistula using methodology prescribed by the AGREE enterprise.

**KEYWORDS**
anal, cryptoglandular, fistula, guidelines

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# 1 | SUMMARY OF RECOMMENDATIONS

## 1.1 | Diagnosis, classification and preoperative investigations

- Immediate fistulotomy at incision and drainage of an acute perianal abscess is *not* recommended. *Low-level evidence. [Upgraded by the Guideline Development Group (GDG), expert opinion]*
- Following incision and drainage of an acute perianal abscess, routine packing *should not* be practiced. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Following incision and drainage of an acute perianal abscess, an empiric course of antibiotics is *not* recommended to prevent fistula development. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- A course of antibiotics *can be considered* following incision and drainage of an acute perianal abscess in patients with systemic sepsis and immunocompromised status. *[GDG expert opinion]*
- Clinical assessment in patients with an anal fistula *must* include history and clinical examination to assess for other causes of fistula formation. *[Upgraded by GDG, expert opinion]*
- Modifiable risk factors for poor wound healing, such as smoking, diabetes and obesity, *should* be assessed and discussed with patients with an anal fistula prior to attempting reparative surgery. *[Upgraded by GDG, expert opinion]*
- Investigations to exclude Crohn's disease *should* be performed in patients with an anal fistula if there is a clinical history in keeping with inflammatory bowel disease or examination that reveals features suspicious for Crohn's disease*. *[Upgraded by GDG, expert opinion]*
- Use of anal manometry is not currently recommended in routine clinical practice in patients with an anal fistula. *[GDG expert opinion]*
- Examination under anaesthesia (EUA) alone *should* not be used as a diagnostic tool in complex fistula as MRI and endoanal ultrasound (EAUS) are superior. *Moderate-level evidence.*
- Imaging by either MRI or EAUS *should* be utilized with a very low threshold in patients, to differentiate patients with simple from those with complex fistulas. *[Upgraded by GDG, expert opinion]*
- Preoperative MRI *should* be used for anal fistula suspected to be complex on clinical assessment, or when EAUS evaluation is not sufficient to assess complexity or is not available. *Moderate level evidence.*
- Preoperative EAUS *can be considered* as a primary tool to assess most patients affected by anal fistula, or where MRI is not readily available or there is a need to assess specific clinical features. *[GDG expert opinion]*

### 1.2 | Perioperative care

- No recommendation can be made for the use of preoperative antibiotics in patients with anal fistula. *[GDG expert opinion]*
- No recommendation can be made for the use of preoperative bowel preparation in patients with anal fistula. *[GDG expert opinion]*
- Sitz bath *can be considered* according to surgeon or patient preference postoperatively in anal fistula. *[GDG expert opinion]*

### 1.3 | Partial sphincter-preserving procedures

- Fistulotomy *should* be used in patients with intersphincteric or low transsphincteric anal fistula and normal preoperative continence, following a thorough assessment of fistula anatomy, symptomatology, involvement of sphincters, risk of incontinence and exploration of patient expectations. *Moderate-level evidence. [Upgraded by GDG, expert opinion]*
- Fistulotomy or fistulectomy and immediate sphincter reconstruction (FISR) *could* be used in highly selected patients with high transsphincteric anal fistula. *Low-level evidence.*
- Marsupialization *could* be performed following fistulotomy and fistulectomy for simple anal fistula. *Low-level evidence.*
- Cutting seton *should not* be used in the management of simple anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Cutting seton is not recommended in high anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Loose setons *can be considered* as a long-term solution in patients who have complex, recurrent fistulas and are at risk of worsening incontinence from further invasive treatment. *Very low-level evidence. [GDG expert opinion]*
- Loose setons *can be considered* as a long-term solution in patients who do not want to have further surgery. *Very low-level evidence. [GDG expert opinion]*
- Bridging setons *can be considered* in patients prior to any sphincter-preserving procedure in the presence of excessive inflammation and suppuration, or for whom poor healing is a concern. *Very low-level evidence. [GDG expert opinion]*

### 1.4 | Sphincter-preserving procedures

- Advancement flap should be used for the management of high anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- There is insufficient data to recommend either core-out or curettage as superior when used with rectal advancement flap. Either method could be selected. *[GDG expert opinion]*
- Ligation of the interspincteric fistula tract (LIFT) should be used in the primary treatment of new, high, transsphincteric anal fistulas. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- No recommendation can be made for the use of BioLIFT because of the lack of high-level evidence for efficacy and long-term outcomes. *Very low-level evidence. [GDG expert opinion]*
- Video-assisted anal fistula treatment (VAAFT) can be considered in the management of complex perianal fistula. *Very low-level evidence.*
- Laser ablation of fistula tract (LAFT) can be considered in patients with a high anal fistula. *Very low-level evidence.*
- Repeated LAFT can be considered in patients following failure from the first attempt. However, repeat procedures should be undertaken with caution, as the cumulative effect of LAFT on the sphincter complex is unknown. *Very low-level evidence. [GDG expert opinion]*
- Fistula plug can be considered in the management of anal fistula. *Low-level evidence. [Downgraded by GDG, expert opinion]*
- No recommendation can be made for the use of over-the-scope clip (OTSC) in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*
- No recommendation can be made for the use of anocutaneous flap in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*
- Fibrin glue should not be used in the management of anal fistula. *Moderate-level evidence.*
- No recommendations can be made for the use of platelet rich plasma (PRP) alone in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*
- PRP can be considered in the management of anal fistula as an add-on treatment to LIFT. *Very low-level evidence [Downgraded by GDG, expert opinion].*
- No recommendation can be made for the use of collagen matrix in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*
- No recommendation can be made for the use of suture repair of the internal opening alone in the management of anal fistula. *[GDG expert opinion]*
- No recommendation can be made for the use of rerouting in high anal fistulas because of a lack of robust data. *[GDG expert opinion]*

### 1.5 | Special considerations

- A palliative seton *can be considered* for the management of recurrent perianal sepsis. *[GDG expert opinion]*
- Palliative seton *can be* offered to patients with an anal fistula who are keen to avoid further surgical intervention and a risk of injury to the sphincter mechanism. *[GDG expert opinion]*
- A defunctioning stoma *can be considered* in patients with severe and locally uncontrollable perianal sepsis with an anal fistula. *[GDG expert opinion]*

## 2 | INTRODUCTION

Cryptoglandular anal fistula has an incidence of 1.2–2.80 per 10,000 people per year in European countries [1]. Men are twice as likely as women to present with an anal fistula, and incidence peaks between the ages of 30 and 50 years [2].

The aim of this guideline was to produce recommendations for clinical management of adult patients with perianal abscess and cryptoglandular anal fistula presenting to secondary care. This guideline does not address cryptoglandular anovaginal fistula, rectovaginal fistula, pouch-related fistula or fistula associated with Crohn's disease, radiotherapy, malignancy or anastomotic leak. The guideline has been developed by an international collaboration of coloproctologists, radiologists and patients, guided by methodologists using the AGREE-S checklist developed by the AGREE enterprise [3].

### 2.1 | What does this paper add to the literature?

This is the first European Society of Coloproctology (ESCP) cryptoglandular anal fistula guideline developed with clinicians, patients and methodologists using the AGREE-S checklist developed by the AGREE enterprise for clinical guidelines.

## 3 | METHODOLOGY

The complete methodology is available in Appendix A.

This guideline addresses the clinical management of perianal abscess and cryptoglandular anal fistula in adult patients presenting to secondary care and has been developed for use by secondary care practitioners, such as general surgeons, coloproctologists and radiologists, involved in the management of anal fistula. Patients interested in clinical evidence for the diagnosis and management of anal fistula in secondary care may find this guideline useful.

The Guideline Development Group (GDG), selected from the European Society of Coloproctology (ESCP) membership, represented geographical variation and demonstrated a breadth of clinical and academic experience of managing anal fistula. The GDG followed methodology established by the AGREE (Appendix B) enterprise and previous ESCP guidelines [4]. The oversight committee (D.Z., P.T., K.G., S.B., L.R. and J.K.) were responsible for managing the study design, the scope of the guideline and conducting GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) and ROBIS (Risk of Bias Assessment Tool) assessments of the evidence selected by the GDG members (G.L., H.E., E.A., J.S., A.N.C., F.A., M.S., M.M., G.B., F.L., S.L., R.J.R., U.G., G.G., P.C.A., E.O., B.G., P.L., C.S. and N.I.). Lillian Reza is a PhD candidate with no affiliations to industry and has no conflict of interest; she led the final literature search, data extraction and grading of the evidence. Jos Kleijnen performed the ROBIS assessment and reviewed the grading of the evidence. The GDG were supported by a patient advisory board consisting of five patients who were involved in drafting the recommendations.

The patient/population, intervention, comparison and outcomes (PICO) framework was used to perform a systematic search of MEDLINE (Ovid), Embase (Ovid), Kleijnen Systematic Reviews (KSR) evidence and the Cochrane database of systematic reviews (Search strategy available in Data S1). The final update of the search was made in October 2022. The highest level of evidence available was used when formulating the recommendations. Where available, the most recent systematic review and meta-analysis publications of randomized controlled trials (RCTs) were reviewed and updated, if necessary, with a new meta-analysis performed using Review Manager 5.4.1. Statistical analysis was conducted using a fixed effects model, with results presented as risk ratio (RR) and 95% CI. Interstudy heterogeneity was reported using the I square statistic. Forest plots were used to visualize the meta-analysis. In the absence of RCTs, systematic reviews and meta-analysis of observational studies were used if they met the inclusion criteria. Systematic reviews of observational data were not updated with new meta-analyses as the GDG took the view that new meta-analyses would not increase the strength of the recommendation because observational data is low-level evidence and prone to considerable bias. The GRADEpro web application was used to perform GRADE assessment of the evidence for each outcome. The overall strength of the recommendation was determined by the lowest certainty level for an outcome in each PICO. Use of expert opinion by the GDG to 'upgrade' or 'downgrade' evidence is explicitly stated in each recommendation. In Table 1, the wording of the recommendation follows the certainty level in the evidence. The final recommendations were produced in four consecutive virtual meetings of the GDG and had complete consensus.

### 3.1 | Wording of recommendations

In previous ESCP guidelines, the wording of the recommendations presented in Table 1 have been useful in creating a hierarchy for the management of conditions based on available evidence. However, it was very difficult to compare the evidence available for the management of anal fistula in a way in which it could be used to develop a stepwise algorithm that includes a hierarchy for treatment modalities. The main limitations were the lack of high-quality RCTs and the heterogenous nature of anal fistula. This reduces the generalizability of the data and does not lend to producing recommendations for every clinical scenario. Surgical modalities need to be offered after assessing individual patients' expectations, sphincter function and willingness to accept the risks of impairment to their continence. For any one clinical scenario, there may be more than one surgical technique that 'should' or 'could' be used and these should be discussed with the patient by a clinician who has performed a thorough assessment of patients' expectations and sphincter function.

**TABLE 1** Grade of evidence and strength of recommendation.

| Grade of evidence | Strength of recommendation |
|---|---|
| High ++++ | 'Must' or 'must not' |
| Moderate +++ | 'Should' or 'should not' |
| Low ++ | 'Could' |
| Very low + | 'Can be considered' |

## 4 | DIAGNOSIS, CLASSIFICATION AND PREOPERATIVE INVESTIGATIONS

### 4.1 | Definition and pathophysiology: Perianal abscess

An abscess usually presents as a painful, erythematous, perianal swelling which may or may not be discharging pus at presentation. Parks cryptoglandular hypothesis of anal fistula development following infection of an anal gland is widely accepted [5]. A perianal abscess is thought to develop in an obstructed intramuscular anal gland. These anal glands have extensions that pass through the internal anal sphincter (IAS) to join the crypts of Morgagni at the dentate line [6]. A chronic phase of inflammation and infection of a blocked anal gland proceeds to drain sepsis through pathways of least resistance, forming tracts that often involve the anal sphincters [7]. These tracts are lined with granulation tissue forming a bridge between the perianal skin and the anal canal.

For this section, the GDG agreed that the critical outcomes for consideration were fistula development following treatment of abscess, abscess recurrence and incontinence, and that the important outcomes were pain and wound healing.

### 4.2 | Review questions for perianal abscess

We considered the following questions for our evidence reviews:

1. What are the effects of immediate fistulotomy versus no immediate fistulotomy at incision and drainage of an acute perianal abscess?
2. What are the effects of packing versus no packing of a cavity following incision and drainage of an acute perianal abscess?
3. What are the effects of antibiotics versus no antibiotics following incision and drainage of an acute perianal abscess?

#### 4.2.1 | Immediate fistulotomy versus no immediate fistulotomy at drainage of an acute perianal abscess

A Cochrane systematic review by Malik et al. [8] included 479 patients from six RCTs in which the effect of immediate treatment of a fistula tract with fistulotomy following incision and drainage of an abscess versus drainage only was evaluated [9]. Most studies [Hebjørn 1987, Schouten 1991, Tang 1996, Ho 1997, Oliver 2003] excluded suprasphincteric, ischiorectal and extrasphincteric fistulas [8, 10–13]. Li et al. [14] included perirectal, ischiorectal and perianal fistulas. Oliver et al. included high transsphincteric and suprasphincteric fistulas but performed delayed progressive fistulotomy using setons. Tang et al. excluded high transsphincteric fistulas and randomized patients once the internal opening had been identified intra-operatively. Hebjørn et al. performed drainage of abscess in all patients and chose to randomize patients to the drainage-alone arm or to fistulotomy on the third postoperative day. Schouten et al. randomized patients to drainage alone or to drainage with fistulectomy and partial primary sphincterotomy. In the intervention arm, in patients for whom the internal opening was identified, the lower part of the internal sphincter was excised, and in patients for whom the internal opening was not identified, the internal sphincter overlying the tract was excised.

This Cochrane systematic review by Malik et al. included studies of patients with submucosal, intersphincteric, and low and high transsphincteric fistula. In four of the six studies, the internal openings of the fistula were identified in 83%–100% of patients, and the remaining two studies included only patients in whom an internal opening was visualized. Follow-up of the drainage-only arm found that 30% of patients subsequently developed a fistula while 5% of patients developed a fistula despite immediate treatment. The proposed benefit of immediate surgery was apparent in only 30% of the patients in the review while a larger proportion of patients were exposed to the risks of impaired continence posed by fistulotomy. The studies did not measure the impact on quality of life or postoperative pain following immediate treatment of a fistula at the time of abscess drainage compared with abscess drainage alone. These are important considerations for patients undergoing drainage and fistula treatment at the index operation.

*Recurrence/persistence or need for further surgery*

Pooled analysis found that immediate fistulotomy at the time of primary abscess drainage was associated with a reduction in recurrence, persistent fistula/abscess and need for further surgical intervention for a fistula (RR = 0.13, 95% CI: 0.07–0.24; Figure 1). Sensitivity analyses were carried out by removing the studies by Hebjørn et al. [13] and Li et al. [14] from the meta-analysis performed by Malik et al. [9] because of bias associated with study design and randomization; however, no significant difference in outcome was found after exclusion of these studies.

*Incontinence*

Malik et al. [9] reported no significant increase in the risk of incontinence 1 year following fistulotomy (RR = 3.06, 95% CI: 0.7–13.45), using random effects analyses, despite a clear effect on continence being seen in two of the six studies [11, 13]. However, analysis in the present study was conducted using a fixed effects model which found a significant difference in the risk of incontinence between groups (RR = 3.14, 95% CI: 1.55–6.37; Figure 2). Postoperative incontinence was reported more frequently in patients with a high transsphincteric fistula.

Heterogeneity in fistula type, intervention and outcome measures for incontinence had reduced confidence in the pooled analysis for incontinence. Oliver et al. [12] included patients with high transsphincteric fistula and, unlike the other studies, treated patients in the intervention group with a cutting seton. Ho et al. [8] found no clinical incontinence, which is in keeping with having only included patients with low transsphincteric and submucosal fistulas. Schouten et al. [11] excised a portion of the internal sphincter from patients in both arms of their study, which could have affected incontinence rates. Six percent of patients were lost to follow-up. However, sensitivity analyses did not find any difference in outcomes following exclusion of the studies by Schouten et al. and Ho et al. [8, 11]. Removal of the study by Oliver et al. [12] led to

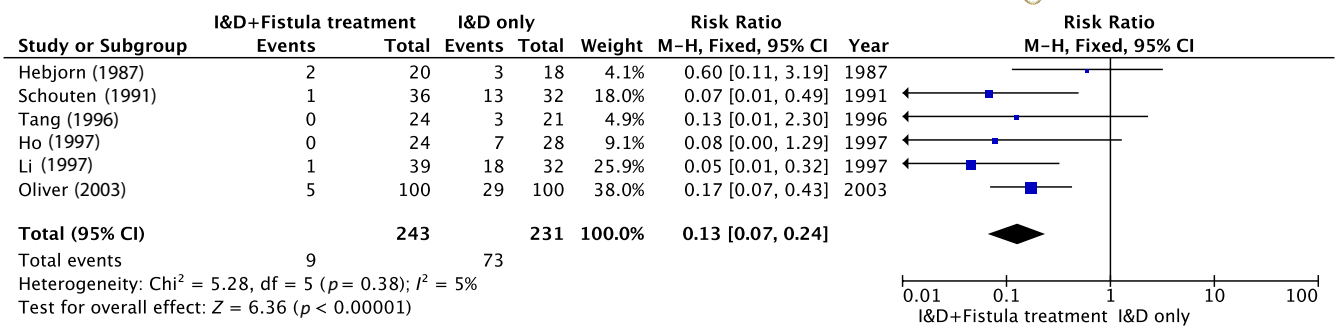


**FIGURE 1** Outcome: Recurrence/persistence or reoperation for fistula. I&D, incision and drainage.

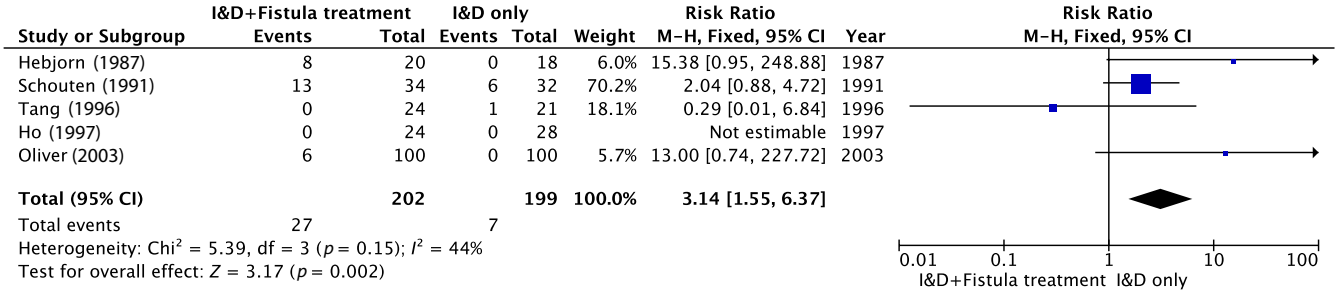


**FIGURE 2** Outcome: Incontinence. I&D, incision and drainage.

a reduced value of the $I^2$ statistic, to 25%, confidence intervals remained wide (pooled RR = 2.47, 95% CI: 0.74–8.18).

Assessment of the primary data sources in the Cochrane review [9] encourages a more cautious interpretation. First, although immediate fistula treatment leads to a reduction in 'recurrence', namely the persistence of a fistula at follow-up after abscess drainage, the rate of fistula 'recurrence' across the studies is only around one third, despite the presence of an internal opening in 83%–100% of patients. This means that at least 50% of fistulas present at the time of primary abscess drainage will resolve spontaneously.

Second, continence impairment is often poorly assessed in studies of fistula treatment, and analysis of this outcome in the Cochrane review reveals a serious risk of bias and low certainty in this critical outcome. Fixed effects analysis of available data at the 1-year follow-up demonstrated a threefold increase in incontinence rate following immediate fistula treatment compared with incision and drainage alone.

In addition, some patients were treated with a seton, and their subsequent fistula treatment (and its risks) were outwith the scope of the studies themselves, so the longer-term effect on continence and on failure of subsequent fistula repair is unknown. Some of the included studies examined only low fistulas, for which continence impairment may be less likely to occur. Finally, injudicious probing by surgeons is thought to contribute to a false passage in some patients.

On the basis that half of patients will not present with a persistent fistula and given that the risks of false passage and continence impairment only occur with probing and lay open of fistula, although the risk of 'recurrence' is lower after immediate fistulotomy, the overall benefit of this intervention is hard to define, and the increased risks associated with it are hard to justify, given the evidence presented in these RCTs. The GDG does not advocate immediate fistula treatment at primary abscess drainage.

### *Meta-analysis of RCTs*

GRADE

**Question:** What are the effects of immediate fistulotomy versus no immediate fistulotomy at incision and drainage of an acute perianal abscess?

**Setting:** Fistula found at drainage of a perianal abscess

**Bibliography:** Hebjørn 1987, Schouten 1991, Tang 1996, Ho 1997, Li 1997, Oliver 2003

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Drainage and immediate fistulotomy | Drainage only | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Recurrence/ persistence or repeat surgery | 6 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 9/243 (3.7) | 73/231 (31.6) | RR = 0.15 (0.08–0.30) | 269 fewer per 1000 (from 291 fewer to 221 fewer) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 5 | Randomized trial | Serious[a,b] | Serious[b] | Not serious | Not serious | None | 27/202 (13.4) | 7/199 (3.5) | RR = 3.14 (1.55–6.37) | 75 more per 1000 (from 19 more to 189 more) | ⨁⨁◯◯ Low | CRITICAL |

Abbreviation: RR, risk ratio.

Explanations. [a]Allocation concealment unclear. [b]Heterogeneity in fistula treatment and fistula type. Inconsistent outcomes for incontinence. Variable follow-up. Schouten 1991 performed fistulectomy as an intervention. Losses to follow-up. Oliver 2003 included high fistulas which were treated with cutting seton.

### 4.2.2 | Packing versus no packing following drainage of a perianal abscess

Two systematic reviews (Mohamedahmed et al. [15] and Smith et al. [16]) have attempted to assess the outcomes of packing (internal dressings) a cavity following drainage of a perianal abscess [15, 16]. Smith et al. included two RCTs in which the effects of packing on time to wound healing, postoperative pain and fistula development were assessed [17,18]. Mohamedahmed et al. [15] assessed packing in all cutaneous abscesses but performed subgroup analysis in 114 patients, with perianal abscess, from three RCTs [17–19]. However, because of incomplete and variable data, it was not possible to perform a meta-analysis on the time taken to achieve wound healing or on postoperative pain scores. Neither systematic review found a significant difference in reintervention rate, abscess recurrence or fistula development between packing and non-packing following drainage of a perianal abscess. Packing was associated with increased pain and economic burden [15, 16]. Pain was assessed as an outcome in all three RCTs [17–19] included in Mohamedahmed et al. [15], but unfortunately the heterogeneity in outcome reporting of pain precluded meta-analysis.

Pearce et al. [20] conducted a multicentre observational study of 141 patients and found that packing was expensive and associated with a two- to threefold increase in pain scores, during and after dressing changes. Following on from this, a multicentre RCT was published by Newton et al. [21]. The primary outcome of this RCT was postoperative pain, measured using a 100 mm visual analogue scale in the first 10 days. Secondary outcomes included perianal fistula development and abscess recurrence. The GDG assessed the meta-analysis findings presented in Figures 3 and 4, which demonstrates that packing does not prevent fistula development or abscess recurrence but is associated with significant postoperative pain. Newton et al. [21] included 433 of participants and found that packing was associated with higher pain scores than non-packing (38.2 for packing vs. 28.2 for non-packing, mean difference = 9.9, $p < 0.0001$). The GDG agreed that, when required, packing may be useful for haemostasis.

*Meta-analysis of RCTs*

GRADE

**Question:** What are the effects of packing versus no packing of an abscess cavity following drainage?

**Setting:** Abscess cavity following drainage of a perianal abscess

**Bibliography:** Tonkin 2004, Perera 2015, Islam 2016, Newton 2022

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Packing | No packing | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula development | 4 | Randomized trial | Serious[a–c] | Not serious | Not serious | Not serious | None | 43/265 (16.2) | 31/275 (11.3) | RR = 0.70 (0.45–1.06) | 34 fewer per 1000 (from 62 fewer to 7 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Abscess recurrence | 4 | Randomized trial | Serious[a–c] | Not serious | Not serious | Not serious | None | 13/265 (4.9%) | 20/284 (7.0%) | **RR = 1.50** (0.77–2.94) | 35 more per 1000 (from 16 fewer to 137 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Pain | 4 | Randomized trial | Serious[a–c] | Not serious | Not serious | Serious[b,d] | None | Median wound pain scores were described in all three studies but follow-up varied and hence data cannot be used in meta-analysis. Newton 2022 included the largest number of participants and found that packing led to higher pain scores compared with non-packing (38.2 vs. 28.2, mean difference 9.9, $p < 0.0001$). | | | | ⨁⨁◯◯ Low | IMPORTANT |

Abbreviation: RR, risk ratio.

Explanations. [a]Unclear blinding of participants and personnel. [b]Incomplete outcome data. [c]Short follow-up. [d]Imprecise estimate.

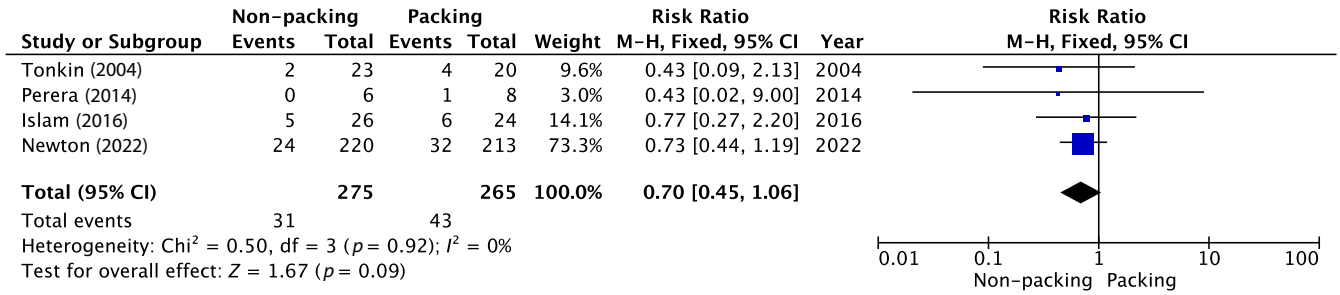


**FIGURE 3** Outcome: Fistula development.

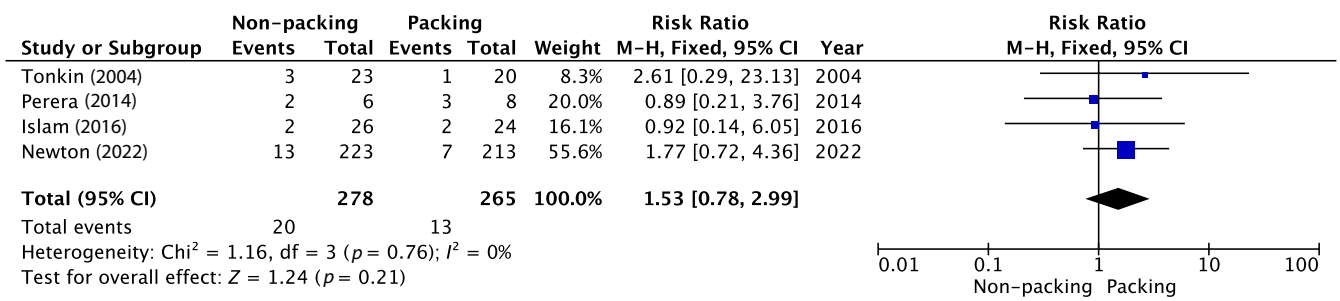


**FIGURE 4** Outcome: Abscess recurrence.

### 4.2.3 | Antibiotics versus no antibiotics following drainage of a perianal abscess

Mocanu et al. [22] conducted a systematic review and meta-analysis of patients with perianal abscess and found a reduced rate of anal fistula formation in patients who were given a course of antibiotics following abscess drainage. ROBIS assessment found that this review is at high risk of bias because of inappropriate pooling of data from observational studies and RCTs.

*Fistula development*

Mocanu et al. [22] reported that the rate of fistula development in subjects receiving postoperative antibiotics was 16% versus 24% in those not receiving postoperative antibiotics. This meta-analysis revealed a statistically significant protective effect for antibiotic treatment (OR = 0.6, 95% CI: 0.43–0.96, $p = 0.03$), but it included an observational study [Lohsiriwat 2010] [24] and two RCTs [Soezner 2011, Ghahramani 2017] [23–25].

The RCTs have been included in the meta-analysis findings presented in Figure 5 which do not show any significant effect of postoperative antibiotics on subsequent fistula development, with a high degree of interstudy heterogeneity, of $I^2 = 92\%$ (RR = 0.80, 95% CI: 0.58–1.11). It is unclear from the available evidence whether treatment with antibiotics following abscess drainage reduces fistula development.

Observational studies and clinical practice guidelines [26] advise that postoperative antibiotic cover should be considered in patients with extensive cellulitis, systemic sepsis, atypical organisms on microbiology or who are immunosuppressed as a result of chemotherapy, malignancy or HIV [27]. The GDG agreed that there is no significant evidence demonstrating that antibiotic treatment following incision and drainage of perianal abscess prevents fistula development; moreover, as injudicious use of antibiotics may contribute to antibiotic resistance, antibiotics should not be used routinely in such patients.

*Meta-analysis of RCTs*

GRADE

**Question:** Antibiotics compared with no antibiotics following drainage of perianal abscess

**Setting:** Antibiotics following drainage of a perianal abscess

**Bibliography:** Ghahramani 2017, Soezner 2011.

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Antibiotics | No antibiotics | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula development | 2 | Randomized trial | Serious[a,b] | Serious[c] | Not serious | Not serious | None | 50/230 (21.7) | 60/220 (27.3) | RR = 0.89 (0.26–3.04) | 30 fewer per 1000 (from 202 fewer to 556 more) | ⨁⨁◯◯ Low | CRITICAL |

Abbreviation: RR, risk ratio.

Explanations. [a]Risk of performance bias (Ghahramani 2017). [b]Heterogeneity in intervention - antibiotic type, duration of treatment and follow-up. [c]Inconsistent results between studies. One study was a single-blind randomized controlled trial (RCT) (Ghahramani 2017) and the other a multicentre double-blind RCT (Soezner 2011). Soezner demonstrated no significant effect on fistula development. Ghahramani 2017 did not include baseline patient characteristics.

Recommendations

- Immediate fistulotomy at incision and drainage of an acute perianal abscess is *not* recommended. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Following incision and drainage of an acute perianal abscess, routine packing *should* not be practiced. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Following incision and drainage of an acute perianal abscess, an empiric course of antibiotics is *not* recommended to prevent fistula development. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- A course of antibiotics *can be considered* following incision and drainage of an acute perianal abscess in patients with systemic sepsis and immunocompromised status. *[GDG expert opinion]*

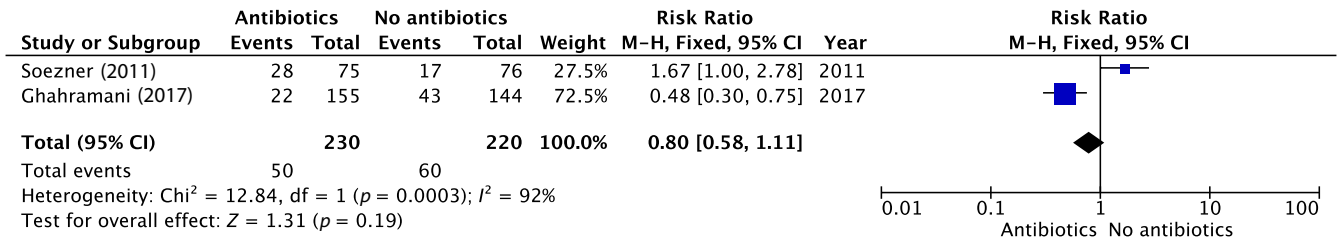


**FIGURE 5** Outcome: Fistula development.

## 4.3 | Definition and pathophysiology: Anal fistula

Anal fistulas are abnormal communications consisting of granulation tissue between the perianal skin and anal canal. These may exist at the time of abscess drainage or present later with perianal discharge or swelling. Following a perianal abscess in cryptoglandular disease, 15% of patients will present with a persistent fistula tract [28]. The following statements address the diagnosis, classification and preoperative assessment of anal fistula. High-level evidence is not available to support this section of the guideline. The statements have been developed with the highest level of evidence available and with GDG consensus opinion.

## 4.4 | Review questions for diagnosis and classification of anal fistula

We considered the following questions for our evidence reviews:

1. Which causative factors should be assessed during history and clinical examination in patients with an anal fistula?
2. Which risk factors for poor fistula healing should be assessed in the clinical history in patients with an anal fistula?
3. When do we need to conduct colonoscopy/faecal calprotectin/small bowel imaging to exclude Crohn's disease?
4. When should we use anal manometry in the management of anal fistula?

### 4.4.1 | Clinical assessment of anal fistula

The clinical history should elicit symptoms suggestive of an anal fistula. These may include discharge of pus, mucus, blood or liquid stools through an external opening at the perineum. Anal fistulas may present spontaneously but most commonly develop following a perianal abscess. The history should also exclude other causes of fistula formation, such as Crohn's disease, tuberculosis, trauma, malignancy or iatrogenic injury following local surgical intervention for other perianal conditions, as these may affect management [29]. An assessment of the patient's bowel habit and continence (including their risk of occult sphincter injury, for example following childbirth) is crucial when determining their suitability for fistulotomy, in addition to considering fistula height and anatomy.

### 4.4.2 | Patient factors that may affect fistula healing

Patient factors that may affect fistula healing are not well understood. Observational studies have attempted to demonstrate associations between specific patient factors and fistula healing for sphincter-preserving procedures. Sugrue et al. [30] conducted a systematic review and presented a narrative summary of patient, microbiological, molecular and histological factors for non-healing or persistence of an anal fistula. This review included observational studies which demonstrated that smoking was associated with poor fistula healing in rectal advancement flap [31], dermal advancement flap [32], anal fistula plug [33] and ligation of the intersphincteric fistula tract (LIFT) [34]. In one study, obesity has also been associated with poor fistula healing following LIFT [35]. ROBIS assessment found high risk of bias, and GRADE demonstrated low-quality evidence because of the observational, retrospective nature of the studies. High-level evidence is not available to demonstrate the effect of smoking, obesity and diabetes mellitus on fistula healing.

Included in Sugrue et al. [30], Zimmerman et al. [31] reported a fistula healing rate of 69%, at a median follow-up of 14 months, for transsphincteric fistulas following rectal advancement flap repair. Smoking was associated with a poor rate of fistula healing, reducing the rate of healing from 79% in non-smokers to 60% in smokers ($p < 0.037$) [31]. Ellis et al. [36] reported outcomes in 95 patients following mucosal flap repair [37] and anodermal flap repair [25] for transsphincteric and rectovaginal fistulas. The overall fistula healing rate was 67%. There was a significant association of fistula recurrence with smoking status ($p < 0.05$). The study has a heterogenous population and variable interventions [36]. Ellis et al. [33] reported a fistula healing rate of 81% in 63 patients following fistula plug treatment, with a mean follow-up of 12 months. Smoking and previous plug failure were significantly associated with poor fistula healing. The study had considerable heterogeneity as it included complex, anovaginal and Crohn's fistulas [33]. Abcarian et al. [34] reported a fistula healing rate of 74% after 41 LIFT procedures in 40 patients. The fistulas in three of eight smokers had failed to heal at a mean follow-up of 18 weeks. Van Koperen et al. (2008) and Abbas et al. (2011) are large cohort studies (of 310 and 179 patients, respectively) in which outcomes are reported following fistulotomy, rectal advancement flap and fistula plug treatment [38, 39]. There were no statistically significant associations between age, sex and smoking and poor fistula healing in these studies.

Mei et al. [40] conducted a systematic review [38] to assess factors that may affect fistula recurrence. Mei et al. included 20 studies and graded the quality of the evidence based on Egger's $p$ value, total sample size and between-study heterogeneity. High-quality observational studies showed no significant difference in fistula recurrence based on gender and smoking habit. Moderate-quality observational studies found that fistula recurrence was not associated with patient factors, such as age, alcohol use, diabetes mellitus and obesity. Several fistula-related factors were found to be associated with recurrence. High transsphincteric fistulas (RR = 4.77, 95% CI: 3.83–5.95), an unidentified internal opening (RR = 8.54, 95% CI: 5.29–13.80) and horseshoe extensions (RR = 1.92, 95% CI: 1.43–2.59) were significantly associated with recurrence. Prior anal surgery (RR = 1.52, 95% CI: 1.04–2.23), seton placement surgery (RR = 2.97, 95% CI: 1.10–8.06) and multiple fistula tracts (RR = 4.77, 95% CI: 1.46–15.51) had moderate-quality evidence to support an association with fistula recurrence. A substantial selection bias is likely to be at play in some of these analyses.

In the absence of high-level evidence, evidence for the effect of smoking on fistula healing following sphincter-preserving repair

is presented in the GRADE table below as it has been most frequently assessed in studies. The GDG discussed the available evidence and produced a statement based on expert opinion. The GDG agreed that an assessment of modifiable risk factors for poor would healing, such as smoking, diabetes and obesity, should be made and discussed with the patient prior to attempting reparative surgery.

GRADE

**Question:** Which risk factors for poor fistula healing should be assessed in the clinical history?

**Setting:** Fistula healing in smokers following sphincter-preserving repair

**Bibliography:** Zimmerman 2002, Ellis 2007, Ellis 2010, Abcarian 2012, van Koperen 2008, Abbas 2011

Recommendations

- Clinical assessment in patients with an anal fistula *must* include history and clinical examination to assess for other causes of fistula formation. *[Upgraded by the GDG, expert opinion]*
- Modifiable risk factors for poor wound healing, such as smoking, diabetes and obesity, *should* be assessed and discussed with patients with an anal fistula prior to attempting reparative surgery. *[Upgraded by the GDG, expert opinion]*
- Investigations to exclude Crohn's disease *should* be performed in patients with an anal fistula, if there is a clinical history in keeping with inflammatory bowel disease, or examination that reveals features suspicious for Crohn's disease*. *[Upgraded by the GDG, expert opinion]*

| | | Certainty assessment | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Outcome assessed** | **No. of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Impact** | **Certainty** | **Importance** |
| Fistula healing | 6 | Observational | Serious[a–c] | Not serious | Not serious | Serious[c] | | Heterogenous studies with inconsistent results | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Lack of blinding, non-RCTs. [b]Incomplete account of patients, loss to follow-up and short follow-up. [c]Small sample size, heterogenous study populations and variable interventions.

### 4.4.3 | Investigations to exclude Crohn's disease

There are no systematic reviews or RCTs regarding this subject. Hospital Episodes Statistics data from the UK indicate that 3% of patients presenting with a primary perianal abscess will be diagnosed with Crohn's disease a median of 14 months later [28]. This represents an opportunity for detection of this disease, which is often diagnosed late. The GDG agreed that an assessment of the patient's risk for Crohn's disease, based on bowel habit, family history and clinical features* (such as the presence of proctitis, other features of perianal Crohn's disease, multiple internal openings or recurrent fistulas) should trigger luminal assessment.

### 4.4.4 | Anal manometry in the management of anal fistula

The are no systematic reviews or RCTs regarding the use of anal manomtry in the assessment of anal fistula. The clinical relevance of any changes between the pre and post-treatment manometry results in observational studies are unclear as there is no agreed definition of the level of resting tone or squeeze pressure that should prompt a change in clinical course. The GDG agreed that there is a need for further research in this area, which will help determine the clinical relevance of manometry in the management of anal fistula.

- Use of anal manometry is not currently recommended in routine clinical practice in patients with an anal fistula. *[GDG expert opinion]*

**Classification and definitions in anal fistula**

Classification of anal fistula is mostly based on clinical assessment, which is prone to observer bias and variability. To assess the risk of injury from operative intervention, a clinical judgement must be made regarding the percentage of sphincter involvement. Although the use of preoperative imaging may reduce heterogeneity in classification and aid clinicians in performing an objective assessment of sphincter involvement, imaging may not be clinically indicated, routinely available or economically feasible for all centres. In retrospective case series, preoperative imaging may not be available for all patients which means fistula classification is based on subjective clinical evaluation.

Anal fistulas are classified according to their relationship with the anal sphincters. However, the definition of a high anal fistula varies enormously from one study to another and no generally agreed definition exists [37]. Examples include a tract passing above the anorectal ring [7] or through the upper third of the anal canal [41]. Fistulas have also been classified as 'simple' or 'complex' [42, 43].

'Simple' anal fistulas include subcutaneous, intersphincteric or low transsphincteric fistulas with minimal involvement of the sphincter complex. 'Complex' anal fistulas are extrasphincteric,

suprasphincteric or high transsphincteric fistulas involving greater than 30% of the external anal sphincter (EAS) and intersphincteric fistulas involving greater than 50% of the IAS [43]. Rectovaginal fistula, anterior fistula in women, recurrent fistula and fistulas with horseshoe or multiple extensions are also classified as complex fistulas [30, 44, 45]. These definitions provide clinicians and patients with insight into the disease process and possibility of cure. Simple anal fistulas involve less of the sphincter complex and may be amenable to fistulotomy, which provides the highest chance of cure, whereas complex anal fistulas may fail to heal despite multiple attempts at fistula repair with increased risk of sphincter injury. A lack of standardized definitions in the literature limits the certainty of effects in the reported outcomes. The GDG opted not to impose strict definitions for fistula complexity in the inclusion criteria for evidence as this would have excluded studies and further limited the pool of available evidence.

## 5 | IMAGING OF ANAL FISTULA

Imaging procedures used to assess perianal fistula include fistulography, MRI, endoanal ultrasound (EAUS) and CT. Imaging has been used to improve preoperative knowledge of secondary tracts, horseshoe extensions and inconspicuous collections, which may contribute to recurrence if left untreated [43, 46]. Imaging is thought to aid surgical planning by producing a precise assessment of the fistula tract and its relationship to the anal canal, pelvic floor and the sphincter complex.

The European Society of Gastrointestinal and Abdominal Radiology (ESGAR) has developed guidance on the use of imaging in anal sepsis and fistula through a modified Delphi process based on RAND/UCLA appropriateness methodology, which included an expert panel of radiologists and a systematic review of the current literature [47]. MRI and EAUS are the most common modalities used in clinical practice [43]. CT and fistulography are rarely used to assess anal fistula, and studies in which these imaging modalities are used are limited to small case series. The literature contains numerous cohort studies in which diagnostic accuracy of MRI and EAUS are described by using the level of concordance of findings on imaging with those on examination under anaesthetic (EUA) or clinical assessment. Examination under anaesthetic is usually set as the reference standard for these studies [47].

The ESGAR recommends MRI as the preferred primary modality for imaging anal fistula, based on several studies assessing clinical outcomes [48–51]. In addition, the ESGAR recommends that EAUS should be used in specific scenarios, such as for assessment of internal openings (as EAUS has better spatial resolution than MRI) or when assessing the sphincter complex, as this will help to guide surgery. CT and contrast fistulography were only recommended for use when MRI and EAUS were unavailable [47]. The ESGAR includes further recommendations on technique, interpretation, reporting and clinical use of various imaging modalities in anal fistula, which are beyond the scope of this guideline.

### 5.1 | Review questions for imaging

We considered the following question for our evidence reviews:

1. What is the effect of preoperative MRI or EAUS on outcomes in anal fistula?

### 5.2 | Effect of preoperative MRI or EAUS on outcomes in anal fistula

#### 5.2.1 | Fistula healing

Sahni et al. [51] conducted a systematic review of the literature to assess how MRI, EAUS and EUA compared in discriminating simple and complex anal fistulas. Blinded prospective studies comparing outcomes following preoperative MRI, EUA and EAUS were included. MRI was found to be more sensitive than EUA (sensitivity = 0.97, 95% CI: 0.92–1.01 for MRI vs. sensitivity = 0.75, 95% CI: 0.65–0.86 for EUA), for discriminating complex perianal fistula. Sensitivity of EAUS, of 0.92 (95% CI: 0.85–0.99), was comparable to that for MRI [51].

Li et al. [52] published a meta-analysis of 12 studies in which the diagnostic accuracy of three-dimensional (3D) EAUS was assessed. The overall diagnostic accuracy rate for all fistula classifications was 91%, with that for suprasphincteric fistula being the poorest. Endoanal ultrasound had high sensitivity (97%) and low specificity (61%) for diagnosis of the internal opening. The 12 studies included in the meta-analysis demonstrated significant heterogeneity ($I^2 = 72.1\%$). The authors concluded that EAUS alone is not sufficient to assess complex fistulas [52]. The studies in the meta-analysis did not report outcomes in patients assessed using EAUS alone.

The literature pertaining to imaging of perianal fistula mostly report diagnostic accuracy, including sensitivity and specificity, for specific features of the fistula. Rarely in the literature has the impact of imaging on clinical outcome been assessed.

This guideline has been developed with clinical outcomes as the focus of recommendations. Only two studies, Chapple et al. and Buchanan et al., could be included in the analysis below, as these have assessed the effect of imaging based on outcomes. Chapple et al. [50] compared the effect of grading fistula complexity using preoperative MRI or EUA on the ability to predict clinical outcomes at the 1-year follow-up in 52 patients. The outcome-based reference standard assessed the persistence and severity of fistula symptoms, such as pain and discharge, and the need for further surgical intervention. Outcomes were subcategorized into satisfactory and unsatisfactory outcomes. Chapple et al. reported significant correlation between MRI-assessed disease severity and clinical outcome ($p < 0.001$). The MRI and EUA results disagreed on fistula complexity in 18 of 52 patients. MRI classified 11 of the 18 discordant pairs as complex anal fistula and these patients had an unsatisfactory outcome. Chapple et al. lacked adequate power to demonstrate statistical significance of discordance between EUA- and MRI-based assessment of fistula severity [51].

Buchanan et al. [53] evaluated the accuracy of preoperative MRI, clinical examination and EAUS by comparing findings from independent, blinded fistula classifications from each modality with an outcome-based reference standard derived from postoperative follow-up (mean ± SD: 23±11 months). Agreement between the three modalities and outcomes were also assessed. The study found that MRI was superior to EAUS and digital examination for the identification of fistula tracts. MRI was accurate in 90% of patients compared with EAUS in 81% and digital examination in 61% ($p<0.001$). MRI was also significantly better at demonstrating horseshoe extension ($p<0.003$) and the location of an internal opening ($p<0.001$). Endoanal ultrasound was almost as accurate as MRI in identifying the location of an internal opening, correctly identifying the internal opening in 91% of patients compared with 97% of patients for MRI. The Kappa statistic was used to assess agreement between the outcome-derived reference standard and fistula classification using the different modalities. Classification of the primary tract was fair ($k=0.38$) using digital examination, good ($k=0.68$) using EAUS and very good ($k = 0.84$) using MRI. This linear trend favouring MRI was similar for classification of abscess and horseshoe extension [51, 53]. The GRADE assessment for Buchanan et al. shows moderate certainty of effect.

GRADE

**Question:** What is the effect of preoperative MRI or EAUS on outcomes in anal fistula?

**Setting:** Choosing imaging modality for primary fistula assessment

**Bibliography:** Buchanan 2004

| Outcome assessed | Certainty assessment | | | | | | | No. of patients[a] | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | MRI | EAUS | Relative (95% CI) | Absolute (95% CI) | | |
| Fistula healing | 1 | Observational | Not serious[b] | Not serious[c] | Not serious[d] | Not serious | | The Kappa statistic was used to assess agreement between the outcome-derived reference standard and fistula classification using the different modalities. Classification of the primary tract was fair ($k=0.38$) using digital examination, good ($k=0.68$) using EAUS and very good ($k$ 0.84) using MRI | | | | ⨁⨁⨁◯ Moderate | CRITICAL |

Abbreviation: EAUS, endoanal ultrasound.

Explanations. [a]All 104 patients had MRI, EAUS and EUA. [b]Independent clinicians were used to classify the fistula on a standardized form. Clinicians were blinded to findings obtained using other modalities. [c]Reference standard was applied to all patients regardless of test result. [d]The patient population includes those with Crohn's disease. Despite the inclusion of patients with Crohn's disease, the comparisons and outcome measure are relevant.

Compared with EAUS or EUA alone, preoperative MRI provides additional information that may affect intra-operative decisions. Preoperative MRI findings may be able to predict the need for further intervention by demonstrating occult sepsis, inconspicuous internal openings and extensions. These features could be dealt with at the primary operation if the clinician was alerted to their presence on preoperative MRI. In complex anal fistula, preoperative MRI has an important role to play.

The GDG deliberated the following recommendations, taking into consideration the availability of resources and varying clinical expertise within the regions. In many regions, EAUS is readily available to clinicians, with appropriate expertise, at the first clinical encounter and may provide sufficient information in simple anal fistula. If a fistula is suspected to be complex following clinical history, examination, EUA or EAUS, then preoperative MRI will be beneficial. MRI is more likely to identify features, described above, that are associated with treatment failure and fistula recurrence.

Recommendations

- EUA alone *should* not be used as a diagnostic tool in complex fistula as MRI and EAUS are superior. *Moderate-level evidence*.
- Imaging using either MRI or EAUS *should* be used with a very low threshold in patients, to differentiate patients with simple fistulas from those with complex fistulas. *[Upgraded by GDG, expert opinion]*
- Preoperative MRI *should* be used for anal fistula suspected, on clinical assessment, to be complex or when EAUS evaluation is either not sufficient to assess complexity or is not available. *Moderate-level evidence*.
- Preoperative EAUS *can be considered* as a primary tool to assess most patients affected by anal fistula, or when MRI is not readily available or there is a need to assess specific clinical features. *[GDG expert opinion]*

## 6 | PERIOPERATIVE CARE

### 6.1 | Review question for perioperative care of cryptoglandular fistula

We considered the following questions for our evidence reviews:

1. What is the effect on fistula healing with the use of preoperative antibiotics?

2. What is the effect on fistula healing with the use of bowel preparation preoperatively in patients with anal fistula?
3. What is the effect on fistula healing with use of postoperative sitz baths in anal fistula?

#### 6.1.1 | Preoperative antibiotics

There are no systematic reviews or RCTs on the benefit of preoperative antibiotics in the management of cryptoglandular anal fistula. Owing to the lack of data, a recommendation for preoperative antibiotics in anal fistula surgery cannot be made. Scarce data exist demonstrating any advantage of antibiotic prophylaxis before anal fistula surgery [54].

#### 6.1.2 | Preoperative bowel preparation

There are no systematic reviews or RCTs on the benefit of preoperative bowel preparation in the management of cryptogadular anal fistula. Owing to the lack of data, a recommendation cannot be made for the use of preoperative bowel preparation in anal fistula surgery. Sparse data exist on perioperative dietary modification with the aim of avoiding straining to protect reconstructing sutures [54, 55].

#### 6.1.3 | Sitz baths

There are no studies specifically assessing sitz bath in the management of anal fistula. There is one systematic review on the use of sitz bath for the management of patients with anorectal disorders. This study includes four RCTs of patients managed with sitz bath following surgical treatment of anal fissure or haemorrhoids [56]. There were conflicting findings for post defecation pain but overall sitz bath did not seem to have an effect on intensity of pain or the presence of postoperative pain. There was no difference in wound or fissure healing with the use of sitz bath. No complications were reported with sitz bath use, and patients were satisfied using sitz bath.

Recommendations

In the absence of high-quality evidence, the following statements are based on GDG expert opinion:

- No recommendation can be made for the use of preoperative antibiotics in patients with anal fistula. *[GDG expert opinion]*
- No recommendation can be made for the use of preoperative bowel preparation in patients with anal fistula. *[GDG expert opinion]*
- Sitz bath *can be considered* according to surgeon or patient preference, postoperatively in anal fistula. *[GDG expert opinion]*

## 7 | PARTIAL SPHINCTER-PRESERVING PROCEDURES

### 7.1 | Fistulotomy

#### 7.1.1 | Review questions for fistulotomy in cryptoglandular fistula treatment

1. What are the indications for fistulotomy?
2. What are the outcomes of fistulotomy compared with other sphincter-preserving procedures in simple anal fistula?

#### 7.1.2 | Indications for fistulotomy

Fistulotomy is a sphincter-cutting technique as it involves laying open the fistula from the internal opening to the external opening and dividing any sphincter muscle along the length of the tract. Continence impairment is the primary concern, making fistulotomy a viable option in a highly selected group of patients with minimal involvement of their fistula in the sphincter complex and with intact sphincter function, also described as 'simple' anal fistulas. Commonly used definitions of simple anal fistulas are intersphincteric or low transsphincteric fistulas that involve less than 30% of the EAS and do not have any features of complexity. There is considerable heterogeneity regarding which fistulas are classified as simple or complex and as high or low, and this has been demonstrated by Iqbal et al. [37] in a systematic review. Lack of standardized definition, and variable use of preoperative imaging that may aid clinicians in classifying and selecting patients for intervention, introduces heterogeneity and bias in studies pertaining to anal fistula [57].

#### 7.1.3 | Fistulotomy in simple anal fistula

Symptomatic simple anal fistulas are often managed with fistulotomy in patients with normal continence [26, 58, 59]. Fistulotomy is thought to be the gold-standard treatment for simple anal fistula as it is associated with a high rate of fistula healing without diminishing continence [60].

Retrospective observational studies of fistulotomy in low transsphincteric and intersphincteric anal fistulas have found a high rate of fistula healing (96%–98%) and acceptable postoperative continence [61]. There was no significant change in continence (defined as incontinence of flatus, mucus or soft and hard stool) following fistulotomy for intersphincteric fistula (IAS divided) and low transsphincteric fistula (IAS and EAS divided). Secondary extensions have been associated with failure [62]. Long-term follow-up data (exceeding 12 months) on continence are sparse.

Some authors recommend that in addition to an appropriate fistula, the presence of a regular bowel habit with a normal stool,

full continence and no predisposition to a loose or frequent stool (for example following ileorectal anastomosis, in irritable bowel syndrome that causes increased diarrhoea [IBS-d] or as a result of inflammatory bowel disease [IBD]) are required for fistulotomy to be consistently safe. Caution should also be exercised in women with anterior fistulas or previous obstetric injury and in patients with previous anorectal surgery. Patients must fully consent to the predicted risk to their continence in their own case.

### 7.1.4 | Fistulotomy in complex anal fistula

Numerous sphincter-preserving fistula repair procedures have been described for patients with complex anal fistula in whom long-term follow-up has demonstrated that fistulotomy poses a higher risk of incontinence [63]. Visscher et al. [63] compared the long-term outcomes of fistulotomy between complex anal fistula and simple anal fistula using the Wexner incontinence score. Fistulotomy in patients with high transsphincteric and suprasphincteric fistulas was associated with a significantly higher Wexner score (mean ± SD = 4.7 ±6.2) than in those treated for a simple anal fistula (Wexner score, mean ± SD = 1.2 ± 2.1) ($p < 0.001$) [63]. It is difficult to ascertain the implication of this finding for patients, as the level of incontinence may be minor (such as incontinence to flatus and mucus) and may not have a significant impact on their quality of life, while symptoms from a persistent fistula may have far greater impact on quality of life. Each patient needs tailored management. Clinicians must assess fistula symptomatology, preoperative incontinence, degree of involvement of anal sphincter and height of the anal fistula, and describe the individual risk of incontinence after fistulotomy and the possible rate of achieving fistula closure when offering options to patients with complex anal fistula.

### 7.1.5 | Outcomes of fistulotomy compared with sphincter-preserving procedures in simple anal fistula

There are limited high-quality RCTs on the management of simple anal fistula in which outcomes between sphincter-cutting and sphincter-preserving procedures have been compared.

Litta et al. [60] published a systematic review in which the outcomes of sphincter-cutting procedures (such as fistulotomy and fistulectomy) were compared with the outcomes of sphincter-preserving procedures (LIFT, fibrin flue, Permacol paste, over-the-scope clip [OTSC] and laser treatment) in simple anal fistulas. This review included 47 observational studies and 19 RCTs in which the management of simple anal fistula was investigated. The RCTs mostly compared outcomes of fistulectomy with primary sphincteroplasty, and fistulotomy with or without marsupialization. The observational studies were retrospective small case series in single institutions. Data on fistula healing, complications, continence, quality of life and patient satisfaction were extracted. The included studies had a weighted average follow-up of 14.7 (1–77) months.

*Fistula healing*

In simple anal fistula, the weighted average fistula healing rate for sphincter-cutting procedures was 93.7% (range: 61%–100%) and for sphincter-preserving procedures (LIFT, glue, Permacol paste, OTSC, laser treatment) was 77.7% (range: 25%–100%). The pooled outcome of sphincter-cutting procedures included data from 19 RCTs and 28 observational studies. This included data from Gottgens et al. [64], the largest retrospective series, in which outcomes of fistulotomy were reported in 537 patients, 6.7% of whom had Crohn's disease. Gottgens et al. [64] reported a primary fistula healing rate of 83.6% with a median follow-up of 38.9 months. The pooled outcome of sphincter-preserving procedures included three RCTs and 20 observational studies.

*Incontinence*

Various methods were used to record incontinence in the included studies. Minor and major incontinence was recorded in 12.7% of patients (and major incontinence alone in 6% of patients) following treatment with sphincter-cutting procedures.

Problems in the measurement of incontinence, including the grouping of patients and comparison of the mean continence scores pre- and postoperatively (rather than comparison of continence data from individual patients pre and postoperatively) may well obscure continence impairment caused by fistula operations. Careful, patient-level assessment of continence impairment has indicated a much higher risk of (usually minor) impairment to continence than was previously believed to occur, in up to one-third of patients. This criticism also holds for sphincter-preserving procedures [65].

In the studies of sphincter-preserving procedures, a weighted average incontinence rate of 0.2% was reported, and the studies only found gas incontinence [60]. Incontinence has not been adequately evaluated to permit pooled analysis and comparison with sphincter-cutting procedures. The main limitations are pooling of outcomes of various sphincter-preserving procedures and the lack of validated tools to measure incontinence.

A limited number of studies have evaluated quality of life and patient satisfaction [63, 66–71]. The postoperative onset of faecal incontinence reduced the quality of life of patients. The recurrence of fistula had a negative impact on quality of life [60]. The value of these findings is unclear as outcomes could not be pooled.

ROBIS assessment found high risk of bias in Litta et al. The studies included in Litta et al. demonstrated significant heterogeneity in fistula aetiology and in outcomes measured, such as fistula healing and incontinence. Heterogeneity has not been statistically reported. The studies are also limited by their short follow-up. Previous guidance on fistulotomy has been based on observational studies owing to the lack of RCTs [43]. The GRADE assessment of the RCTs included in this systematic review suggest a low level of certainty for the incontinence outcome. Continence impairment can have a significant impact on quality of life and therefore clinicians should perform a detailed assessment of fistula anatomy, individual risk of incontinence and patients' expectations prior to offering fistulotomy for simple anal fistula.

GRADE

**Question:** What are the outcomes of fistulotomy in simple anal fistula compared with sphincter-preserving procedures?

**Bibliography:** Ho 1998, Ho 2001, Shahbaz 2002, Lindsey 2002, Sahakitrungruang 2011, Nazeer 2012, Jain 2012, Kamal 2012, Wang 2012, Chalya 2013, Sheikh 2015, Sabre 2016, Ganesan 2017, Shahid 2017, Mittal 2018, Gupta 2018, Anan 2019, Sahai 2019, Sanad 2019

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 19 | Randomized trial | Serious[a] | Not serious | Not serious | Not serious[b] | None | Litta et al. included 47 observational studies and 19 RCTs to compare outcomes of sphincter-cutting and sphincter-sparing techniques in simple anal fistula. The observational studies were of low quality and demonstrated significant heterogeneity, which reduces the strength of the conclusions. Fistula healing rate was higher (93.7% vs. 77.7%) following sphincter-cutting procedures[a,b] | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 19 | Randomized trial | Not serious | Serious[c] | Not serious | Serious[c,d] | None | Continence impairment (major and minor) weighted average rate was 12.7% for sphincter-cutting procedures. For sphincter-sparing procedures, continence impairment weighted average rate was 0.2% | ⨁⨁◯◯ Low | CRITICAL |

Explanations. [a]Randomization unclear. Varying definitions of fistula healing and recurrence. [b]Follow-up data are limited. Most studies do not include 12-month follow-up data. [c]Continence impairment following sphincter-cutting procedures showed a wide variation in reported incontinence rates, from 0% to 45%. [d]Studies that included follow-up data of longer than 12 months reported increasing rates of incontinence. Unfortunately, most studies included had a follow-up of shorter than 12 months.

Recommendations

- Fistulotomy *should* be used in patients with intersphincteric or low transsphincteric anal fistula and normal preoperative continence, following a thorough assessment of fistula anatomy, symptomatology, involvement of sphincters, risk of incontinence and exploration of patient expectations. *Moderate-level evidence. [Upgraded by GDG, expert opinion]*

## 7.2 | Fistulotomy or fistulectomy and immediate sphincter reconstruction

### 7.2.1 | Review questions for fistulotomy or fistulectomy and immediate sphincter reconstruction in cryptoglandular fistula treatment

1. What are the indications for fistulotomy or fistulectomy and immediate sphincter reconstruction (FISR)?
2. What are the effects on fistula healing, recurrence and incontinence following FISR in cryptoglandular anal fistula?
3. What are the outcomes of FISR compared with the outcomes of sphincter-preserving procedures?
4. What are the effects of marsupialization following fistulotomy or fistulectomy?

### 7.2.2 | Indications for FISR

Fistulotomy or fistulectomy and immediate sphincter reconstruction is performed in patients with high anal fistula who would require division of a significant portion of the sphincter complex following laying open of the fistula [37]. The FISR procedure is also thought to avoid formation of a 'keyhole' deformity that may affect sphincter function [72].

### 7.2.3 | Effects on fistula healing, recurrence and incontinence following FISR

Literature review found two meta-analyses on FISR. Ratto et al. [72] included 14 studies and Iqbal et al. [40] included 21 studies in which the efficacy and safety of FISR in cryptoglandular anal fistula were assessed [37, 72]. Both reviews included RCTs and observational studies. Iqbal et al. is an updated review including recent studies on FISR. Iqbal et al. excluded studies based primarily on patients with Crohn's disease to avoid the confounding effects of biologics on fistula healing and reported outcomes of fistulotomy or fistulectomy with primary sphincter repair in 1700 patients, of whom 56% were male and 1.6% had Crohn's disease. Of the included studies, only two were RCTs and had a total of 43 patients [Perez 2006, Mascagni 2019] [73, 74].

*Fistula healing*

Iqbal et al. [37] conducted pooled analysis of fistula healing in 21 studies and reported a primary fistula healing rate of 93% (95% CI: 91%–95%, $I^2 = 51\%$, $p < 0.004$) after FISR. Ratto et al. reported a similar success rate for primary fistula healing, with a weighted average healing rate of 93.2% (range: 85.7–100), at a follow-up of 28.9 (range: 12–81) months. Ratto et al. [72] reported a weighted average time to recurrence of 8.9 (range: 1.5–20) months.

Iqbal et al. specifically assessed outcomes for 'high' anal fistula following FISR as the studies included many patients with low transsphincteric anal fistula. Of the 1700 patients included, 777 were identified as having high transsphincteric, suprasphincteric or extrasphincteric fistulas. Definitions of high anal fistula were not always reported in every study, and in some studies results were not reported according to fistula height; therefore, not all studies

were eligible for inclusion in this subanalysis. Studies in which fistula height was described, defined 'high anal fistula' variably, according to percentage involvement of the EAS, ranging between 30% and 70%. Data could only be extracted from 12 studies, including one RCT and 11 observational studies of FISR in high anal fistula. Following pooled analysis, the rate of fistula healing after FISR was reported as 89% (95% CI: 84%–94%, $I^2 = 76\%$, $p < 0.001$) in high anal fistula [37].

fistula morphology is unclear. Furthermore, there are only two RCTs included within Iqbal et al., and the quality of the other studies analysed was generally low.

GRADE

**Question:** FISR compared with sphincter-preserving procedures for adult patients with anal fistula

**Bibliography:** Mascagni 2019, Perez 2006

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 2 | Randomized trial | Serious[a–c] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | Iqbal et al. conducted a pooled analysis of 21 studies including 19 observational studies. Primary fistula healing rate was 93% (95% CI: 91%–95%) with FISR. Healing rate in high anal fistula was 89% (95% CI: 84%–94%) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 2 | Randomized trial | Serious[a–c] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | Iqbal et al. conducted a pooled analysis of 16 studies, including 14 observational studies, in which an overall rate of continence disturbance of 11% (95% CI: 6%–18%) with FISR was found. The rate of continence disturbance in high anal fistula was 16% | ⨁⨁◯◯ Low | CRITICAL |

Abbreviation: FISR, fistulotomy or fistulectomy and immediate sphincter reconstruction.

Explanations. [a]Unclear method of randomization, no allocation concealment. [b]Blinding not possible. [c]Small cohort of patients.

*Incontinence*

Iqbal et al. reported an overall rate of continence disturbance, after FISR, of 11% (95% CI: 6%–18%, $I^2 = 87\%$, $p < 0.001$) from 16 studies. The studies excluded had failed to report outcomes or to provide data that could be pooled. Pooled analysis of worsening continence was performed using the results from 10 studies in which data for preoperative and postoperative continence were included. Worsening continence was reported in 8% (95% CI: 4%–12%, $I^2 = 74\%$, $p < 0.001$) of patients. Major and minor incontinence were poorly described in the included studies. Of the 83 patients with a deterioration in continence after FISR, only 36 had outcomes for which a distinction could be made between major and minor incontinence. One (2.8%) patient was found to have major incontinence (liquid or solid stools).

Iqbal et al. also reported the rate of continence disturbance following treatment of high anal fistulas, from nine studies, to be 16% (95% CI: 7%–27%, $I^2 = 89\%$, $p < 0.001$). Seven studies included data on worsening continence from baseline in high anal fistulas. Pooled analysis found that this occurred in 8% (95% CI: 2%–16%, $I^2 = 80\%$, $p < 0.001$) of patients. The findings are limited by the lack of standardized definitions of incontinence, inability to distinguish major incontinence from minor incontinence, and the use of unvalidated scores to measure continence.

Ratto et al. did not find any significant differences in outcomes, after FISR, between the type of excision (fistulotomy or fistulectomy) or method of sphincter repair. End-to-end sphincteroplasty demonstrated higher rates of dehiscence, but overlapping repair was found to be associated with worsening continence in two studies [73, 75]. Further research is needed to clarify the optimal technique. Although most patients included in the two meta-analyses were reported to have complex fistulas, there is no standardized description of how this was defined or homogenous measurement of the height of the fistula. The ideal candidate for FISR in terms of

### 7.2.4 | Outcomes of FISR compared with sphincter-preserving procedures

Perez et al. [73] compared advancement flap and fistulotomy with sphincter reconstruction in the management of complex cryptoglandular anal fistula. Outcomes were reported in 55 patients with similar fistula complexity (high transsphincteric and suprasphincteric) from a median follow-up period of 38 (range: 24–52) months. Over-the-scope clip (OTSC) has also been compared with FISR in a RCT. This is further discussed in the section dedicated to OTSC.

*Recurrence*

The fistula recurrence rate was 7.1% in the FISR group. There was no significant difference in the fistula recurrence rate between groups. However, following sphincter reconstruction, 71% of patients experienced dehiscence and healing by secondary intention.

*Incontinence*

There was no significant difference in mean incontinence scores between groups (advancement flap and FISR). Anal manometry was recorded pre and post procedure, with no significant differences found between groups.

Perez et al. was reviewed by Jacob et al. in their Cochrane review of the management of anal fistula, published in 2010. This study was excluded because of the lack of clear randomization in their methodology [57].

GRADE

**Question:** FISR compared with advancement flap for anal fistula in adult patients

**Bibliography:** Perez 2006

| Outcome assessed | Certainty assessment: No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | No. of patients: FISR | Advancement flap | Effect: Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fistula healing | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | 26/28 (92.9) | 25/27 (92.6) | RR: 1.00 (0.86– 1.16) | 0 fewer per 1000 (from 130 fewer to 148 more) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | 9/28 (32.1) | 8/27 (29.6) | RR = 1.08 (0.49–2.40) | 24 more per 1000 (from 151 fewer to 415 more) | ⨁⨁◯◯ Low | CRITICAL |

Abbreviations: FISR, fistulotomy or fistulectomy and immediate sphincter reconstruction; RR, risk ratio.
Explanations. [a]Unclear method of randomization, no allocation concealment. [b]Blinding not possible. [c]Small cohort of patients.

There is no evidence of superiority of FISR over advancement flap in the treatment of high anal fistula. Studies in delayed and immediate sphincteroplasty following obstetric injury demonstrate worsening faecal incontinence over time [76]. It is unclear whether there are similar outcomes following FISR because relevant long-term follow-up data are not available.

The FISR procedure can result in high levels of healing in patients who have been appropriately counselled regarding the risks of continence disturbance. The ideal patient candidate and operative technique have not been clearly identified. Quality of life and patient satisfaction have not been consistently assessed in the available literature. Although existing data support the safety of the FISR procedure, there are concerns regarding the quality of the evidence for the risk of continence impairment, which limits our confidence in this technique for high anal fistula.

### 7.2.5 | Effects of marsupialization following fistulotomy or fistulectomy

Marsupialization involves suturing the edges of the wound, following fistulotomy or fistulectomy, to the perianal skin. This reduces the surface area of unepithelialized tissue and is thought to reduce the time to complete wound healing [77]. Sahebally et al. [77] conducted a meta-analysis of six RCTs, comparing outcomes in time to wound healing, pain scores at 24 h, fistula recurrence and incontinence following fistulotomy or fistulectomy, with or without marsupialization, in simple anal fistula. Simple anal fistula was defined as intersphincteric or low transsphincteric fistula of cryptoglandular origin, comprising less than 30% of the EAS.

#### *Time to complete wound healing*

Pooled analysis of four studies [Anan 2019, Chalya 2013, Ho 1998, Jain 2012] including 365 patients found that marsupialization was associated with a significantly shorter time to achieve complete wound healing compared with no marsupialization in simple anal fistula: standard mean difference was −0.87 (95% CI: −1.09 to −0.66) weeks ($I^2 = 64\%$, $p < 0.00001$; Figure 6). There was a high level of interstudy heterogeneity [78]. Sensitivity analysis was conducted using studies of fistulotomy only, as fistulectomy wounds are considerably larger than fistulotomy wounds and may impact the rates of wound healing. Sensitivity analysis found that wound healing was complete in a considerably shorter time following fistulotomy and marsupialization compared with fistulotomy and no marsupialization.

#### *Meta-analysis of RCTs*

#### *Pain scores*

Only two observational studies included an assessment of postoperative pain [Pescatori 2006, Jain 2012] [79, 80]. There was no difference in postoperative mean pain scores between groups.

#### *Recurrence*

Five studies were included in the assessment of fistula recurrence [Sahakitrungruang 2011, Anan 2019, Chalya 2013, Ho 1998, Jain 2012]. No significant difference was found in the rate of fistula recurrence between groups with or without marsupialization [79–82].

#### *Incontinence*

Six studies were included in the meta-analysis to assess disturbance of continence between groups. No significant difference was found.

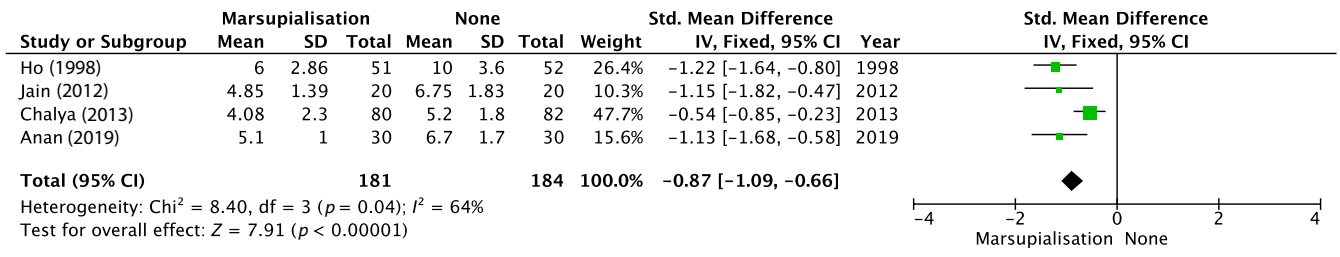


**FIGURE 6** Outcome: Time to wound healing (weeks).

GRADE

**Question:** Marsupialization compared with none for anal fistula in adult patients

**Bibliography:** Anan 2019, Chalya 2013, Ho 1998, Jain 2012, Sahakitrungruang 2011, Pescatori 2006

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Marsupialization | None | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Time to wound healing (weeks) | 4 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 181 | 184 | - | SMD = 0.87 SD lower (0.66 lower to 1.09 lower) | ⨁⨁⨁◯ Moderate | IMPORTANT |
| Incontinence | 6 | Randomized trial | Serious[a,b] | Not serious | Not serious | Serious[c] | None | 3/228 (1.3) | 9/233 (3.9) | RR = 0.38 (0.12–1.26) | 24 fewer per 1000 (from 34 fewer to 10 more) | ⨁⨁◯◯ Low | CRITICAL |
| Fistula healing | 5 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 205/206 (99.5) | 208/209 (99.5) | RR 1.00 (0.98–1.03) | 0 fewer per 1000 (from 20 fewer to 30 more) | ⨁⨁⨁◯ Moderate | CRITICAL |

Abbreviations: RR, risk ratio; SMD, standardized mean difference.

Explanations. [a]Selection bias because of lack of allocation concealment. [b]Computer-generated randomization carried out in two studies. [c]Imprecision; 95% CI crosses the line of no effect.

The studies included are heterogenous in their definitions of wound healing, use of antibiotics and analgesia. Risk of bias in methodology of the included RCTs reduces the strength of the meta-analysis.

Recommendations

- FISR *could* be used in highly selected patients with high transsphincteric anal fistula. *Low-level evidence*.
- Marsupialization *could* be performed following fistulotomy and fistulectomy for simple anal fistula. *Low-level evidence*.

## 7.3 | Cutting seton

### 7.3.1 | Review questions for cutting seton in cryptoglandular fistula treatment

1. What are the indications for a cutting seton?
2. What are the effects on fistula healing, recurrence and incontinence following the use of a cutting seton in cryptoglandular anal fistula?
3. What are the outcomes of using a cutting seton compared with the outcomes following use of other sphincter-preserving procedures?

### 7.3.2 | Indications for a cutting seton

Cutting setons have been used in patients for whom fistulotomy poses a considerable risk of incontinence because the fistula encompasses a moderate proportion of the sphincter complex. Cutting setons are thought to cause minimal sphincter disruption and allow the sphincter to heal above the seton through fibrosis as the seton is gradually moved caudad through serial tightening. There is a lack of evidence to support this theory [26, 42, 43].

### 7.3.3 | Effects on fistula healing, recurrence and incontinence with the use of a cutting seton

Literature search found several small case series [Hamalainen 1997, Ibister 2001, Chuang-wei 2008, Ege 2013, Rosen 2015, Patton 2015] with considerable heterogeneity in the use of seton material, period of follow-up, measurement of incontinence and whether partial sphincterotomy was performed prior to insertion of the cutting seton. Data from case series are difficult to pool because of differences in fistula anatomy arising from the level of the internal opening and the proportion of internal or external sphincter involvement [83–88].

There is one RCT [Ho 2001] in which the use of ayurvedic cutting seton is compared with conventional fistulotomy for low anal fistula [89].

*Fistula healing*

In Ho et al., the only RCT in which a cutting seton (46 patients) was compared with fistulotomy (54 patients) in low transsphincteric and intersphincteric fistula, there was one recurrence following fistulotomy over a 2-month follow-up (OR = 0.38, 95% CI: 0.02–9.64). The overall healing rate for a cutting seton was 100% compared with 96% for fistulotomy.

Chuang-wei et al. [87] conducted a retrospective analysis of cutting seton in 112 patients with complex anal fistula. The rate of recurrence was 0.9% with a median follow-up of 38.6 months. Several observational studies of complex cryptoglandular anal fistula with a median follow-up of at least 12 months found that recurrence rates ranged from 0.9% to 6.8% [84–88].

*Incontinence*

In Ho et al., post procedure incontinence was measured following treatment with either fistulotomy or cutting seton. Following treatment with cutting seton, five patients reported gas ($n = 2$) or liquid

stool ($n=3$) incontinence. There were three patients with gas ($n=1$) or liquid stool ($n=2$) incontinence in the fistulotomy group. There was no difference in disturbance to continence between ayurvedic cutting seton and fistulotomy (OR = 2.07, 95% CI: 0.47–9.19).

Incontinence is a critical concern associated with cutting seton. Previously, observational studies reported short-term follow-up data in which incontinence was measured with unvalidated scoring systems. In recent studies with longer follow-up periods, it is suggested that major incontinence may be a concern with time. Chuang-wei et al. included 28 patients with extrasphincteric fistula and 84 patients with either transsphincteric or suprasphincteric fistula. Disturbance to continence was reported in 24% of patients, of whom 21% had gas incontinence and 5.4% had liquid incontinence at a median follow-up of 38.6 months [87]. Several recent studies with at least a 12-month follow-up report variable rates of continence disturbance. Patton et al. [85] reported moderate incontinence in 13.5% of patients and severe incontinence in 8.5%, following placement of a cutting seton. Women had significantly higher incontinence scores than men. Hamalainen et al. [88] reported that 51% of patients had gas incontinence, 34% complained of soiling undergarments weekly and 6% reported occasional incontinence to liquid stool. Ege et al. [86] reported worsening incontinence in 5.5% of patients. Interpretation of continence outcomes from these studies is challenging as they include patients with heterogenous fistula anatomy, varying in extent of sphincter involvement and previous surgical exposure, which is likely to affect function. Outcome reporting is also heterogenous, which precludes pooled analysis of results.

*Pain*

Ho et al. reported significant differences in post procedure pain between patients treated with fistulotomy and those treated with cutting seton. Cutting seton was more painful than fistulotomy in the first 24 h ($p<0.001$) [89]. There was a trend for cutting seton continuing to be associated with higher pain scores in the first 7 days, but this did not reach statistical significance.

GRADE

**Question:** Ayurvedic cutting seton compared with fistulotomy for anal fistula in adult patients

**Bibliography:** Ho 2001

Other considerations in developing recommendations for cutting seton include the need for frequent clinical review to tighten the seton, which may affect patient satisfaction and is burdensome on resources. The impact on quality of life from pain, frequent clinical reviews and long-term continence is unclear.

An RCT of fistulotomy compared with cutting seton in patients with a fistula too high to lay open, with a major risk of continence impairment, would be unethical and hence such data will never exist. We are therefore limited to case series of cutting seton in high anal fistula. These too are lacking in number and quality. Consequently, it is difficult to advocate for the use of cutting seton in high anal fistulas.

### 7.3.4 | Outcomes of using a cutting seton compared with other sphincter-preserving procedures

There are no RCTs that compare cutting seton with other reparative treatments.

Recommendations

- Cutting seton *should not* be used in the management of simple anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- Cutting seton is not recommended in high anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*

## 8 | SPHINCTER-PRESERVING PROCEDURES

### 8.1 | Bridging/draining seton

#### 8.1.1 | Review questions for bridging seton use in cryptoglandular fistula treatment

1. What are the indications for a bridging/draining seton?
2. What are the effects on fistula healing, recurrence and incontinence of using a draining seton alone in cryptoglandular fistula?
3. What are the effects on fistula healing, recurrence and incontinence of using a bridging seton prior to sphincter-preserving procedures?

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Ayurvedic cutting seton | Fistulotomy | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 46/46 (100.0) | 52/54 (96.3) | RR = 1.04 (0.97–1.11) | 39 more per 1000 (from 29 fewer to 106 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 1 | Randomized trial | Not serious | Not serious | Not serious | Serious[a,b] | Publication bias strongly suspected[c] | 5/46 (10.9) | 4/54 (7.4) | RR = 1.47 (0.42–5.15) | 35 more per 1000 (from 43 fewer to 307 more) | ⨁⨁◯◯ Low | CRITICAL |
| Pain | 1 | Randomized trial | Not serious | Not serious | Not serious | Not serious | None | Higher pain scores reported following cutting seton in the first 24 h ($p<0.001$). | | | | ⨁⨁⨁⨁ High | IMPORTANT |

Abbreviation: RR, risk ratio.

Explanations. [a]Small sample size, the number of events is low with short follow-up, suggesting the possibility of recurrence with either intervention. [b]Sequence generation not adequately described. [c]One randomized controlled trial (RCT) with short follow-up of incontinence.

### 8.1.2 | Indications for bridging/draining seton

A bridging or draining seton is usually used to drain sepsis and to prepare, and mature, a fistula tract prior to attempting sphincter-preserving procedures. Bridging or draining setons tend to be loose and do not impinge on the sphincter complex. There are a number of different types of seton material in use and there is no high-level evidence to recommend a certain seton material. A seton should be comfortable for the patient, durable and drain sepsis adequately.

### 8.1.3 | Effects on fistula healing, recurrence and incontinence following draining seton

There are no RCTs in which the outcomes of using a draining seton in cryptoglandular fistula are compared only with the outcomes of fistula treatment using other sphincter-preserving procedures. There are RCTs of rerouting with a draining seton and mucosal advancement. These are discussed separately below (Section 9.2.1). Limited retrospective observational studies exist regarding the use of draining seton for fistulas of various complexity, including intersphincteric and high transsphincteric [90, 91]. Two studies with the largest cohort of patients and the longest follow-up periods are discussed. Daodu et al. [90] conducted a retrospective review of 76 patients with a draining seton inserted for a fistula comprising greater than 10% of the sphincter complex. The setons were removed 6 months after they had been placed. Mean follow-up was 72 (range: 14–126) months. Symptom resolution was the primary outcome. Daodu et al. [90] reported complete resolution of symptoms in 73.7% of patients and significant amelioration of symptoms in 18.4%. Persistent symptoms or recurrence were reported in 15% of patients. Kelly et al. [92] reported the outcomes of loose seton insertion in 200 patients, of whom only 38% had a fistula secondary to cryptoglandular disease. The fistulas included were of varying complexity (35% were transsphincteric, 42.5% were intersphincteric, 6% were suprasphincteric and 8% were extrasphincteric). Of this cohort, 93% of patients had a fistulotomy following seton insertion and only 7% reported a healed fistula with a seton alone [92].There is no high-level evidence to support the use of a loose seton on its own with the intention of achieving fistula closure.

GRADE

**Question:** Outcomes of loose seton for anal fistula in adult patients

**Bibliography:** Daodu 2018, Kelly 2013

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 2 | Observational | Serious[a–c] | Serious[d] | Serious[e] | Serious[d,e] | [d] | Variable rates of overall fistula healing, of 7%-73%, were reported in two studies | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Retrospective case series. [b]Heterogenous fistula anatomy. [c]Unclear follow-up. [d]Inconsistent outcomes.

### 8.1.4 | Effects on fistula healing, recurrence and incontinence using a bridging seton

Placer-Galán et al. [93] conducted a systematic review on the outcomes of using a bridging seton prior to performing the LIFT procedure. The meta-analysis included 10 observational studies with a median follow-up of 12 months. Galán et al. did not find a significant difference in the fistula recurrence rate between groups (bridging seton and no bridging seton prior to LIFT). The overall healing rate was 60% in patients with a bridging seton compared with 48.7% in patients without a bridging seton [93]. The main limitations were the retrospective nature of the data and the inclusion of patients with Crohn's perianal fistula. In the included studies, the choice of a preoperative seton was not random, suggesting that these were probably placed in patients for whom the surgeon anticipated a lower likelihood of fistula healing. The finding of either no difference or an increase in healing in these – presumably more difficult – fistulas suggests that setons are of benefit.

Giamundo et al. [94] have published their 10-year experience of laser ablation of fistula tract (LAFT) in 175 patients with cryptoglandular fistula. They found that patients who had a seton inserted for drainage as a first-stage procedure prior to LAFT had a significantly higher rate of fistula healing, of 70.4%, than the fistula-healing rate of 51.5% achieved without a bridging seton ($p < 0.03$) [94].

GRADE

**Question:** Bridging seton prior to LIFT compared with no bridging seton for anal fistula

**Bibliography:** Espin 2011, Wallin 2012, Liu 2013, Wang 2013, Sileri 2014, Hall 2014, Ye 2015, Vander Mijns 2019, Placer-Galan 2017

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 10 | Observational | Serious[a,b] | Not serious | Not serious | Not serious | | Overall healing rate of 60% with bridging seton and 48.7% without. | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Small case series, heterogenous fistula, heterogenous fistula aetiology. [b]Selection bias.

Setons are commonly used for draining a fistula tract or bridging in preparation for a fistulotomy or a sphincter-preserving procedure. There are no additional outcomes reported that are important to patients, such as patient quality of life and satisfaction with a bridging seton.

Recommendations

- Loose setons *can be considered* as a long-term solution in patients who have complex, recurrent fistula and are at risk of worsening incontinence from further invasive treatment. *Very low-level evidence. [GDG expert opinion]*
- Loose setons *can be considered* as a long-term solution in patients who are not keen to have further surgery. *Very low-level evidence. [GDG expert opinion]*
- Bridging setons *can be considered* in patients prior to any sphincter-preserving procedure in the presence of excessive inflammation and suppuration, or for whom poor healing is a concern. *Very low-level evidence. [GDG expert opinion]-*

## 8.2 | Advancement flap

### 8.2.1 | Review questions for advancement flap in cryptoglandular fistula treatment

1. What are the indications for advancement flap?
2. What are the effects on fistula healing, recurrence and incontinence following advancement flap in cryptoglandular fistula?
3. What are the outcomes of advancement flap compared with outcomes of other sphincter-preserving procedures?

### 8.2.2 | Indications for advancement flap

Rectal advancement flaps, subsequently referred to as advancement flaps, were initially described in rectovaginal fistulas and later adapted as a sphincter-preserving strategy for complex anal fistulas [95]. Different types of advancement flaps have been described based on the thickness of the flap, or level of involvement of the IAS muscle. The three main types of advancement flap are mucosal, partial or full thickness. Full-thickness flaps involve the entire IAS. The fistula tract is managed either with curettage or with core-out fistulectomy.

### 8.2.3 | Effects on fistula healing, recurrence and incontinence following advancement flap in cryptoglandular anal fistula

Literature search found a systematic review by Stellingwerf et al. [96] in which the overall rate of fistula healing following use of advancement flap in cryptoglandular anal fistula was assessed. A meta-analysis has also been conducted by Balciscueta et al. [97], of studies reporting outcomes in recurrence and incontinence following treatment with mucosal, partial and full-thickness advancement flaps. Although they did not report overall fistula healing rate as an outcome, they assessed recurrence rate based on flap thickness.

*Fistula healing*

Stellingwerf et al. [96] reported an overall rate of fistula healing, following the use of advancement flap in high cryptoglandular anal fistula, of 74.6% (95% CI: 65.6–83.7). The weighted overall success rate was based on observational studies.

Balciscueta et al. conducted a pooled analysis of 25 observational studies and one RCT (1655 patients) on the use of advancement flap in complex cryptoglandular anal fistula. They found an overall fistula recurrence rate of 21% (95% CI: 15.3%–26.8%) at a mean follow-up of 30.3 months. The fistula recurrence rate in individual studies ranged from 0% to 47.2%. There was significant heterogeneity between studies ($I^2 = 90.3\%$, $p < 0.0001$), especially in studies of mucosal-thickness advancement flaps (MTAF; $I^2 = 93.1\%$, $p < 0.001$) and partial-thickness advancement flaps (PTAF; $I^2 = 81.6\%$, $p < 0.001$). Low heterogeneity was noted between studies of full-thickness advancement flaps (FTAF; $I^2 = 28.9\%$, $p = 0.3$). Heterogeneity was reduced by conducting a sensitivity analysis according to quality of data. This led to the exclusion of outlier studies, which improved the pooled recurrence rate to 19% (95% CI: 15.5%–22.6%). Subgroup analysis found that the lowest recurrence rate occurred for FTAF (7.4%, 95% CI: 4%–10%), followed by PTAF (22.9%, 95% CI: 15.6%–30.2%) and then MTAF (26.7%, 95% CI: 13.7%–39.7%). Balciscueta et al. also found no marked difference in the recurrence rate between curettage (18.9%, 95% CI: 14.9%–23%) and core-out fistulectomy (21%, 95% CI: 14.9%–25.5%) [97].

Balciscueta et al. included one RCT in which partial-thickness and mucosal advancement flaps were compared; it was found that PTAFs resulted in a significantly higher overall healing rate than MTAFs (90% vs. 60%, $p < 0.05$) [97].

*Incontinence*

Pooled rates of incontinence were reported by Stellingwerf et al. [96]; however separate analyses of the outcomes following use of advancement flap in patients with cryptoglandular and Crohn's perianal fistula were not carried out due to the small number of studies. The weighted incontinence rate reported by Stellingwerf et al., of nine studies, was 7.8% (95% CI: 3.3%–12.4%, $I^2 = 56.7\%$).

Balciscueta et al. [97] included 12 studies in their analysis of the effect of advancement flap on incontinence. Most of the incontinence symptoms were defined as minor. Pooled analysis of the incontinence rate following MTAF was 9.3% (95% CI: 5.4%–13.1%, $I^2 = 39.4\%$; $p = 0.17$), for PTAF it was 10.2% (95% CI: 0.5%–14.6%, $I^2 = 0\%$; $p = 1.0$) and for FTAF it was 20.4% (95% CI: 14.2%–26.6%, $I^2 = 44.5\%$; $p = 0.17$). Subgroup analysis found that the incontinence rate following core-out fistulectomy was 14.3% (95% CI:

7.2%–21.3%, $I^2 = 78.83\%$; $p < 0.001$) and following curettage it was 12% (95% CI: 4%–19.2%, $I^2 = 49.5\%$; $p = 0.1$) [97]. There were no significant differences in recurrence rates and incontinence between core-out and curettage of the fistula tract. Mean follow up was 30.3 months (95% CI: 29–31.6) months.

Increasing flap thickness decreases the fistula recurrence rate. Full-thickness flaps are associated with a lower rate of fistula recurrence compared with partial-thickness or mucosal flaps, which could be attributed to maintenance of vascularity. However, increasing the flap thickness increases the risk of faecal incontinence. Mucosal flaps are associated with a lower risk of incontinence compared with partial-thickness and full-thickness flaps. It is important to note that most of the incontinence reported was minor incontinence only.

The limitations of the studies reporting incontinence include the use of various measurement tools for incontinence, heterogenous fistula complexity and the probable variation in surgical technique that is likely to affect the outcomes of flaps of different thickness.

The GRADE assessment has been performed on the only available RCT of partial-thickness and mucosal advancement flaps in cryptoglandular anal fistula. GRADE assessment of observational studies on advancement flaps would yield low to very-low certainty of evidence. The GDG developed recommendations based on the outcomes of the two systematic reviews of observational studies of advancement flaps in cryptoglandular anal fistula [Stellingwerf 2019, Balciscueta 2017] and consensus of expert opinion. The ROBIS assessment of the study by Stellingwerf et al. demonstrates low risk of bias, while the study by Balciscueta et al. was found to have high risk of bias.

Advancement flap has a high rate of fistula healing and is associated with minor incontinence which increased in severity with increases in flap thickness.

Grade

**Question:** Partial-thickness rectal advancement flap compared with mucosal advancement flap for anal fistula in adult patients

**Bibliography:** Khafagy 2010

| | Certainty assessment | | | | | | | No, of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Partial-thickness rectal advancement flap | Mucosal advancement flap | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Not serious | Not serious | Not serious | Not serious | Publication bias strongly suspected | 18/20 (90.0) | 12/20 (60.0) | RR = 1.50 (1.02–2.21) | 300 more per 1000 (from 12 more to 726 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Serious[c] | Publication bias strongly suspected | 2/20 (10.0) | 0/20 (0.0) | RR = 5.00 (0.26–98.00) | 0 fewer per 1000 (from 0 fewer to 0 fewer) | ⨁◯◯◯ Very low | CRITICAL |

Abbreviation: RR, risk ratio.

Explanations. [a]Single study, small number of cases. [b]Selection bias. [c]Wide confidence intervals.

## 8.2.4 | Outcomes of advancement flap compared with other sphincter-preserving procedures

There are two RCTs in which outcomes following treatment with LIFT are compared with outcomes following advancement flap in cryptoglandular anal fistula. This is discussed in the section pertaining to LIFT.

There is one RCT in which mucosal advancement flap is compared with fibrin glue in the treatment of cryptoglandular fistula [85]. This is discussed further under the section pertaining to fibrin glue.

Recommendations

- Advancement flap *should* be used for the management of high anal fistula. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- There are insufficient data to recommend either core-out or curettage as superior when used with rectal advancement flap. Either method *could be selected. [GDG expert opinion]*

## 8.3 | Ligation of the intersphincteric fistula tract

Ligation of the intersphincteric fistula tract can be used in simple and complex perianal fistulas. The procedure involves identifying the tract in the intersphincteric space, dividing it there and ligating it at the level of the EAS and IAS.

### 8.3.1 | Review questions for LIFT in cryptoglandular fistula treatment

1. What are the indications for LIFT?
2. What are the effects on fistula healing, recurrence and incontinence following the use of LIFT in cryptoglandular fistula?
3. What are the outcomes of LIFT compared with those of other sphincter-preserving procedures?
4. What are the indications for BioLIFT?

### 8.3.2 | Indications for LIFT

The LIFT procedure is a sphincter-preserving technique for transsphincteric anal fistula. The fistula tract should cross the intersphincteric space relatively directly and not travel within it. There should be no intersphincteric complexity (such as branching or

horseshoeing), the intersphincteric space must be appreciable and the IAS should be intact, meaning a small internal opening without IAS loss. There should also be adequate space cephalad to the fistula to dissect around the fistula completely without risk to rectal wall or vagina, making some very high tracts unsuitable for LIFT.

### 8.3.3 | Effects on fistula healing, recurrence and incontinence following the use of LIFT

*Fistula healing*

Literature search identified the most recent meta-analysis, conducted by Stellingwerf et al. [96], in which fistula healing following advancement flap and LIFT in cryptoglandular and Crohn's perianal fistula was assessed. Subgroup analysis included eight studies of LIFT in patients with cryptoglandular anal fistula with a median follow-up of 12 months. There were only two RCTs of LIFT. Pooled weighted analysis found a success rate, for LIFT, of 69.1% (95% CI: 53.9%–84.3%) [96]. There was high heterogeneity between studies, of $I^2 = 91.3\%$.

In the meta-analysis by Emile et al. [99], some recurrences of fistula following LIFT were treated with a fistulotomy or simple curettage. Although the LIFT procedure may not have healed the fistula, it succeeded in downstaging the fistula tract from transsphincteric to intersphincteric, which would qualify for a fistulotomy. This represents true secondary success. Some tracts recurred in the same morphology as the original fistula. A proportion of patients then underwent a repeat LIFT procedure with a successful outcome, implying that LIFT may still be a valid option after initial failure. Some patients in whom LIFT fails, seem to develop both recurrence of the original transsphincteric fistula and a new tract in the intersphincteric wound created during the LIFT procedure. These patients have 'upstaging' of their fistula, which is now more complex and difficult to treat.

Factors associated with persistence or recurrence following LIFT surgery include horseshoe fistulas, fistulas associated with Crohn's disease and a history of previous fistula surgery [99]. Horseshoe fistulas are challenging to treat and are a determinant factor for failure following LIFT. Recurrence following previous surgery is challenging to treat because of postoperative scarring and fibrosis obscuring the anatomical planes. This can sometimes cause associated extensions and collections that are difficult to identify. Meta-analysis demonstrated that previous surgery was a predictor for failure following LIFT repair [99].

*Incontinence*

Stellingwerf et al. [96] reported an incontinence rate of 1.6% (95% CI: 0.4%–2.8%) in patients following LIFT. This is similar to the rate reported in the meta-analysis published by Emile et al. [99], namely that incontinence of a minor grade was 1.4%. The weighted mean rate of faecal incontinence was 0.6% [99].

The authors state that it is not fully understood why a LIFT procedure would result in incontinence, given that the anal sphincters are completely spared. They have postulated that there may be a degree of compromise to the IAS during dissection in the intersphincteric space [99].

### 8.3.4 | Outcomes of LIFT compared with other sphincter-preserving procedures

A meta-analysis of surgical management of cryptoglandular anal fistula included two RCTs in which LIFT was compared with advancement flap (the control group); no statistically significant difference in fistula healing rate was found between LIFT and advancement flap [100, 101]. In the LIFT group, the fistula healing rate was 85% compared with 79.5% in the advancement flap group. There was no significant difference in postoperative incontinence. Pooled analysis of incontinence yielded an RR of 0.20 (95% CI: 0.02–1.74, $p = 0.14$, $I^2 = 0\%$). Postoperative pain scores were significantly lower in the LIFT group than in the advancement flap group [102]. Our meta-analysis is presented in Figures 7 and 8.

There were no statistically significant differences in fistula healing. The main outcome of interest was that LIFT seemed to be associated with less postoperative pain than advancement flap.

*Meta-analysis of RCTs*

GRADE

**Question:** LIFT compared with advancement flap for anal fistula

**Bibliography:** Mushaya 2012, Madbouly 2014

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | LIFT | Advancement flap | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 2 | Randomized trial | Serious[a] | Not serious | Not serious | Not serious | None[a] | 51/60 (85.0) | 39/49 (79.6) | RR = 1.04 (0.88–1.24) | 32 more per 1000 (from 96 fewer to 191 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 2 | Randomized trials | Serious[a] | Not serious | Not serious | Serious[b] | None[a] | 0/60 (0.0) | 3/49 (6.1) | RR = 0.20 (0.02–1.74) | 49 fewer per 1000 (from 60 fewer to 45 more) | ⨁⨁◯◯ Low | CRITICAL |
| Pain | 2 | Randomized trial | Not serious | Not serious | Not serious | Not serious | Publication bias strongly suspected[a] | Pain scores in the LIFT group were significantly lower than those in the AF group in the first 1–2 weeks following the procedure. | | | | ⨁⨁⨁◯ Moderate | IMPORTANT |

Abbreviations: AF, advancement flap; RR, risk ratio.

Explanations. [a]Small sample size in both studies. [b]Wide confidence intervals.

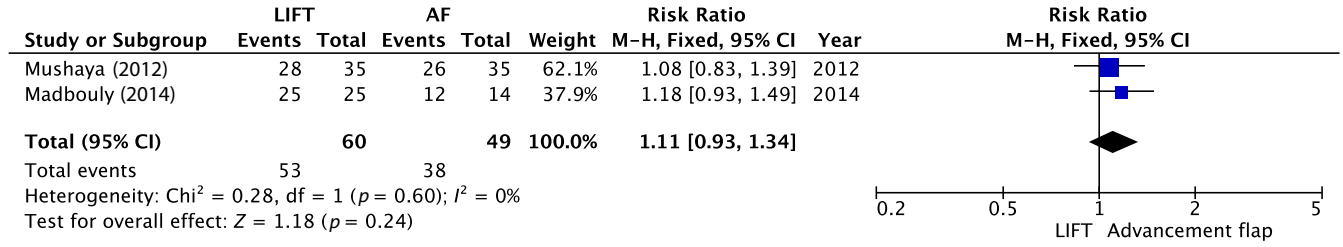


**FIGURE 7** Outcome: Fistula healing. AF, advancement flap; LIFT, ligation of the intersphincteric fistula tract.

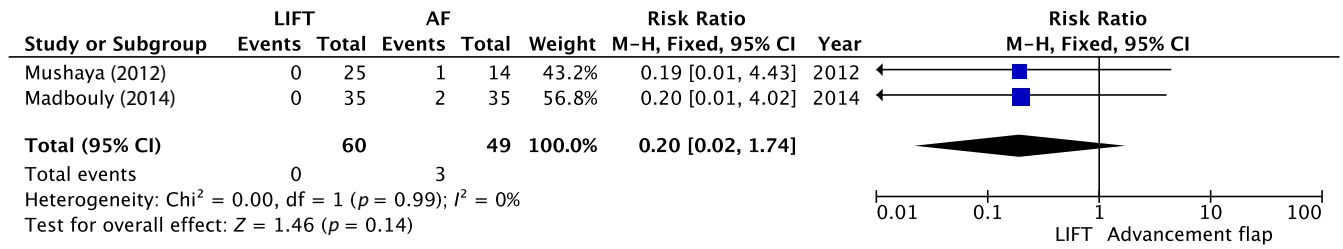


**FIGURE 8** Outcome: Incontinence. AF, advancement flap; LIFT, ligation of the intersphincteric fistula tract.

*BioLIFT*

In this modification to LIFT, a bioprosthetic mesh is placed between the ligated ends of the intersphincteric portion of the fistula tract. The use of BioLIFT has been described in two studies with a total of 44 patients; an overall success rate of 60%–68.8% was reported at a mean follow-up of around 2 years. There are no randomized data comparing LIFT with BioLIFT, so a comparison between the two procedures cannot be made.

Recommendations

- LIFT *should* be used in the primary treatment of new, high transsphincteric fistulas. *Low-level evidence. [Upgraded by GDG, expert opinion]*
- No recommendation can be made for the use of BioLIFT because of the lack of high-level evidence for efficacy and long-term outcomes. *Low-level evidence. [GDG expert opinion]*

## 8.4 | Video-assisted anal fistula treatment

### 8.4.1 | Review questions for video-assisted anal fistula treatment in cryptoglandular fistula treatment

1. What are the indications for video-assisted anal fistula treatment (VAAFT)?
2. What are the effects on fistula healing, recurrence and incontinence following the use of VAAFT in cryptoglandular fistula?
3. What are the outcomes of VAAFT compared with those of other sphincter-preserving procedures?

### 8.4.2 | Indications for VAAFT

Video-assisted anal fistula treatment is a relatively new procedure that has been used in patients with complex fistulas for diagnostic and therapeutic purposes [103]. There are observational studies of VAAFT in cryptoglandular and Crohn's anal fistula. There are no RCTs. The main advantage of VAAFT is described as the ability to identify the internal opening of the fistula using fistuloscopy and fulgurate the fistula tract under direct vision. However, the straight fistuloscope is a drawback of VAAFT in horseshoe fistula [103]. In observational studies, VAAFT has been combined with closure of the internal opening using suture, staple or a flap procedure [104]. More recently, VAAFT has been considered as more of a diagnostic and preparatory tool than a therapeutic tool, as a specific method of closure always has to be added to the procedure. It is not always clear if the proposed reported benefits of VAAFT are a result of application of the fistuloscope or the novel closure methods used in conjunction.

### 8.4.3 | Effects on fistula healing, recurrence and incontinence following the use of VAAFT

*Fistula healing*

Garg et al. [104] published a systematic review and meta-analysis of eight observational studies and found that, following VAAFT, fistula healing ranged from 52.5% to 92.5% and the net pooled rate after proportional meta-analysis using a random effects model was 76.01% (95% CI: 68.1%–83.9%, $I^2 = 82.4\%$).

Emile et al. [105] published a systematic review and meta-analysis of 11 studies, in which a fistula recurrence rate of 14.2%, at a median follow-up of 9 (range: 3.2–34) months, was reported following VAAFT. Using the random effects model, the weighted mean recurrence rate across the studies was 17.7% (95% CI: 11.8%–23.7%, $I^2 = 69.5\%$, $p < 0.001$). Redo VAAFT was applied in 58% of instances of fistula recurrence [105]. This systematic review includes one study in which 13 patients with perianal fistulas caused by Crohn's disease were treated using VAAFT.

*Incontinence*

In the systematic review by Garg et al., incontinence was reported in six studies [Selvarajan 2015, Liu 2015, Chowbey 2015, Walega 2014, Meinero 2014, Kochhar 2014]. Anal manometry was used in one study [Kochhar 2014] and an objective scoring scale, the Faecal Incontinence Severity Index (FISI), was used in one study [Walega 2014]. In the other studies, incontinence was not measured using a validated scoring system [Selvarajan 2015, Liu 2015, Chowbey 2015, Meinero 2014]. No study reported a significant deterioration in continence.

### 8.4.4 | Outcomes of VAAFT compared with other sphincter-preserving procedures

No studies have been found in which VAAFT has been compared with other sphincter-preserving procedures.

GRADE

**Question:** What are the outcomes of VAAFT in anal fistula?

**Bibliography:** Selvarajan 2015, Liu 2015, Zarin 2015, Chowbey 2015, Walega 2014, Meinero 2014, Kochhar 2014, Mendes 2014

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No.of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 8 | Observational | Serious[a–c] | Not serious | Not serious | Not serious | [a] | Pooled rate of fistula healing was 76% using proportional meta-analysis (Garg et al.).<br>Chowbey (2015) reported a 73.8% healing rate in 416 patients, Meinero (2014) reported a 70% healing rate in 203 patients and Kochhar (2014) reported an 84% healing rate in 82 patients. Selvarajan 2015 reported a healing rate of only 52% for eight patients | ⨁◯◯◯ Very low | CRITICAL |
| Incontinence | 5 | Observational | Serious[c,d] | Not serious | Not serious | Not serious | [a] | No significant change in continence was reported | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Small sample size. [b]Selection bias. [c]Heterogeneity in fistula complexity, closure of internal opening and duration of follow-up. Only two studies (Chowbey 2015, Meinero 2014) had a follow-up of at least 12 months. In four studies (Liu 2015, Chowbey 2015, Walega 2014, Zarin 2015) there were no defined inclusion and exclusion criteria. Chowbey 2015 could not identify the internal opening in 24% (100) patients. [d]Rates of incontinence were not reported in two studies. Various tools were used to measure incontinence in the other studies. Only in one study was a validated scoring system used to assess postoperative incontinence.

Efficacy of VAAFT is unclear and further studies are required to assess the long-term outcomes of VAAFT on incontinence, fistula recurrence and quality of life.

Recommendations

- VAAFT *can be considered* in the management of complex perianal fistula. *Very low-level evidence*.

## 8.5 | Laser ablation of fistula tract

### 8.5.1 | Review questions for LAFT in cryptoglandular fistula treatment

1. What are the indications for LAFT?
2. What are the effects on fistula healing, recurrence and incontinence following the use of LAFT in cryptoglandular fistula?
3. What are the outcomes of LAFT compared with those of other sphincter-preserving procedures?

### 8.5.2 | Indications for LAFT

Laser ablation of fistula tract was first described by Wilhelm et al., in 2011 [106], in 11 patients with cryptoglandular anal fistula. In all patients, the perianal abscess was initially drained, the internal opening was identified and a seton was inserted for drainage. Fistula repair was attempted at a later date, whereby the internal opening was closed using an advancement, anodermal or mucosal flap, and the remaining tract was obliterated using a radially emitting laser probe. Laser therapy is thought to destroy the fistula epithelium, promote healing and reduce the chance of persistence without significantly affecting the sphincter complex. The LAFT procedure has been used to treat fistula tracts with or without closure of the internal opening [107]. Wilhelm et al. [106] describes the use of LAFT in straight fistulas (without branching or horseshoeing) with a narrow calibre (diameter not specified).

### 8.5.3 | Effect of LAFT on fistula healing, recurrence and incontinence

Literature search found two meta-analyses published in 2019 [108] and 2020 [109]. Both included observational studies of fistula closure following laser therapy in patients with cryptoglandular and Crohn's perianal fistula.

*Fistula healing*

Elfeki et al. conducted a systematic review of seven studies including 454 patients. Three studies reported outcomes of LAFT in cryptoglandular anal fistula [Terzi 2018, Ozturk 2014, Quaresimini 2016], two studies included patients with Crohn's and cryptoglandular anal fistula [Giamundo 2015, Wilhelm 2017] and two studies did not specify fistula aetiology [Donmez 2017 and Lauretta 2018] [108]. Fistulas of variable complexity were included, comprising transsphincteric (69.1%),

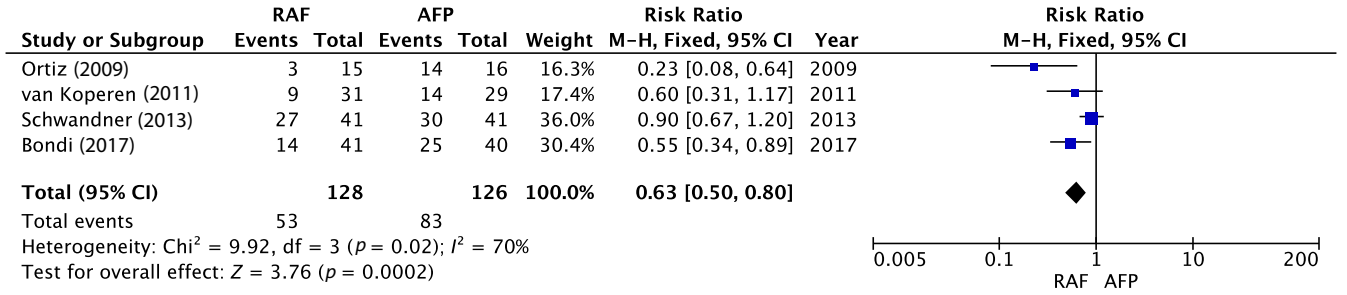


**FIGURE 9** Outcome: Fistula healing. AFP, anal fistula plug; RAF, rectal advancement flap.

intersphincteric (20.93%), suprasphincteric or extrasphincteric (8.37%) and superficial (1.54%). Recurrent fistulas (35%) were also included in the studies. The primary outcome was the primary healing rate of the fistula following the first LAFT procedure. Secondary outcomes were secondary healing rates if LAFT was reattempted. Failure was defined as non-healing or recurrence of the fistula. Pooled analysis was reported as weighted mean rates. The primary healing rate was 67.3% (95% CI: 51.3%–83.4%, $I^2$=4.2%, $p$<0.001). Repeat of the LAFT procedure in 19 patients achieved a 42% success rate. The overall healing rate was reported as 69.7% (95% CI: 54.4%–85.0%, $I^2$=93.9%, $p$<0.001). The median follow-up was 23.7 months.

Frountzas et al. conducted a similar meta-analysis but included an additional case series [Marref 2019] of 69 patients with Crohn's anal fistula (9%) and cryptoglandular anal fistula (91%). Pooled analysis found a fistula healing rate of 63% (95% CI: 50%–75%, $I^2$=87.63%).

There is significant heterogeneity between studies in terms of fistula aetiology, tract complexity, thickness of laser diode, wattage of energy applied, speed of diode retraction and treatment of the internal opening. All studies used a radial laser fibre with a wavelength of 1470 nm but with various wattage of energy applied, ranging between 10 and 12 W. The speed of fibre withdrawal also varied, but most studies withdrew the fibre at a speed of 1 mm/s. Median follow-up was longer than 12 months in all studies except for that by Marref et al., which had the shortest follow-up, of 6.3 months [110].

All studies apart from Wilhelm et al. reported the effect of LAFT without any additional treatment to the internal opening. Wilhelm et al. [106] closed the internal opening in all patients in addition to performing laser therapy of the fistula tract. Wilhelm et al. included the largest number of patients ($n$=117) and found a primary fistula healing rate of 64% for cryptoglandular anal fistula. The overall fistula healing rate (following a second treatment with LAFT) was 85.5% in cryptoglandular anal fistula, which is similar to the healing rate reported by others [Giamundo 2015, Ozturk 2014, and Donmez 2017], in which no additional steps were taken to close the internal opening [111–113].

Since publication of the systematic review by Elfeki et al., on the outcomes following LAFT, three further observational series have been published on the use of LAFT. Giamundo et al. published their 10-year experience of LAFT with closure of the internal opening in cryptoglandular anal fistula in 175 patients, and a median follow-up of 60 months. A primary healing rate of 66.8% was reported in their study, which is similar to the rates presented in the meta-analysis by Elfeki et al., of previous observational studies. Giamundo et al. found a significant difference in fistula healing rate between patients treated with a drainage seton preceding LAFT and those who were not treated with seton drainage (70.4% with draining seton vs. 51.5% with no draining seton, $p$<0.03) [94]. Wolicki et al. [114] published their series of LAFT in 83 patients with a median follow-up of 42 months; the majority of fistulas treated were of cryptoglandular aetiology and two were related to Crohn's disease. The primary healing rate was 74.7%. The overall healing rate following a second LAFT procedure did not improve substantially, at 78.3%. Isik et al. published outcomes of 100 patients following LAFT with a median follow-up of 48 months. They reported an overall success rate of 62% [115].

Elfeki et al. [108] suggested that failure may be attributed to several factors, including undetected secondary tracts and inadequate fistula tract drainage using a draining seton prior to LAFT. Ozturk et al. [112] suggested curetting the tract to enhance the sealing effect of the laser. In most studies, the fistula tracts were prepared using a draining seton to ensure adequate drainage of sepsis prior to LAFT treatment [94, 108].

*Incontinence*

Elfeki et al. found a 1% weighted mean rate of incontinence in the form of minor soiling. This outcome was not measured objectively using validated scores in any study. The radial thermal damage to the sphincter could affect incontinence. It is assumed that repeated LAFT may have a cumulative effect and cause sphincter damage [116].

### 8.5.4 | Outcomes of LAFT compared with other sphincter-preserving procedures

Laser ablation of fistula tract has not been compared in an RCT with other sphincter-preserving procedures. Recommendations will be based on observational series only.

GRADE

**Question:** What are the outcomes of LAFT in anal fistula?

**Bibliography:** Ozturk 2014, Giamundo 2015, Quaresimini 2016, Wilhelm 2017, Domes 2017, Terzi 2018, Lauretta 2018, Giamundo 2021, Isik 2020, Wolicki 2021

| Outcomes assessed | Certainty assessment | | | | | | | Impact | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|
| | No.of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | | | |
| Fistula healing | 10 | Observational | Serious[a–c] | Serious[d] | Not serious | Serious[a] | [e] | Elfeki et al. reported a 67.3% weighted mean rate of primary healing[d] | ⨁◯◯◯ Very low | CRITICAL |
| Incontinence | 6 | Observational | Serious[a,f] | Not serious | Not serious | Serious[a,f] | [a] | Wilhelm et al. reported four patients with minor soiling[f] | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Small sample size. [b]Possible selection bias. [c]Heterogeneity in fistula aetiology, complexity, tract length, secondary tracts, thickness of diode, wattage of laser energy and treatment of internal opening. Wilhelm et al. and Giamundo et al. had the largest cohort of patients with cryptoglandular anal fistula and closed the internal opening using an advancement flap whereas the other studies did not. [d]Ozturk 2014, Giamundo 2015, Quaresimini 2016, Wilhelm 2017, Donmez 2017, Isik 2020 and Wolicki 2021, reported an overall fistula healing rate of 62%–93%, whereas Terzi 2018 and Lauretta 2018 reported a healing rate of 40%. [e]High statistical heterogeneity and small sample size. [f]Validated tools were not used in all studies to measure incontinence.

Recommendations

- LAFT *can be considered* in patients with a high anal fistula. *Very low-level evidence*.
- Repeated LAFT *can be considered* in patients following primary failure from the first attempt. However, repeat procedures should be undertaken with caution as the cumulative effect of LAFT on the sphincter complex is unknown. *Very low-level evidence. [GDG expert opinion]*

## 8.6 | Fistula plug

### 8.6.1 | Review questions for fistula plug in cryptoglandular fistula

1. What are the indications for fistula plug?
2. What are the effects on fistula healing, recurrence and incontinence following the use of fistula plug in cryptoglandular fistula compared with the use of rectal advancement flap?
3. What are the outcomes of fistula plug compared with those of other sphincter-preserving procedures?

### 8.6.2 | Indications for fistula plug

Anal fistula plug was first described in 2006 as a simple, minimally invasive sphincter-preserving procedure to achieve closure of a primary fistula tract. The efficacy of fistula plug is not well established because of the variable rates of fistula healing and recurrence reported in published studies. Fistula plug has been compared with rectal advancement flap, an established procedure used in the management of complex anal fistula. Anal fistula plugs have been mostly trialled in patients with complex anal fistula. The current literature is mainly limited by small patient cohorts and short-term follow-up (less than 12 months).

### 8.6.3 | Effects on fistula healing, recurrence and incontinence following the use of fistula plug in cryptoglandular fistula compared with rectal advancement flap

*Fistula healing*

Literature search found a meta-analysis conducted by Lin et al. which included subgroup analysis of fistula healing, recurrence, and complication rates from five RCTs (in which rectal advancement flap was compared with anal fistula plug in cryptoglandular anal fistula) and from six non-RCT studies of fistula plug [117]. Analysis of the RCTs found an overall fistula healing rate of 52% in the anal fistula plug group and 65% in the rectal advancement flap group. Pooled analysis using a random effects model found no difference in fistula healing in the RCTs (OR = 0.46, 95% CI: 0.16–1.34, $p = 0.16$).

However, subgroup analysis of four RCTs [Ortiz 2009, Van Koperen 2011, Schwandner 2013, Bondi 2017] with a median follow-up of at least 12 months, excluding Ba-bai-ke-re et al., in which a shorter follow-up interval was reported, yielded different results. Patients in the rectal advancement flap group were found to have a significantly higher healing rate than patients in the anal fistula plug group (healing rate: 48% for rectal advancement flap vs. 29% for anal fistula plug; OR = 0.32, 95% CI: 0.13–0.78, $p = 0.01$). Heterogeneity was high because of inclusion of the study by Ortiz et al. [118], which stopped recruitment at 3 months because of a high recurrence rate in the anal fistula plug group. Further analysis with exclusion of this study did not change outcomes. Our meta-analysis is presented in Figure 9.

A scatter plot was produced to demonstrate healing rate at 12 months for anal fistula plug compared with rectal advancement flap. The scatter plot showed that, at a follow-up of 12 months, the healing rate following treatment with rectal advancement flap was higher than that following treatment with anal fistula plug. The healing rate was greater than 60% in the rectal advancement flap group, whereas none of the studies achieved a healing rate of 60% at 12 months in the anal fistula plug group.

*Incontinence*

Lin et al. assessed the overall rate of complications, including incontinence, bleeding and infection, following treatment with an anal fistula plug. In only one study was incontinence assessed using a validated scoring system. There was no significant difference in incontinence between groups [119]. Data on complications were available from three RCTs; a complication rate of 7.7% was reported for the anal fistula plug group and a complication rate of 6.7% was reported for the rectal advancement flap group [118–120]. There was no significant difference in complications between groups from RCTs (OR = 1.16; 95% CI: 0.34–3.94, $p = 0.81$).

*Pain*

Lin et al. found three RCTs [Bondi 2017, van Koperen 2011, Ba-bai-ke-re 2010] in which postoperative pain measured; however, different

pain-measurement methods were used among these studies which prevented meta-analysis of results. Ba-bai-ke-re et al. found that patients treated with anal fistula plug had a shorter duration of postoperative pain [120]. No significant differences in postoperative pain between groups were reported in the other two RCTs [119, 121].

*Meta-analysis of RCTs*

GRADE

**Question:** Fistula plug compared with rectal advancement flap for anal fistula

**Bibliography:** Ortiz 2009, Ba-bai-ke-re 2010, Van Koperen 2011, Schwandner 2013, Bondi 2017

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study decide | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fistula plug | Rectal advancement flap | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 4 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 53/128 (41.4) | 83/126 (65.9) | RR=0.63 (0.50–0.80) | 244 fewer per 1000 (from 329 fewer to 132 fewer) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 1 | Randomized trial | Not serious | Not serious | Not serious | Serious[d] | Publication bias strongly suspected[b] | 9/31 (29.0) | 14/29 (48.3) | RR=0.60 (0.31–1.17) | 193 fewer per 1000 (from 333 fewer to 82 more) | ⨁⨁◯◯ Low | CRITICAL |
| Pain | 3 | Randomized trial | Serious[b,c] | Serious[b,c] | Not serious | Not serious | None | There were no significant differences in pain scores between groups in most studies, except for Ba-bai-ke-re et al. who found that patients treated with anal fistula plug had a shorter period of postoperative pain | | | | ⨁⨁◯◯ Low | IMPORTANT |

Abbreviation: RR, risk ratio.

Explanations. [a]Attrition bias. [b]Small sample size. [c]Different methods used to assess postoperative pain.

## 8.6.4 | Outcomes of fistula plug compared with other sphincter-preserving procedures

Jayne et al. published results from FIAT (Fistula-In-Ano-trial) in 2021. This was a multicentre RCT in which safety, efficacy and cost-effectiveness were compared between patients treated with anal fistula plug and patients treated according to their surgeon's preference (cutting seton, fistulotomy, advancement flap, and LIFT). This trial included 304 patients randomized to fistula plug, cutting seton, fistulotomy, advancement flap and the LIFT procedure for treatment of transsphincteric anal fistula. Preoperative MRI confirmed fistula anatomy. The primary outcome was faecal incontinence quality of life (FiQoL). There were no differences in quality of life between groups. Twelve months post-treatment, fistula healing occured in 54% of patients treated with a fistula plug compared fistula healing in 55% of patients treated according to surgeon's preference. There were no differences in overall rate of fistula healing between patients treated with a fistula plug and those treated according to their surgeon's preference. Plug extrusion rate was 16%. A higher rate of unexpected pain (65%) was reported by patients treated with fistula plug than by patients treated with surgeon's preference (36%). The pooled rate of complications, including unexpected pain, septic events and bleeding, were also significantly higher in the group of patients treated with a fistula plug (35%) than in the control group (18%) (RR=1.89; 95% CI: 1.24–2.88, $p=0.002$). There was no difference in FiQoL scores between groups.

GRADE

**Question:** Fistula plug compared with fistulotomy/cutting seton/advancement flap/LIFT for anal fistula

**Bibliography:** Jayne 2021

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fistula plug | Fistulotomy/ cutting seton/ advancement flap/LIFT | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Complications | 1 | Randomized trial | Not serious | Not serious | Not serious | Serious[a,b] | None | 49/142 (34.5) | 25/137 (18.2) | RR=1.89 (1.24–2.97) | 162 more per 1000 (from 44 more to 359 more) | ⨁⨁⨁◯ Moderate | IMPORTANT |
| Pain | 1 | Randomized trial | Not serious | Not serious | Not serious | Serious[a,b] | None | 32/49 (65.3) | 9/25 (36.0) | RR=1.81 (1.03–3.18) | 292 more per 1000 (from 11 more to 785 more) | ⨁⨁⨁◯ Moderate | IMPORTANT |
| Fistula healing | 1 | Randomized trial | Serious[c] | Not serious | Not serious | Not serious | None | 66/122 (54.1) | 66/119 (55.5) | RR=0.98 (0.78–1.23) | 11 fewer per 1000 (from 122 fewer to 128 more) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 3.22 | 3.65 | - | MD 0.44 lower (1.66 lower to 0.79 higher) | ⨁⨁⨁◯ Moderate | CRITICAL |

Abbreviations: MD, mean difference; RR, risk ratio.

Explanations. [a]Wide confidence intervals. [b]Small sample size. [c]Selection bias.

The meta-analysis of RCTs of fistula plug and rectal advancement flap demonstrate that healing rates at 12 months are higher following treatment with advancement flap than with fistula plug and that there are no differences in the outcome for pain. The FIAT trial found that pain and complications were increased with the use of fistula plug compared with the surgeons' own preference of treatment without demonstrating any increase in the rate of fistula healing with the use of fistula plug. This was considered by the GDG in the development of the recommendation. Whilst advancement flap is superior in terms of healing in those patients suitable for treatment with either technique, the fistula plug remains an option for appropriate fistulas.

Recommendations

- Fistula plug can be considered in the management of anal fistula. *Low-level evidence*. [Downgraded by GDG, expert opinion]

## 8.7 | Over-the-scope clip

Over-the-scope clip involves the placement of a self-contracting nitinol clip to close the internal opening of a fistula tract. This was first described in 2012 by Prosst et al. [122], in a case series of 10 patients; since then, several retrospective and prospective studies have been reported [123–128]. The primary limitations of the existing studies are the heterogenous nature of the groups of patients included in the study and limited follow-up data. Outcomes are reported in mixed series, including for fistulas of cryptoglandular and Crohn's aetiology, fistulas of simple and complex classifications, recurrent fistulas and rectovaginal fistulas. This heterogenous nature of reporting precludes meta-analysis and identification of subpopulations in whom OTSC may be of benefit.

Proponents claim that the malleable nature of the clip means that it will flex with tissue expansion and contraction, thus maintaining a consistent pressure on the tissues, which leads to a more effective closure of the internal opening.

### 8.7.1 | Review questions for OTSC in cryptoglandular fistula treatment

1. What are the indications for OTSC?
2. What are the effects on fistula healing, recurrence and incontinence following treatment with OTSC in cryptoglandular fistula?
3. What are the outcomes of OTSC compared with the outcomes of other sphincter-preserving procedures?

### 8.7.2 | Indications for OTSC

Over-the-scope clip has been used in simple and complex fistulas. It is a sphincter-preserving strategy, developed to close the internal opening and promote fistula closure without the potential risk of incontinence. The existing literature reports better outcomes in fistula healing following OTSC as a primary procedure compared with OTSC as a secondary or salvage procedure for recurrent anal fistula [129].

### 8.7.3 | Effects on fistula healing, recurrence and incontinence following treatment with OTSC

There are only three studies in which outcomes after treatment with OTSC are reported exclusively for cryptoglandular anal fistula [123, 126, 130]. The rate of fistula healing ranged from 47% to 90% and included patients with various levels of fistula complexity. Pooled analysis showed a fistula healing rate of 67% in 61 patients. Follow-up data were limited to less than 6 months in two studies [126, 130]. Dango et al. [123] had the longest median follow-up, of 36.9 months and reported a fistula recurrence rate of 41%. In Dango et al., no significant postoperative pain was reported, as measured using a visual analogue scale. Prosst et al. [130] reported that two patients required elective removal of the OTSC because of pain and clip migration. Incontinence either was not reported [129] or was not measured [126, 129] in the studies.

GRADE

**Question:** Outcomes of treatment with an OTSC in adults with an anal fistula

**Bibliography:** Prosst 2014, Dango 2017, Grossberg 2020

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 3 | Observational | Serious[a] | Serious[a] | Serious | Serious[b] | | Prosst et al. (2014) reported 90% fistula healing in 20 patients at 6 months of follow-up | ⨁◯◯◯ Very low | CRITICAL |
| Pain | 2 | Observational | Serious[a] | Serious[c] | Serious[d] | Serious | | Dango et al. measured pain using VAS and noted complications such as necrosis, ulceration and foreign-body reaction. There were no significant pain or other complications reported in their series. Prosst et al. did not measure pain using an objective scoring system | ⨁◯◯◯ Very low | CRITICAL |

Abbreviation: VAS, visual analogue scale.

Explanations. [a]Heterogeneous fistula anatomy. [b]No objective measurement tool/assessment protocol of fistula healing. [c]Short-term follow-up. [d]Pain assessment score not used to measure pain.

### 8.7.4 | Outcomes of OTSC compared with other sphincter-preserving procedures

Over-the-scope clip has been compared with FISR in an RCT for patients with low transsphincteric cryptoglandular anal fistula [74]. Patients were randomized in a 1:1 consecutive process to either OTSC ($n=15$) or FISR ($n=15$). All patients completed a 3-year follow-up. Primary outcomes were fistula healing at 12 months and recurrence at 3 years. Incontinence was measured using the Wexner score at 60 days. The fistula healing rate was 93% in the OTSC group and 100% in the FISR group. There were no significant differences in the Wexner scores at the 2-month follow-up. One patient required early clip removal because of pain, and one patient presented with recurrence of symptoms at 30 days post-surgery.

GRADE

**Question:** OTSC compared with FISR for anal fistula

**Bibliography:** Mascagni 2018

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | OTSC | FISR | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | 14/15 (93.3) | 15/15 (100.0) | RR=0.94 (0.78–1.12) | 6 fewer per 100 (from 22 fewer to 12 more) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | Publication bias strongly suspected[c] | After 1 month, the Wexner score was 0 for the OTSC group and 3 for the FIPS group. At the 2-month follow-up there were scores suggesting no postoperative incontinence in either group | | | | ⨁⨁◯◯Low | |

Abbreviations: FISR, fistulotomy or fistulectomy and immediate sphincter reconstruction; RR, risk ratio.

Explanations. [a]Unclear randomization yields concern for allocation concealment. [b]Small sample size. [c]One study with a small sample size.

Variable rates of fistula healing following treatment with OTSC have been reported in observational studies. A high rate of fistula recurrence has been suggested in studies with a follow-up of longer than 12 months. The only RCT of OTSC included a small study sample with unclear methodology and a risk of bias but reported a high success rate in both OTSC and FISR arms.

Recommendations

- No recommendation can be made for the use of OTSC in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*

## 8.8 | Anocutaneous flap

### 8.8.1 | Review questions for anocutaneous flap in cryptoglandular fistula treatment

1. What are the indications for anocutaneous flap?
2. What are the effects on fistula healing, recurrence and incontinence following treatment with anocutaenous flap?
3. What are the outcomes of anocutaneous flap compared with the outcomes of other sphincter-preserving proced-ures?

### 8.8.2 | Indications for anocutaneous flap

Anocutaneous flaps have been used in simple and complex fistulas. There is one RCT in which outcomes in transsphincteric anal fistula following treatment with anocuatenous flap (also known as dermal island flap) have been compared with outcomes following conventional therapy, such as fistulotomy or seton insertion. This study recruited only 10 patients to each arm, and all patients had preoperative EAUS to delineate the anatomy of their fistula [95].

### 8.8.3 | Effects on fistula healing, recurrence and incontinence following anocutaenous flap

Ho et al. [95] reported no recurrence of fistula in patients in either arm (anocutaneous flap or fistulotomy/seton) of their RCT at a mean follow-up of 16 months. Faecal incontinence was measured at 16 weeks and no difference was found between the groups.

### 8.8.4 | Outcomes of anocutaneous flap compared with other sphincter-preserving procedures

There are no RCTs in which outcomes for anal fistula following treatment with anocutaneous flap are compared with outcomes following treatment with other sphincter-preserving procedures.

GRADE

**Question:** Anocutaneous flap (Dermal island flap) compared with fistulotomy/seton insertion for anal fistula in adult patients

**Bibliography:** Ho 2005

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Dermal island flap | Fistulotomy/ seton insertion | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula recurrence | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Serious[b] | | 0/10 (0.0) | 0/10 (0.0) | Not estimable | | ⨁◯◯◯ Very low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a–c] | Not serious | Not serious | Serious[b,d] | | 0/10 (0.0) | 0/10 (0.0) | Not estimable | | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]No mention of sequence generation or allocation concealment. [b]Small sample size. [c]Control group consisted of patients who had fistulotomy or loose draining seton. [d]Short follow-up of 16 weeks.

Evidence is limited in anocutaneous flap. Data on continence status are mostly missing in case series. One RCT is limited by small numbers, a very short follow-up of outcomes in continence and lacks other outcomes, such as pain and quality of life. The RCT was not adequately powered to produce any useful results for recommendations.

Recommendations

- No recommendation can be made for the use of anocutaneous flap in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*

## 8.9 | Fibrin glue

### 8.9.1 | Review questions for fibrin glue in cryptoglandular fistula treatment

1. What are the indications for fibrin glue?
2. What are the effects on fistula healing, recurrence and incontinence following treatment with fibrin glue?

*Fibrin glue versus advancement flap*

Van der Hagen et al. randomized patients with complex cryptoglandular anal fistula to treatment with either mucosal advancement flap or fibrin glue. The overall fistula healing rate was 40% for treatment with fibrin glue compared with 80% for mucosal advancement flap. Fistula recurrence was higher for patients in the fibrin glue group (60%) than for patients in the mucosal advancement flap group (20%) ($p < 0.03$) at a median 12-month follow-up. There was no difference between groups in median Vaizey incontinence scores after treatment and at 12 months.

GRADE

**Question:** Fibrin glue compared with mucosal advancement flap for anal fistula in adult patients

**Bibliography:** Van der Hagen 2011

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fibrin glue | MAF | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a–c] | Not serious | Not serious | Serious[a,c] | None | 6/15 (40.0) | 12/15 (80.0) | RR = 0.50 (0.26–0.98) | 400 fewer per 1000 (from 592 fewer to 16 fewer) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | Publication bias strongly suspected[a] | The Vaizey incontinence score was used to measure postoperative incontinence. There were no differences between groups in incontinence scores postoperatively. Continence disturbance was not reported in either arm | | | | ⨁⨁◯◯ Low | CRITICAL |

Abbreviations: MAF, mucosal advancement flap; RR, risk ratio.

Explanations. [a]Small number of patients. [b]Lack of allocation concealment. [c]Wide confidence interval.

### 8.9.2 | Indications for fibrin glue

Fibrin glue has been used in simple, complex and recurrent anal fistulas. Many observational studies exist regarding the treatment of fistula using fibrin glue and these report variable rates of success. The observational studies are limited by heterogenous fistula aetiology, fistula anatomy and follow-up data of less than 12 months. It is unclear from these non-RCTs whether fibrin glue is at least equivalent to procedures that currently exist in the treatment of anal fistula [57, 131].

### 8.9.3 | Effects on fistula healing, recurrence and incontinence following treatment with fibrin glue

There are two RCTs in which treatment of anal fistula with fibrin glue is described [131]. Generally poor outcomes resulting from early fistula recurrence following the use of fibrin glue are reported. Van der Hagen et al. [132] compared the use of fibrin glue with advancement flap, and Altomare et al. [131] compared fibrin glue with seton.

*Fibrin glue versus Seton*

Altomare et al. (2009) compared outcomes of fibrin glue treatment with seton treatment in transsphincteric fistulas using a prospective randomized crossover trial. They used cutting or loose setons. Patients randomized to seton treatment following failure of previous treatment were given a loose seton. The overall rate of fistula healing was lower following treatment with fibrin glue (38%) than following treatment with seton (73.8%) (RR = 0.51, 95% CI: 0.35–0.77) at a median follow-up of 12 months.

Altomare et al. also measured the change in continence using the Wexner score. There was significant worsening of continence function for patients in the seton group (mean Wexner score: 1.79–5.1, $p = 0.0017$) than for patients in the fibrin glue group (mean Wexner score: 0.67–0.49, $p = 0.070$).

GRADE

**Question:** Fibrin glue compared with cutting/loose seton for anal fistula

**Bibliography:** Altomare 2009

| Outcome assessed | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Fibrin glue | Cutting/loose seton | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a,b] | Not serious | Not serious | Not serious | None | 19/50 (38.0) | 31/42 (73.8) | RR = 0.51 (0.35–0.77) | 362 fewer per 1000 (from 480 fewer to 170 fewer) | ⨁⨁⨁◯ Moderate | CRITICAL |
| Incontinence | 1 | Randomized trials | Serious[c] | Not serious | Not serious | Not serious | None | Change in continence function after intervention was measured using Wexner score. Seton group had a significant worsening of continence function compared with fibrin glue group | | | | ⨁⨁⨁◯ Moderate | CRITICAL |

Abbreviation: RR, risk ratio.

Explanations. [a]Unclear process of randomization. [b]Recurrences in the seton group were treated surgically and not randomized. [c]Recurrences in the seton group may have an increased chance of worsening continence function as they were all treated surgically and not randomized.

Randomized trials do not demonstrate fibrin glue to be equivalent or superior to existing management strategies for anal fistula.

Recommendations

- Fibrin glue *should not* be used in the management of anal fistula. *Moderate-level evidence*.

## 8.10 | Platelet rich plasma

### 8.10.1 | Review questions for platelet rich plasma in cryptoglandular fistula treatment

1. What are the indications for platelet rich plasma (PRP)?
2. What are the effects of PRP on fistula healing, incontinence and pain in cryptoglandular anal fistula?

### 8.10.2 | Indications for PRP

Platelet rich plasma is obtained using centrifugation to concentrate a patient's own plasma, thus increasing the numbers of platelets and growth factors. It has been used in complex anal fistula, often as an adjunct to other sphincter-preserving procedures, such as LIFT and mucosal advancement flap.

### 8.10.3 | Effects of PRP on fistula healing, incontinence and pain

Luo et al. [133] conducted a meta-analysis of PRP, which included outcomes from six observational case series and three RCTs [Madbouly 2021, Mortagy 2021, Portilla 2019]. The observational case series were limited by heterogenous fistula aetiology (two studies included fistula associated with Crohn's disease), small numbers of study participants, and lack of data on incontinence, fistula healing time and complications [133].

The meta-analysis [133] of the RCTs in PRP [Madbouly 2021, Mortagy 2021, Portilla 2019] did not find a significant improvement in fistula healing with the addition of PRP [100, 134, 135]. The pooled data were limited by the inclusion of heterogenous fistula aetiology, low patient numbers and short follow-up. Portilla et al. compared the outcomes between PRP and fibrin glue in patients with high anal fistula but because patients with Crohn's disease were included, the results cannot be used as evidence in this guideline. Mortagy et al. randomized patients with high transsphincteric cryptoglandular anal fistula either to curettage of fistula tract and injection of PRP ($n = 9$) or to LIFT ($n = 9$). There was no difference in overall fistula healing between the groups at 5 weeks of follow-up. Following curettage and PRP, fistula healing was reported for six patients, and fistula healing was reported for seven patients treated with LIFT alone. Mortagy et al. could not be included in this guideline as it is limited by small numbers of participants in each arm of the study and a very short follow-up.

Madbouly et al. compared outcomes following LIFT, with or without the addition of autologous PRP, in high transsphincteric fistula of cryptoglandular origin. They found that primary healing improved with the addition of PRP to LIFT (85.7%, $p < 0.03$) compared to LIFT without PRP (65%) at a follow-up of 12 months. Patients had significantly lower levels of pain following LIFT plus PRP on day 1 ($3.6 \pm 1.01$ for LIFT vs. $2.0 \pm 1.1$ for LIFT+PRP; $p < 0.01$) and day 7 ($2.7 \pm 1.3$ for LIFT vs. $1.2 \pm 0.71$ for LIFT+PRP; $p < 0.01$) post-treatment. Quality-of-life scores at 4 weeks were higher in patients treated with LIFT plus PRP than in patients treated with LIFT without PRP. The study by Madbouly et al. had the longest follow-up (median 12 months) among the reported RCTs on PRP.

GRADE

**Question:** LIFT, with or without PRP, for anal fistula in adult patients

**Bibliography:** Madbouly 2021

| Outcome assessed | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | LIFTwith PRP | LIFT without PRP | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Not serious | Not serious | Not serious | Serious[a] | None | 42/49 (85.7) | 32/49 (65.3) | RR = 1.31 (1.04–1.66) | 202 more per 1000 (from 26 more to 431 more) | ⨁⨁⨁◯ Moderate | CRITICAL |

Abbreviations: LIFT, ligation of the intersphincteric fistula tract; PRP, platelet rich plasma; RR, risk ratio.

Explanations. a. Wide confidence interval.

There is a lack of robust evidence for benefit of PRP in treatment of anal fistula. Further research and long-term follow-up are required to assess whether there is a significant difference in overall fistula healing with the use of PRP on its own for the management of fistula healing. One RCT has investigated the use of PRP as an additional treatment to LIFT. This study reported greater fistula healing in LIFT with the addition of PRP.

Recommendations

- No recommendations can be made for the use of PRP alone in the management of anal fistula. *Very low-level evidence. [GDG expert opinion]*
- PRP *can be considered* in the management of anal fistula as an add-on treatment to LIFT. *Very low-level evidence [Downgraded by GDG, expert opinion].*

## 8.11 | Collagen matrix

### 8.11.1 | Review questions for collagen matrix in cryptoglandular fistula treatment

1. What are the indications for collagen matrix?
2. What are the effects on fistula healing, incontinence and pain following the use of collagen matrix in cryptoglandular anal fistula?
3. What is the effect of adding collagen matrix to rectal advancement flap?

### 8.11.2 | Indications for collagen matrix

Collagen matrix is a porcine dermal matrix that can be prepared as a collagen paste and has been used in small experimental studies to fill a fistula tract, with the aim of promoting cell invasion and tissue regeneration within the tract [136, 137]. Collagen dermal matrix has been advocated for use in simple intersphincteric and transsphincteric fistulas with short, straight tracts [66].

### 8.11.3 | Effects on fistula healing, incontinence and pain following the use of collagen matrix

*Fistula healing*

Giordano et al. [66] conducted a prospective observational study of collagen dermal matrix in 100 patients with solitary, primary or recurrent intersphincteric and transsphincteric fistulas of cryptoglandular origin. Fistulas with secondary tracts and horseshoe extensions were excluded. The primary fistula healing rate was 53.5% at 12 months of follow-up [66]. Observational studies of collagen paste in cryptoglandular anal fistula have demonstrated variable rates of healing, ranging between 20% and 77% [Hammond 2011, Giordano 2017, Bayrak 2018, Schiano di Visconte 2019] [66, 138–140]. Most studies consisted of a small number of participants with varying fistula complexity and had a short follow-up.

Vollebregt et al. [141] have published the largest observational study to date on the use of collagen matrix in complex cryptoglandular anal fistulas. A retrospective analysis was conducted in 90 patients, of whom 80% had complex fistula (comprising more than 30% of the EAS), as determined using preoperative imaging. At a median follow-up of 30 months, the primary fistula healing rate was only 20%. A significant association was found between complex fistulas and failure of the fistula to heal (OR = 3.53; 95% CI: 1.12–11.09, $p < 0.03$). Out of 20 patients with an unhealed fistula following primary infiltration, six healed with one ($n = 3$) or two ($n = 3$) further infiltrations of collagen paste.

### 8.11.4 | Effects of adding collagen matrix to rectal advancement flap

There are no RCTs in which the effect of adding collagen matrix to rectal advancement flap is assessed.

GRADE

**Question:** Collagen matrix compared with none for anal fistula treatment in adult patients

**Bibliography:** Hammond 2011, Giordano 2017, Bayrak 2018, Schiano di Visconte 2019, Vollebregt 2020

| | Certainty assessment | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Impact | Certainty | Importance |
| Fistula healing | 5 | Observational | Serious[a–c] | Not serious | Not serious | Serious[b,c] | | Fistula healing rate varied greatly between studies. Most studies included very small numbers of patients with complex anal fistula. Studies reported outcomes from short time periods of follow-up. Fistula healing rate ranged between 20% and 77% | ⨁◯◯◯ Very low | CRITICAL |

Explanations. [a]Heterogenous fistula anatomy. [b]Retrospective, small case series. [c]Primary fistula healing rates vary.

There is a lack of robust evidence demonstrating a benefit of collagen matrix in the treatment of anal fistula. Fistula healing rate is variable. Further research and long-term follow-up are required to establish whether treatment of the fistula tract with collagen matrix results in a significant difference in overall fistula healing.

Recommendations

- No recommendation can be made for the use of collagen matrix in the management of anal fistula. *Very low-level evidence*. *[GDG expert opinion]*

## 9 | OTHER PROCEDURES

### 9.1 | Suture repair of internal opening

#### 9.1.1 | Review questions for suture repair of internal opening in cryptoglandular fistula treatment

1. What is the effect of suture repair in the management of cryptoglandular anal fistula?

There are no RCTs or large case series in which the outcomes of oversewing the internal opening in anal fistula, as the only treatment, are reported. This was previously highlighted by Jacob et al., in 2010, in a Cochrane review of the management of anal fistula [57].

Suture repair of the internal opening is carried out as an adjunct to other sphincter-preserving procedures, but success rates of suture repair alone are unclear.

Further research with long-term follow-up is required to assess the effect of suture repair in fistula healing.

### 9.2 | Rerouting

#### 9.2.1 | Review questions for rerouting in cryptoglandular fistula treatment

1. What is the effect of rerouting in the management of cryptoglandular anal fistula?

Literature search was conducted using 'rerouting' as a key word in studies of cryptoglandular anal fistula. There is no standard definition of rerouting, but this has been reported sporadically in the literature and usually describes attempts to minimize division of the IAS or EAS whilst attempting fistula repair. A few observational studies were found in which "partial fistulotomy" and placement of a cutting seton or a loose draining seton are mentioned but this was not described as "rerouting". In these studies, a staged fistulotomy is performed after leaving the seton in place for varying periods of time. This makes analysis of the evidence more difficult.

The search found three RCTs in which different approaches to rerouting, and comparison of rerouting with conventional management, were described. The outcomes of these are detailed below with a description of the procedures and a narrative review.

*Rerouting by preserving the IAS*

Zbar et al. [142] described the outcomes of an RCT in which a conventional cutting seton (16 patients) was compared with a modified technique that involves rerouting the fistula tract to only encompass the EAS with a cutting seton (18 patients) in high transsphincteric (involving greater 30% of the EAS) cryptoglandular fistula. This procedure first involves excising the internal opening and creating a U-shaped mucosal flap to close the internal opening without involving the IAS muscle. Intersphincteric dissection is used to pass a cutting seton around the EAS. The IAS is closed at the internal opening using a 2/0 polyglactin suture, and the internal opening is then covered with mucosal advancement flap. The cutting seton is tightened at 2-weekly intervals in the clinic [142].

There were no significant differences between groups in the rates of fistula healing. The fistula healing rate was 89% in the group in which the IAS-preserving seton was used compared with 94% in the control group (conventional cutting seton), at a median follow-up of 12 months [142]. The average fistula healing time for the group in which the IAS-preserving seton was used was 14 weeks and for the group in which the cutting seton was used was 12 weeks. In the group in which the IAS-preserving seton was used, one patient reported minor incontinence to flatus and in the control group one patient reported minor incontinence to flatus and one patient reported occasional faecal leakage [142].

It is important to note that 4/18 patients in the group in which the IAS-preserving seton was used and 4/16 patients in the control group (conventional cutting seton) had a secondary fistulectomy for slow progress once the seton had descended below the puborectalis sling. The study lacked allocation concealment and adequate description of randomization. Small sample size and short follow-up data limit its use.

GRADE

**Question:** IAS-preserving seton compared with cutting seton for anal fistula in adult patients

**Bibliography:** Zbar 2003

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | IAS-preserving seton | Cutting seton | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a] | Not serious | Not serious | Serious[b,c] | None | 16/18 (88.9) | 15/16 (93.8) | RR=0.95 (0.77–1.17) | 47 fewer per 1000 (from 216 fewer to 159 more) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a] | Not serious | Not serious | Serious[b] | None | 1/18 (5.6) | 2/16 (12.5) | RR=0.44 (0.04 to 4.45) | 70 fewer per 1000 (from 120 fewer to 431 more) | ⨁⨁◯◯Low | CRITICAL |

Abbreviation: RR, risk ratio.

Explanations. [a]Lack of allocation concealment. [b]One study with small sample size. [c]Wide confidence intervals.

*Rerouting by preserving the EAS*

Omar et al. conducted an RCT in which outcomes following an EAS-preserving rerouting technique with seton insertion (30 patients) were compared with those following placement of a conventional draining seton (30 patients). High transsphincteric, suprasphincteric and horseshoe fistulas of cryptoglandular origin were included. The fistulas were classified using preoperative MRI. All patients had their fistula tract excised up to the EAS. In the control group, a loose draining silk suture was placed as a seton through the remaining tract. In the rerouting group, the intersphincteric space was dissected and a silk suture was guided through the space and the internal opening, encircling the IAS. The point where the fistula tract passed through the EAS was closed using a Vicryl suture [143].

All patients in the draining seton group required a second-stage fistulotomy, whereas only two patients in the rerouting group required fistulotomy ($p<0.0001$) for fistula persistence at 3 months. The primary outcome was time to fistula healing, which was significantly shorter in the rerouting group (46 ± 18 days) than in the draining seton group (103 ± 47 days), $p<0.0001$. At a mean follow-up of 12 months (range: 10–19 months), four (13%) patients in the draining seton group and one (3%) patient in the rerouting group had fistula persistence or recurrence of fistula ($p=0.35$). The overall healing rate following treatment with an EAS-preserving seton was 96.7%. Patients in the control group initially had a draining seton inserted but all were then subjected to a second-stage fistulotomy; an overall healing rate of 86.7% was reported. Postoperative pain was significantly higher in the first 24 h and at 1 week in the draining seton (control) group than in the rerouting (EAS-preserving seton) group (5.5 ± 1.6 (draining seton) vs. 3.3 ± 1.3 (EAS-preserving seton); $p<0.0001$) [143].

The study was single-blinded and included allocation concealment and random sequence generation. A power calculation was performed. The study was limited by heterogeneity in fistula anatomy and complexity and would have benefitted from long-term follow-up.

GRADE

**Question:** EAS-preserving seton compared with draining seton for anal fistula in adult patients

**Bibliography:** Omar 2019

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | EAS-preserving seton | Cutting seton | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a] | Not serious | Not serious | Serious[b,c] | None | 16/18 (88.9) | 15/16 (93.8) | RR = 0.95 (0.77–1.17) | 47 fewer per 1000 (from 216 fewer to 159 more) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a] | Not serious | Not serious | Serious[b] | None | 1/18 (5.6) | 2/16 (12.5) | RR = 0.44 (0.04–4.45) | 70 fewer per 1000 (from 120 fewer to 431 more) | ⨁⨁◯◯ Low | CRITICAL |

Abbreviations: EAS, External anal sphincter; RR, risk ratio.

Explanations. [a]Heterogenous fistula anatomy. [b]One study with small sample size. [c]Wide confidence intervals.

Abdelnaby et al. [144] conducted a RCT in which outcomes in patients with high transsphincteric anal fistula treated with mucosal advancement flap and a drainage seton rerouted around the EAS were compared with outcomes in patients treated with rerouting seton around the IAS. The procedure used was similar to that described in the studies above. There was no difference in fistula healing and recurrence between groups at 20 months of follow-up. The overall rate of fistula healing was 95.9% following mucosal advancement with EAS rerouting compared with 91.7% following IAS rerouting alone. The faecal incontinence rate was higher in the group treated with rerouting seton around the IAS than in the group treated with rerouting seton around the EAS (14.5% vs. 2%, $p<0.03$).

GRADE

**Question:** Mucosal advancement/EAS rerouting compared with IAS rerouting for anal fistula in adult patients

**Bibliography:** Abdelnaby 2019

| | Certainty assessment | | | | | | | No. of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Outcome assessed | No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Mucosal advancement/EAS rerouting | IAS rerouting | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| Fistula healing | 1 | Randomized trial | Serious[a,b,c] | Not serious | Not serious | Serious[c] | None | 47/49 (95.9) | 44/48 (91.7) | RR = 1.05 (0.88–1.08) | 46 more per 1000 (from 110 fewer to 73 more) | ⨁⨁◯◯ Low | CRITICAL |
| Incontinence | 1 | Randomized trial | Serious[a,b,c] | Not serious | Not serious | Serious[c] | None | 1/49 (2.0) | 7/48 (14.6) | RR = 0.14 (0.01–1.03) | 125 fewer per 1000 (from 144 fewer to 4 more) | ⨁⨁◯◯ Low | CRITICAL |

Abbreviations: EAS, external anal sphincter; IAS, internal anal sphincter; RR, risk ratio.

Explanations. [a]Lack of allocation concealment. [b]Inadequate sequence generation. [c]One study with small sample size.

Further research with long-term follow-up is required to assess whether either of the various methods of rerouting may be of benefit in selected patients.

Recommendations

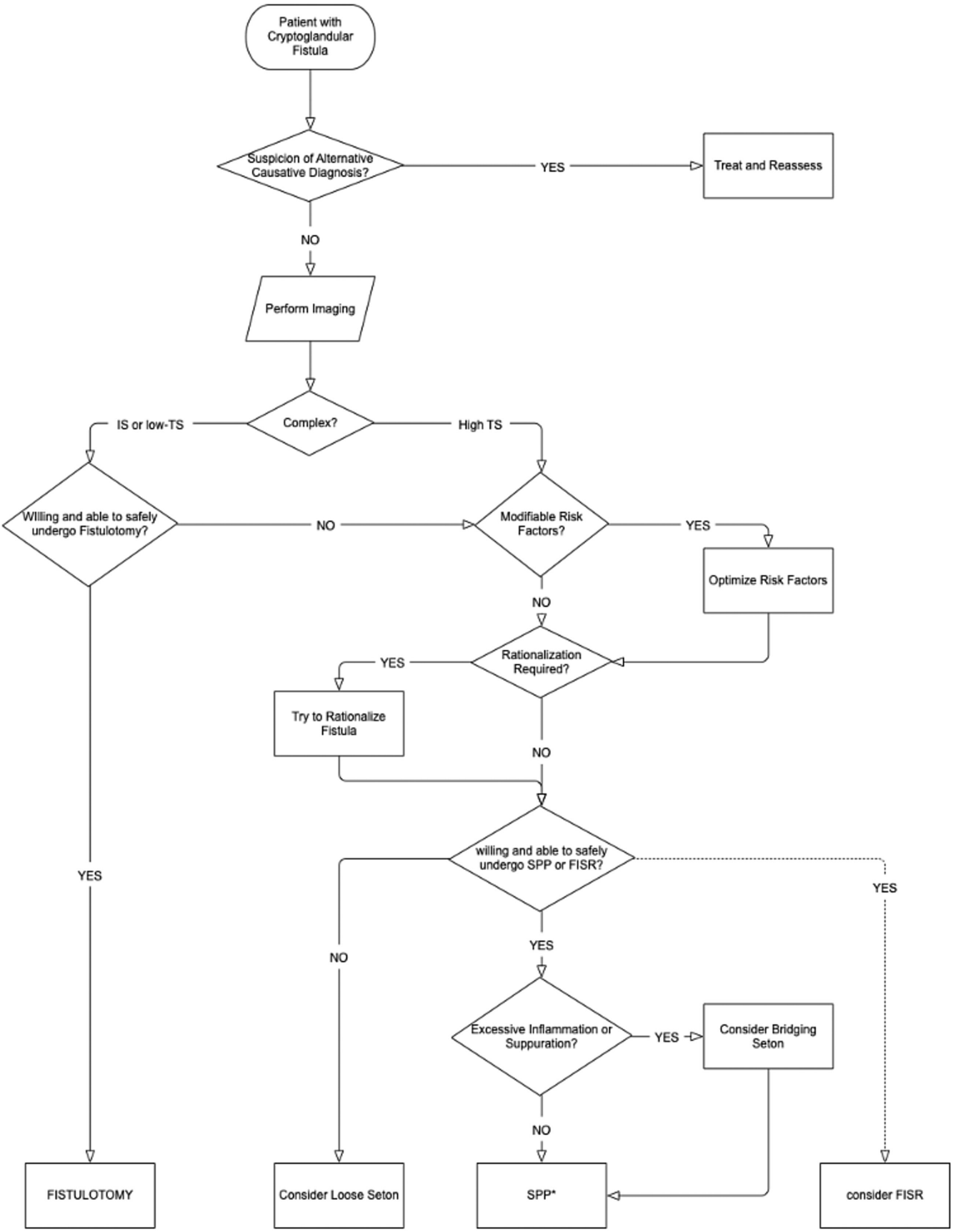


**FIGURE 10** Proposed algorithm for managing a patient with a new fistula. FISR, fistulotomy or fistulectomy and immediate sphincter reconstruction; IS, intersphincteric; SPP, sphincter-preserving procedure; TS, transsphincteric.

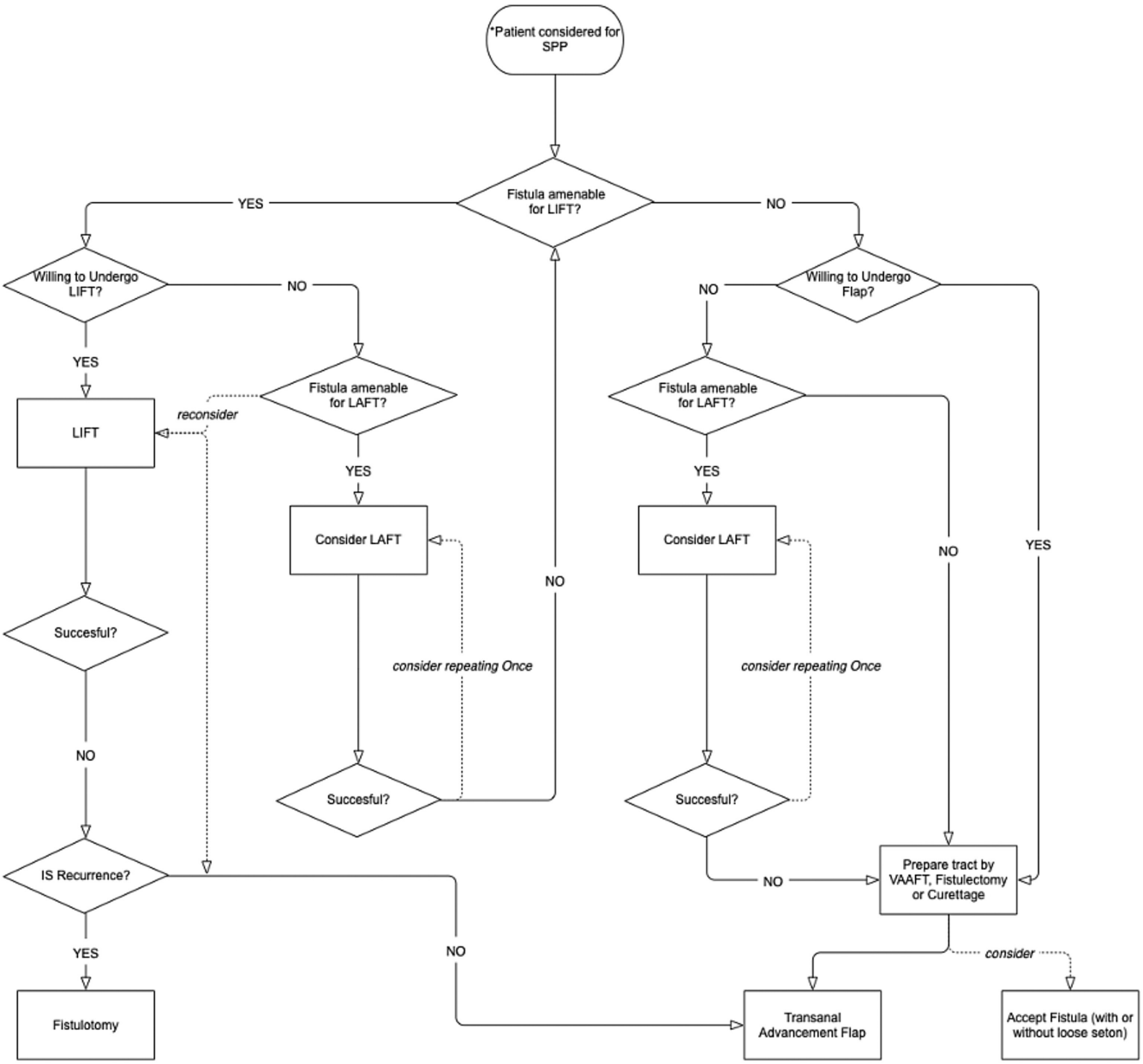


**FIGURE 11** Proposed algorithm for treating a fistula using sphincter-preserving procedures. IS, intersphincteric; LAFT, laser ablation of fistula tract; LIFT, ligation of the intersphincteric fistula tract; SPP, sphincter-preserving procedure; VAAFT, video-assisted anal fistula treatment.

- No recommendation can be made for the use of suture repair of the internal opening alone in the management of anal fistula. *[GDG expert opinion]*
- No recommendation can be made for the use of rerouting in high anal fistulas because of a lack of robust data. *[GDG expert opinion]*

## 10 | SPECIAL CONSIDERATIONS

### 10.1 | Review questions in cryptoglandular fistula treatment

1. What is the effect of palliative seton in the management of cryptoglandular anal fistula?
2. What is the effect of defunctioning colostomy or enterostomy in the management of cryptoglandular anal fistula?

#### 10.1.1 | Palliative seton

No systematic reviews or RCTs have been found in which the impact on quality of life of different seton techniques, materials, knots or other features in palliative loose seton treatment is considered.

#### 10.1.2 | Defunctioning colostomy or enterostomy

No systematic reviews or RCTs have been found on the significance of faecal diversion on fistula healing or patient satisfaction in

cryptoglandular fistula-in-ano. While some surgeons use a covering stoma in procedures such as advancement flaps and fistulectomy with sphincter repair, there is no evidence to support this strategy. It is well established that a significant proportion of patients with perianal fistula associated with Crohn's disease undergo faecal diversion.

Faecal diversion has been associated with clinical remission of perianal Crohn's fistulas; however, few patients have their stoma reversed. Corresponding data for cryptoglandular fistulas have not been identified.

Recommendations

- A palliative seton *can be considered* for the management of recurrent perianal sepsis. *[GDG expert opinion]*
- Palliative seton *can* be offered to patients with an anal fistula who are keen to avoid further surgical intervention and the risk of injury to the sphincter mechanism. *[GDG expert opinion]*
- A defunctioning stoma *can be considered* in patients with severe and locally uncontrollable perianal sepsis with an anal fistula. *[GDG expert opinion]*

## 11 | MANAGEMENT ALGORITHMS

The GDG have proposed two algorithms incorporating the various elements discussed in this guideline. These have been developed as an aid for clinical decision making when managing a new fistula (Figure 10) or a complex fistula with sphincter-preserving procedures (Figure 11).

## 12 | PATIENT INFORMATION

A patient information chapter will be produced with patient representation to describe each procedure with illustrations and lay language.

## 13 | IMPLEMENTATION

Implementation of this guideline is likely to be limited by resource constraints and the availability of expertise. Competing service demands may prevent many surgeons from developing the skills and experience required to master the wide range of interventional procedures discussed here. It is possible that within a region, specific units will specialize in certain procedures to ensure efficiency and high-volume case experience. Variable access to MRI and possible ease of access to EAUS in some regions may continue to limit the use of MRI in the assessment of anal fistula. This was extensively discussed by the GDG, and recommendations were developed to accommodate variations in practice. Patient expectations of cure and willingness to accept risk to continence will vary with regional cultural norms, values and the financial burden of disease. Some recommendations may be more acceptable and easily implemented than others.

Readers are requested to provide feedback to the corresponding authors using escpfistula@gmail.com on possible barriers of implementation in their clinical setting of any of the recommendations in this guideline. These will be reviewed and considered in future updates of this guideline.

## 14 | UPDATING

We plan to update this guideline in 2 years by conducting a search of the literature and incorporating any new, relevant research into our recommendations. The GDG members will reassess the need for an annual update at the annual ESCP conference if new, compelling research requires an adaptation of or earlier changes to our current recommendations.

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### AUTHOR CONTRIBUTIONS

**Lillian Reza:** Investigation; writing – original draft; writing – review and editing; formal analysis; data curation; methodology; software. **Kevin Gottgens:** Writing – review and editing; validation; formal analysis; data curation; writing – original draft. **Jos Kleijnen:** Methodology; validation; formal analysis; data curation; resources. **Stephanie Breukink:** Writing – review and editing; data curation; validation; supervision. **Peter C. Ambe:** Writing – review and editing; data curation; investigation. **Felix Aigner:** Writing – review and editing; data curation; investigation. **Erman Aytac:** Writing – review and editing; data curation; investigation. **Gabriele Bislenghi:** Writing – review and editing; data curation; investigation. **Andreas Nordholm-Carstensen:** Writing – review and editing; data curation; investigation. **Hossam Elfeki:** Writing – review and editing; data curation; investigation. **Gaetano Gallo:** Writing – review and editing; data curation; investigation. **Ugo Grossi:** Writing – review and editing; data curation; investigation. **Baris Gulcu:** Writing – review and editing; data curation; investigation. **Nusrat Iqbal:** Writing – review and editing; data curation; investigation. **Rosa Jimenez-Rodriguez:** Writing – review and editing; data curation; investigation. **Sezai Leventoglu:** Writing – review and editing; data curation; investigation. **Giorgio Lisi:** Writing – review and editing; data curation; investigation. **Francesco Litta:** Data curation; writing – review and editing; investigation. **Philip Lung:** Writing – review and editing; validation. **Monica Millan:** Writing – review and editing; data curation; investigation. **Ersin Ozturk:** Writing – review and editing; data curation; investigation. **Charlene Sackitey:** Writing – review and editing; data curation; investigation. **Mostafa Shalaby:** Writing – review and editing; data curation; investigation. **Jasper Stijns:** Writing – review and editing; data curation; investigation. **Phil Tozer:** Writing – review and editing; conceptualization; project administration; supervision; visualization; writing – original draft; validation. **David Zimmerman:**

Supervision; conceptualization; visualization; writing – review and editing; writing – original draft; project administration; validation.

## AFFILIATIONS

[1]St Mark's Hospital, London, UK
[2]Máxima MC Eindhoven, Eindhoven, Netherlands
[3]KSR Ltd & Maastricht University Medical Center (MUMC+) -CAPHRI, Maastricht, Netherlands
[4]Maastricht University Medical Center (MUMC+), Maastricht, Netherlands
[5]Witten/Herdecke University, Witten, Germany
[6]St. John of God Hospital, Graz, Austria
[7]Acibadem University, Istanbul, Turkey
[8]University Hospital Leuven, Leuven, Belgium
[9]Bispebjerg University Hospital, Copenhagen, Denmark
[10]Mansoura University Hospital, Mansoura, Egypt
[11]Sapienza University of Rome, Rome, Italy
[12]Treviso Regional Hospital, Treviso, Italy
[13]Medicana Bursa Hospital, Bursa, Turkey
[14]St Mark's Hospital, London, UK
[15]Virgen del Rocío University Hospital, Seville, Spain
[16]Gazi University Medical School, Ankara, Turkey
[17]Sant'Eugenio Hospital, Rome, Italy
[18]Gemelli Hospital Foundation, Rome, Italy
[19]St Mark's Hospital, London, UK
[20]La Fe University and Polytechnic Hospital, Valencia, Spain
[21]Medicana Bursa Hospital, Bursa, Turkey
[22]St Mark's Hospital, London, UK
[23]Mansoura University Hospitals, Mansoura, Egypt
[24]Universitair Ziekenhuis Brussel, Jette, Belgium
[25]St Mark's Hospital, London, UK
[26]Elisabeth-TweeSteden Hospital, Tilburg, Netherlands

## CONFLICT OF INTEREST STATEMENT

Jos Kleijnen (Kleijnen Systematic Reviews Ltd) has been part of the development process of this guideline and is co-author of the ROBIS, PRISMA, QUADAS, STARD and PROBAST tools.

## ETHICS STATEMENT

Since the study does not use health data of individuals, ethics apporval was not required.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

## ORCID

*Lillian Reza* https://orcid.org/0000-0002-1993-2989
*Kevin Gottgens* https://orcid.org/0000-0002-8774-5317
*Erman Aytac* https://orcid.org/0000-0002-8803-0874
*Gabriele Bislenghi* https://orcid.org/0000-0002-9212-9287
*Hossam Elfeki* https://orcid.org/0000-0003-0704-4068
*Nusrat Iqbal* https://orcid.org/0000-0003-3264-7362
*Rosa Jimenez-Rodriguez* https://orcid.org/0000-0001-8587-8768
*Mostafa Shalaby* https://orcid.org/0000-0002-0358-2398
*Jasper Stijns* https://orcid.org/0000-0002-5256-6167

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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## APPENDIX A

### Methodology

The European Society of Colproctology (ESCP) guideline development process was first described in the ESCP guideline for haemorrhoidal disease. The protocol for ESCP guideline development has been published (https://www.escp.eu.com/images/guidelines/documents/Development-ESCP-Guideline-Haemorrhoidal-Disease.pdf). We outline the steps taken to recreate the guideline developement process with the aim of developing an ESCP guideeline for anal fisutla.

### A.1. | Why is there a need for a new guideline in anal fistula?

The primary aim was to develop recommendations according to a transparent and robust process. The existing guidelines for cryptoglandular anal fistula were not developed using the AGREE-S toolkit [145]. Moreover, the existing guidelines are limited by geographical representation and do not consider differences in regional practice

and availability of resources. This guideline has been primarily developed with the ESCP membership in mind.

### A.2. | *What challenges were anticipated in the development of anal fistula guidelines?*

At the outset it was clear to the oversight committee that there would be challenges in the guideline development process for anal fistula.

There are a vast range of possible surgical interventions for the management of complex anal fistula in secondary care. Ideally, recommendations should be made using high-level, good-quality evidence. As there are limited numbers of good-quality randomized trials in the surgical management of anal fistula because of the heterogenous presentation of anal fistula with varying levels of anatomical complexity, many recommendations may need to be developed using expert consensus and low-level evidence. As recommendations would be reliant on the clinical experience of managing anal fistula in secondary care using a vast range of interventions, the oversight committee ensured that the GDG comprised members with an academic interest and clinical experience of managing complex anal fistula in secondary care.

### A.3. | Setting the scope

#### A.3.1. | Target population

The guideline addresses the clinical management of perianal abscess and cryptoglandular anal fistula in adult patients presenting to secondary care. The guideline does not include recommendations for ileoanal pouch fistula, rectovaginal fistula or Crohn's perianal fistula.

#### A.3.2. | Target audience

The guideline was developed for use by secondary care practitioners involved in the management of anal fistula, including general surgeons, coloproctologists and radiologists. Patients interested in the clinical evidence for the diagnosis and management of anal fistula in secondary care may find this guideline useful.

#### A.3.3. | Compilation of the GDG

Applications to the GDG were encouraged from the current ESCP membership. The GDG was selected to ensure a broad geographical representation of its members. Surgeons were required to demonstrate extensive surgical experience of managing anal fistula and involvement in clinical research of anal fistula. The radiologist selected for inclusion in the GDG demonstrated extensive clinical experience in anal fistula radiology and has an academic interest in anal fistula.

The final GDG group represented 10 countries (The Netherlands, United Kingdom, Italy, Egypt, Turkey, Belgium, Denmark, Austria, Spain, and Germany), eight of which were in Europe. There were 21 colorectal surgeons with concurrent practice in general surgery, three colorectal clinical research fellows (PhD candidates in perianal fistula), one radiologist with a subspecialist interest in anal fistula radiology and one methodologist (Table A1). A team of methodologists (Kleijnen Systematic Reviews Ltd) advised and guided the development process.

The oversight committee (D.Z., P.T., K.G., S.B., L.R. and J.K.) was responsible for managing the study design, scope of the guideline and conducting GRADE (Grading of Recommendations Assessments, Development and Evaluation) and ROBIS (Risk Of Bias In Sytematic reviews) assessments of the evidence selected by the GDG members (G.L., H.E., E.A., J.S., A.N.C., F.A., M.S., M.M., G.B., F.L., S.L., R.J.R., U.G., G.G., P.C.A., E.O., B.G., P.L., C.S. and N.I.). Lillian Reza is a PhD candidate with no affiliations to industry and has no conflict of interest; she led the final literature search, data extraction and grading of the evidence. Jos Kleijnen performed the ROBIS assessment and reviewed the grading of the evidence.

### A.4. | Formulating review questions

The GDG submitted 250 questions with themes for review. The questions were categorized as being of high, moderate or low value based on their frequency of submission by the oversight committee. High- and intermediate-value questions were those that were submitted by a large proportion of the GDG. Low-value questions usually addressed themes that were beyond the scope set for this guideline.

The preliminary list of questions submitted by the GDG enabled the group to understand the pertinent clinical themes that require recommendations or a statement. The oversight committee categorized the questions under broad themes.

- Diagnosis, classification and preoperative investigations
  - Perianal abscess and anal fistula
  - Diagnosis of anal fistula
  - Perioperative care
- Partial sphincter-preserving procedures
  - Fistulotomy
  - Fistulectomy and immediate sphincter repair
  - Cutting seton
- Sphincter-preserving procedures
  - Bridging/draining seton
  - Advancement flap
  - Ligation of intersphincteric tract
  - Video-assisted anal fistula treatment
  - Laser ablation of fistula tract
  - Fistula plug
  - Over-the-scope clip
  - Platelet rich plasma
  - Collagen matrix
  - Suture repair of internal opening
  - Rerouting
- Special considerations
  - Palliative seton
  - Defunctioning colo- or enterostomy

**TABLE A1** Guideline development group.

| Name | Profession | Country | Function |
|---|---|---|---|
| David Zimmerman | Colorectal surgeon (EBSQ-certified) | The Netherlands | Oversight committee |
| Phil Tozer | Colorectal surgeon | United Kingdom | Oversight committee |
| Kevin Gottgens | Colorectal surgeon (EBSQ-certified) | The Netherlands | Oversight committee |
| Lillian Reza | Clinical research fellow | United Kingdom | Oversight committee |
| Jos Kleijnen | Methodologist | UK/The Netherlands | Oversight committee |
| Stephanie Breukink | Colorectal surgeon | The Netherlands | Oversight committee |
| Giorgio Lisi | Colorectal surgeon | Italy | GDG member |
| Hossam Elfeki | Colorectal surgeon | Egypt | GDG member |
| Erman Aytac | Colorectal surgeon (EBSQ-certified) | Turkey | GDG member |
| Jasper Stijns | Colorectal surgeon (EBSQ-certified) | Belgium | GDG member |
| Andreas Nordholm-Carstensen | Colorectal surgeon | Denmark | GDG member |
| Felix Aigner | Colorectal surgeon (EBSQ-certified) | Austria | GDG member |
| Mostafa Shalaby | Colorectal surgeon | Egypt | GDG member |
| Monica Millan | Colorectal surgeon (EBSQ-certified) | Spain | GDG member |
| Gabriele Bislenghi | Colorectal surgeon (EBSQ-certified) | Belgium | GDG member |
| Francesco Litta | Colorectal surgeon | Italy | GDG member |
| Sezai Leventoglu | Colorectal surgeon (EBSQ-certified) | Turkey | GDG member |
| Rosa Jimenez-Rodriguez | Colorectal surgeon (EBSQ-certified) | Spain | GDG member |
| Ugo Grossi | Colorectal surgeon | Italy | GDG member |
| Gaetano Gallo | Colorectal surgeon (EBSQ-certified) | Italy | GDG member |
| Peter C. Ambe | Colorectal surgeon (EBSQ-certified) | Germany | GDG member |
| Ersin Ozturk | Colorectal surgeon (EBSQ-certified) | Turkey | GDG member |
| Baris Gulcu | Colorectal surgeon | Turkey | GDG member |
| Philip Lung | Radiologist | United Kingdom | GDG member |
| Charlene Sackitey | Clinical research fellow | United Kingdom | GDG member |
| Nusrat Iqbal | Clinical research fellow | United Kingdom | GDG member |

The population, intervention, comparator and outcome (PICO) framework was then used to formulate the review questions for use in literature search and possible subgroups for each PICO were explored.

The draft PICO questions were reviewed by all members of the GDG, who had the opportunity to suggest changes by email. A GDG virtual meeting was used to discuss the final questions for inclusion. The PICO questions within the components and the complete search strategy have been included in the Appendix. An example of a PICO question and its components are as follows:

| | |
|---|---|
| Population | Adult patients with a perianal abscess and cryptoglandular anal fistula |
| Intervention | Immediate fistulotomy/fistulectomy/repair of anal fistula and drainage of perianal abscess |
| Comparator | Drainage of perianal abscess |
| Outcome | Recurrence/persistence of fistula/repeat surgery, incontinence |

### A.5. | Establishing outcomes for extraction

The core set of outcomes produced by the Anal Fistula Core Outcome Set (AFCOS) study [146] were used in selecting outcomes for inclusion in guideline development. The AFCOS study, led by Nusrat Iqbal (a PhD candidate), generated a core set of outcomes that should be reported in all interventional studies pertaining to cryptoglandular anal fistula. These outcomes were generated using a systematic review, qualitative patient interviews and a Delphi process according to COMET (Core Outome measures in Effectivenes Trials) guidance [147]. This list of outcomes was presented to the GDG at a virtual meeting to stimulate discussion. The GDG also had the opportunity to add to the list of outcomes that should be extracted from each PICO. The GDG discussed outcomes that were frequently reported in clinical studies and used in clinical decision making. Critical outcomes were those that were necessary to assess the efficacy of an intervention and were also relevant to patients. The AFCOS study helped to ensure that the GDG prioritized outcomes that were relevant to patients. The long list of outcomes was ratified and prioritized on a Likert scale.

The GDG selected fistula healing and incontinence as critical outcomes and pain as an important outcome based on a balance of patient priority (from AFCOS, which was patient driven and centred) and utility. Existing interventional fistula studies use these outcomes frequently and they are therefore useful for comparing efficacy of treatment (overall fistula healing, recurrence/persistence, fistula development) and risk of harm (change in continence, minor incontinence, major incontinence) across studies. Variations in definitions of outcome reporting were discussed for each critical outcome and these are listed below. Studies that did not report predefined outcomes were not included for review. Figure A1 demonstrates the list of outcomes discussed at the GDG virtual meeting and how these were rated on a Likert scale for decision making. Where available, quality-of-life measures were described in each section as these are relevant to patients.

### A.6. | Definitions for outcomes

1. Fistula healing

Fistula healing, closure, recurrence, persistence, overall healing, fistula development, need for repeat surgery for fistula, time to wound healing.

2. Incontinence

Change in continence, minor or major incontinence, Wexner scale, Vaizey incontinence score.

3. Pain

**Discomfort, pain scores (Table A2).**

### A.7. | Conducting a search for the evidence and statistical analysis

The GDG anticipated challenges in meta-analysis of outcomes as they were aware of the significant heterogeneity in reporting outcomes in anal fistula management. Heterogeneity also arises from variations in anal fistula anatomy, fistula complexity and the association of fistula with the sphincters. Published data in anal fistula are mainly retrospective observational studies that are prone to selection bias and reporting bias. Therefore, meta-analysis of observational studies may not always be possible or appropriate, and when conducted should be viewed with caution. The GDG set out to report recommendations for simple and complex anal fistula separately where evidence allowed.

The GDG members formed eight teams and were allocated specific PICO questions to review. Literature searches were developed with the methodologist and evidence was extracted, according to inclusion criteria, by each team (PICO and search strategy in Appendix). A literature search was performed of MEDLINE (Ovid), Embase (Ovid), the KSR evidence database and the Cochrane Database of Systematic Reviews. The first searches were performed between January 1980–August 2021 and January 1980–October 2021. The most recent search was conducted in October 2022 for studies published since the first search between October 2021–October 2022.

The highest level of evidence available was included to answer each PICO question. The highest levels of evidence were systematic reviews and meta-analysis of randomized controlled trials (RCTs). The most recent systematic review and meta-analysis of RCTs were included and updated where necessary. In the presence of a new RCT, published since the publication of a systematic review, or if an RCT was not included in the original review but met the criteria for inclusion, a new meta-analysis of RCT evidence was conducted using Review Manager 5.4.1.

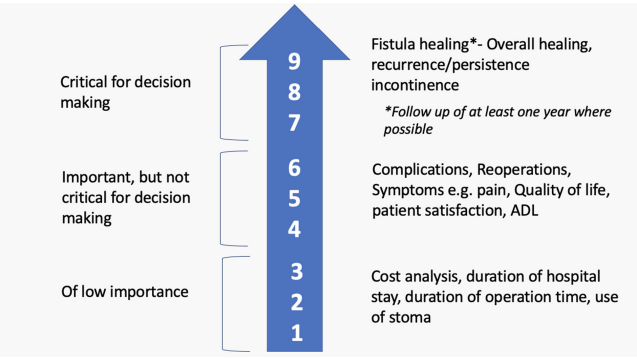


**FIGURE A1** Likert scale used to prioritize outcomes.

**TABLE A2** Long list of outcomes described by GDG members.

| |
|---|
| Overall fistula healing<br>Clinical healing<br>Radiological healing |
| Failure<br>Failure of fistula healing<br>Fistula persistence<br>Recurrence |
| Incontinence (minor/major/change) |
| Symptoms of anal fistula<br>Pain<br>Discharge |
| Quality of life |
| Follow up<br>Consider length of follow-up where \1-year follow-up data would be ideal |
| Ability to perform activities of daily living |
| Patient satisfaction |
| Complications/adverse effects |
| Reoperations |
| Cost analysis |
| Duration of hospital stay |
| Duration of operation time |
| Use of a stoma |

Data were analysed in Review Manager 5.4.1 using risk ratio with fixed effects and a 95% CI. Interstudy heterogeneity was also presented using $I^2$ statistic. Forest plots were used to present the data.

In the presence of RCT evidence, no lower-level evidence was included. In the absence of randomized controlled studies, the most recent meta-analysis of observational studies was included. The GDG did not consider any benefit to updating the meta-analysis of systematic reviews of observational studies as GRADE assessment would classify this type of evidence as low grade. An updated meta-analysis would not increase the certainty in the evidence or the strength of the recommendation. Single observational studies were utilized with caution as these are prone to considerable bias.

*Characteristics of studies included for review*:

1. Systematic review and meta-analysis of RCTs
2. RCTs
3. Systematic review and meta-analysis of observational studies
4. Observational studies
5. Case series with more than five participants
6. Existing guidelines

*Broad inclusion and exclusion criteria for the evidence are listed below*:

*Inclusion criteria*

- Idiopathic/cryptoglandular anal fistula
- Adult patients
- Critical or important outcomes

*Exclusion criteria*

- Predominantly Crohn's disease-related fistula
- Pouch, anovaginal or rectovaginal fistula

### A.8. | Developing recommendations

GRADE assessments of quality were conducted of the highest level of available evidence for each outcome in a PICO question by two members (L.R. and K.G.), using the principal categories for GRADE (study design, risk of bias, inconsistency, indirectness, imprecision and publication bias). These assessments were further reviewed by the methodologist to ensure consistency. GRADE assessments were conducted using the GRADEpro web application. GRADE was performed on each study (randomized or observational) included in data extraction for an outcome.

The main considerations were confidence in estimates of effect and the level of certainty. The GDG assessed the size of the effect and level of certainty in the evidence of the risk of harm (incontinence) against the size of effect and level of certainty in the evidence of benefit (fistula healing). The strength of recommendation was determined by the lowest level of certainty for an outcome in the PICO question.

ROBIS assessments were performed by the methodologist (J.K.). The ROBIS tool was used to assess the risk of bias in systematic reviews. ROBIS assessments highlighted areas of concern within the systematic reviews. During the systematic search of the evidence, these meta-analyses were updated if randomized studies were found that had not been included in the original systematic review, either because they had been published since the review or had been missed from the original review. The randomized studies included in the systematic review were reviewed to assess whether they met the inclusion criteria and data were extracted for analysis and production of forest plots using Review Manager 5.4.1.

**TABLE A3** Grade of evidence and strength of recommendation.

| GRADE | Strength of recommendation |
|---|---|
| High ++++ | 'Must' or 'must not' |
| Moderate +++ | 'Should' or 'should not' |
| Low ++ | 'Could' |
| Very low + | 'Can be considered' |

The GDG developed the recommendations using the highest level of available evidence, GRADE assessments and expert opinion. The wording used in the recommendations has been established in a previous guideline [4]. Table A3 outlines the GRADE of evidence and strength of recommendations. For each PICO question, the strength of the recommendation is based on the lowest GRADE achieved by a critical or important outcome. The GDG was able to upgrade or downgrade the available evidence, which has an impact on the strength of the final recommendation. Where the GDG has chosen to use expert opinion and clinical practice to affect the strength of the recommendation, this is explicitly stated.

The strength of the recommendations is limited by the availability of randomized trials in the management of anal fistula. Heterogeneity in fistula anatomy and complexity, as well as the challenges of recruiting large numbers of patients with similar features, have been barriers to conducting large-scale randomized trials in anal fistula [148]. Meta-analysis of RCTs is considered as high-level evidence, and previous guidance has striven to include these where possible [4]. This guideline has been developed with a similar intention, but the GDG were aware at the outset that evidence would largely consist of small series of observational studies and meta-analysis of cohort studies, as found in previous attempts to develop recommendations for anal fistula [58].

In the absence of high-level evidence and where it was unclear whether there is significant benefit of an intervention, the GDG opted to make no recommendation. For interventions with evidence demonstrating low confidence in estimates of effect and unclear harm in terms of risk of incontinence or pain to patient, the GDG chose to not recommend the intervention.

### A.9. | Patient involvement in the guideline

The final draft recommendations have been reviewed by five patient representatives. These patients attended two virtual meetings to discuss the evidence and suggest amendments. Patient feedback has been incorporated into the guideline. A parallel chapter will be

produced, with input from patient representatives, in which each procedure will be described with illustrations and lay language. Patients have also suggested a number of PICO questions that were not within the scope of this guideline but will be addressed in a separate chapter.

### A.10. | Finalizing recommendations

The draft recommendations and evidence tables were emailed to all GDG members. Members reviewed these recommendations and made suggestions to the draft. These recommendations were discussed in four consecutive virtual meetings. Each recommendation was verbally discussed, and the final wording was confirmed once there was whole-group consensus at the virtual GDG meeting. The final draft recommendations were subsequently reviewed by all members of the GDG.

### A.11. | Wording of recommendations

In previous ESCP guidelines, the wording used in Table A3 has been useful for creating a hierarchy, based on available evidence, for the management of conditions. It is very difficult to compare evidence for the management of anal fistula for use in developing a stepwise algorithm which includes a hierarchy for treatment modalities. The main limitations are the lack of high-quality randomized studies and the heterogenous nature of anal fistula. This reduces the generalizability of the data and does not lend to the production of recommendations for every clinical scenario. Surgical modalities need to be offered by assessing individual patients' expectations, sphincter function and willingness to accept the risks of impairment to their continence. For any one clinical scenario, there may be more than one surgical technique that 'should' or 'could' be used and these should be discussed with the patient by a clinician who has performed a detailed assessment of patients' expectations and sphincter function.

## APPENDIX B

**AGREE-S Reporting Checklist. Copyright: The GAP Consortium.**

Title of guideline: ESCP cryptoglandular anal fistula guideline

Name of first author: _Lillian Reza

Sponsoring organization (if applicable): ____European Society of Coloproctology____

| Section | Checklist item | ✓ | Reported in: (page # or manuscript section) |
|---|---|---|---|
| Protocol | The guideline has been developed according to a protocol and the link to the protocol is provided. | Yes | Methodology document<br>Lines 5-7. We have developed the guideline based on previously published protocol for ESCP guidelines.<br>https://www.escp.eu.com/images/guidelines/documents/Development-ESCP-Guideline-Haemorrhoidal-Disease.pdf |
| Objective | The overall objective(s) of the guideline is (are) specifically described. | Yes | Methodology document<br>Line 12 |
| Health question(s) | The health question(s) covered by the guideline (patient, interventions/procedures, outcomes) are specifically described. | Yes | Methodology document: Line 18<br>Patient/population, intervention, comparison and outcomes (PICO) and Search strategy: Includes all the PICO questions and search terms |
| Methodological support | The guideline reports on whether it was supported by a guideline development committee, including a guideline methodologist. | Yes | Methodology document: Line 47, Line 59 |
| Stakeholder involvement | Representation of professional groups and patients included in the guideline development group is reported. | Yes | Methodology document: Line 281 |
| Target users | The target users of the guideline are specifically described. | Yes | Methodology document: Line 41 |
| Systematic review | The methods that were used to search for evidence are clearly described. | Yes | Methodology document: Line 180 |
| Selection criteria | The criteria for selecting the evidence are clearly described. | Yes | Methodology document: Line 207 and Line 216 |
| Strengths/limitations of evidence | The strengths and limitations of the body of evidence are clearly described. | Yes | Methodology document: Line 264 |
| Patient/public input | The views and preferences of the target population (patients, public, etc.) are reported. | Yes | Methodology document: Line 122, Line 279 |

| Section | Checklist item | ✓ | Reported in: (page # or manuscript section) |
|---|---|---|---|
| Formulation of recommendations | The methods for formulating the recommendations are clearly described. | Yes | Methodology document: Line 251 |
| Link between evidence and recommendations | The health benefits, side effects and risks have been considered in formulating the recommendations. | Yes | Methodology document: Line 235 |
| Link between evidence and recommendations | The link between the recommendations and the supporting evidence is explicitly reported. | Yes | Methodology document: Line 253 |
| Clarity of recommendations | The recommendations are specific and unambiguous. | Yes | Methodology document: Line 260 |
| Alternative options | The different options for management of the condition or health issue are clearly presented. | Yes | Figure 2: Proposed algorithm for treating a fistula with sphincter-preserving procedures |
| Identification of recommendations | Key recommendations are easily identifiable. | Yes | Section 1: Summary of recommendations |
| Resource considerations | The potential resource implications of applying the recommendations have been considered. | Yes | Section 13: Implementation |
| Practice variability | The guideline discusses potential variability in surgical expertise of those performing the interventions/procedures. | Yes | Section 13: Implementation |
| Role of funder | The role of the funding body is described. | Yes | Section 16: Role of funder |
| Conflicts of interest | Competing interests of guideline development group members are reported in detail. | Yes | Section 15: Conflict of interest |
| Facilitators and barriers | The guideline describes facilitators and barriers to its application. | Yes | Section 13: Implementation |
| Update | A procedure for updating the guideline is provided. | Yes | Section 14: Updating |
| Implementation | The guideline provides advice and/or tools on how the recommendations can be put into practice. | Yes | Section 13: Implementation |
| Monitoring | The guideline presents monitoring and/or auditing criteria. | Yes | Section 13: Implementation |