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REVIEW

A meta-analysis of marsupialisation versus none in the treatment of simple fistula-in-ano

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Abstract

Introduction Marsupialisation of post-fistulotomy wounds results in a smaller raw surface area and may improve postoperative outcomes. However, it remains a variable practice. We performed a systematic review and meta-analysis to evaluate the effectiveness of marsupialisation in the treatment of simple fistula-in-ano.

Materials and methods PubMed, EMBASE and Cochrane databases were searched for relevant articles from inception until April 2020. All trials that reported on marsupialisation in anal fistula treatment were included. The primary outcome measure was time to complete healing, while secondary outcomes included recurrence, pain scores and incontinence. Random effects models were used to calculate pooled effect size estimates. A sensitivity analysis was performed.

Results Six randomised controlled trials were included capturing 461 patients. The mean (SD) age of the cohort was 39.31 (± 8.71) years. There were 395 males (85.7%). All fistulae were of the cryptoglandular aetiology. On random effects analysis, marsupialisation was associated with a significantly shorter time to healing compared with no marsupialisation (SMD − 0.97 weeks, 95% CI = − 1.36 to − 0.58, $p < 0.00001$). However, there was no difference in recurrence (RD = − 0.00, 95% CI = − 0.02 to 0.02, $p = 0.72$), pain scores at 24 h (SMD − 0.03, 95% CI = − 0.56 to 0.50, $p = 0.91$) or incontinence (RD = − 0.01, 95% CI = − 0.05 to 0.02, p = 0.42). On sensitivity analysis, focusing exclusively on fistulotomy for simple fistula-in-ano, the results for time to healing, recurrence and incontinence remained similar.

Conclusions Marsupialisation of fistulotomy wounds for simple fistula-in-ano is associated with a significantly shorter healing time, but similar recurrence, pain scores at 24 h and incontinence rates, compared with omitting marsupialisation.

Keywords Marsupialisation · Fistulotomy · Fistula-in-ano · Healing · Incontinence · Recurrence

Introduction

Fistula-in-ano contributes a significant workload in colorectal surgical practice and negatively impacts patients' quality of life [1]. The historical incidence of fistula-in-ano stems from a Finnish population-based study that described 0.86 cases per 10,000/year [2]. However, a study by Zanotti et al. [3] revealed an incidence varying from 1.04 to 2.32 cases per 10,000/year across four European countries. A fistula-in-ano usually results in perianal pain and/or swelling and/or discharge of pus from the external opening [4]. Simple anorectal fistulae have a single external opening and tract, whilst complex fistulae are characterised by multiple skin openings, branched tracts or significant (i.e. ≥ 30%) external sphincter involvement [5]. The aetiology underpinning primary (or idiopathic) fistula-in-ano is sepsis originating from anal glands located in the intersphincteric space (i.e., cryptoglandular theory), whilst secondary anorectal fistulae are associated with Crohn's disease, hidradenitis suppurativa, malignancy, tuberculosis and radiotherapy [5]. The cornerstone of surgical management revolves around the eradication of sepsis, maintenance of continence and prevention of recurrence [6]. For simple fistula-in-ano, this is achieved with fistulotomy (laying open of the entire tract from internal to external opening) or

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fistulectomy (excision of the tract) with or without advancement flaps. However, the latter procedures may result in substantial continence disturbance in complex fistulae [7], and hence, sphincter-sparing techniques are used.

Both fistulotomy and fistulectomy wounds result in raw, unepithelialised tissue that prolongs wound healing and requires serial dressings, thus incurring significant costs together with the added risks of wound sepsis. Marsupialisation is a technique that involves suturing the perianal skin to the edges of the laid open fistula tract and, by doing so, reduces the surface area of unepithelialised tissue and consequently speeds up wound healing [8]. However, its practice remains entirely surgeon-dependent. We aimed to appraise the existing literature on marsupialisation in the treatment of simple fistula-in-ano and perform a systematic review and meta-analysis to evaluate its efficacy.

Materials and methods

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [9] and AMSTAR (Assessing the Methodological Quality of Systematic Reviews) [10] guidelines. A study protocol was published in the Open Science Foundation Registry (DOI 10.17605/OSF.IO/KB9RD; https://osf.io/kb9rd/).

Eligibility criteria

All randomised studies that directly compared marsupialisation versus none of fistulotomy (or fistulectomy) wounds for simple fistulae-in-ano were eligible for inclusion. Unpublished reports and studies that evaluated solely complex, recurrent or horseshoe fistulae were excluded. Studies evaluating sphincter-sparing approaches for fistula-in-ano (such as fibrin glue or plugs) were also excluded as were studies assessing other modalities of treatment (e.g. ligation of fistula tract).

Search strategy

The online databases of Medline, CINAHL, EMBASE, and Cochrane Central Register of Controlled Trials as well as Google Scholar were examined for pertinent studies from inception until April 2020. Studies were restricted to English language. The following medical subject heading (MeSH) terms were used in different combinations as well as free-text words: fistula-in-ano, anal fistula, perianal fistula, fistulotomy, marsupialisation or marsupialization. The related search function in Medline was also used to ensure maximization of results. The last search was carried out on April 30, 2020. Two authors (SMS and LOB) independently assessed the title and abstract of citations, and full texts of potentially eligible studies were retrieved. The bibliographies of the latter studies were further examined for potential additional studies for inclusion.

The primary outcome measure was time to complete healing, while secondary outcomes included recurrence, pain scores at 24 h and incontinence.

Data collection

Data were gathered independently by SMS and LOB onto a password-protected Microsoft Excel Sheet, using a predefined template. The following information was noted from the eligible studies: authors' names, journal, year of publication, gender, mean age, sample size, aetiology of fistulae, inclusion and exclusion criteria, details of fistulotomy and marsupialisation technique, pain scores, time to complete healing, incontinence, recurrence and length of follow-up.

Data analysis

The extracted data were entered into Review Manager software (RevMan, version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) for analysis. For dichotomous parameters (recurrence and incontinence), the risk difference (RD) was analysed with its variance and 95% confidence interval (CI). For continuous variables (time to complete healing and pain scores), the standard mean difference (SMD) together with its 95% CI was calculated. All pooled outcome measures were determined using the random effects model as described by DerSimonian and Laird [11]. The results of each outcome evaluated were displayed on a forest plot with 95% CI. A sensitivity analysis was also performed.

The prevailing heterogeneity between different trials for the studied outcome was calculated by the I^2 inconsistency test. No observed statistical heterogeneity was reflected by a value of 0%, while larger values signified increasing heterogeneity. The risk of bias of the included studies was assessed using the Cochrane Collaboration tool [12] and the methodological quality, using the Jadad score [13]. Publication bias could not be evaluated, as there were fewer than 10 studies included in the final meta-analysis.

Sensitivity analysis

A sensitivity analysis was carried out examining marsupialisation versus no marsupialisation on fistulotomy wounds (excluding fistulectomy wounds) for simple fistula-in-ano only and excluding complex and recurrent fistulae.

Table 1 Clinical characteristics of included studies

Author, year	Number of patients in marsupialisation/non-marsupialisation group	Gender (male: female)	Type of fistula included	Surgical intervention (s)	Mode of anaesthesia and patient position	Technique of marsupialisation	Postoperative analgesia	Follow-up	Jadad score
Ho, 1998	51/52	90:13	Simple only	Fistulotomy only	General and lithotomy	Interrupted polyglactin	Not described	9 months	2
Pescatori, 2006	22/24	28:18	Simple, complex and recurrent	Fistulotomy and fistulectomy	General or spinal and lithotomy	Continuous locking 3-0 Vicryl	Ketorolac 30 mg IV[a] TDS[b] x 24 hours	3–46 months	2
Sahakitrungruang, 2011	25/25	43:7	Simple only	Fistulotomy only	Spinal and prone	Continuous 4-0 Vicryl Rapide	Pethidine 50 mg IM[c] and/or paracetamol 500 mg PO[d]	Not defined	2
Jain, 2012	20/20	34:6	Simple only	Fistulotomy and fistulectomy	General and regional (position not defined)	Interrupted 3-0 catgut sutures	Pethidine 50–100 mg TDS × 24 h followed by PO diclofenac 50 mg BD[e] × 3 days	3 months	3
Chalya, 2013	80/82	150:12	Simple only	Fistulotomy and fistulectomy	General and regional (position not defined)	Interrupted 3-0 catgut sutures	Pethidine 50–100 mg TDS × 24 h followed by PO diclofenac 50 mg BD[e] × 3 days	3 months	2
Anan, 2019	30/30	50:10	Simple only (MRI[f] confirmed)	Fistulotomy only	Spinal and modified lithotomy	Interrupted 3-0 polyglactin	Diclofenac IV (dose unspecified)	6 months	3

[a] Intravenous

[b] Three times daily

[c] Intra muscular

[d] Per oral

[e] Twice daily

[f] Magnetic Resonance Imaging

Table 2 Definition of outcome measures

Author, year	Outcome measures				Use of prophylactic antibiotics
	Complete wound healing	Recurrence	Assessment of VAS pain scores	Continence assessment	
Ho, 1998	Not defined	Not defined	Not measured	Manometry pre- and postoperatively	Not reported
Pescatori, 2006	Not defined	Not defined	At 24 h	Pescatori score	Ceftriaxone
Sahakitrungruang, 2011	Not defined	Not defined	At first defecation	Clinical continence score	Not reported
Jain, 2012	Defined as complete wound epithelialisation	Not defined	At 24 h	3-point Likert scale	Ciprofloxacin and metronidazole
Chalya, 2013	Defined as complete wound epithelialisation	Not defined	At 24 h	3-point Likert scale	Ciprofloxacin and metronidazole
Anan, 2019	Defined as complete wound epithelialisation	Reappearance of fistula within 1 year following complete healing	At 1 week	Wexner score	Not reported

Results

Study selection and characteristics

The initial search yielded 420 citations. Following application of inclusion and exclusion criteria, 8 full-text studies were assessed for eligibility. Of those, 2 were subsequently excluded as they were non-randomised [14], comparing fistulectomy with fistulotomy without marsupialisation [15, (Supplementary Table 1)]. Therefore, 6 trials [16–21] describing a total of 461 patients were included in the final analysis. A flow diagram of the selection process is shown in Fig. 1. The study characteristics are summarised in Table 1. Outcome definitions are summarised in Table 2 (Reviewer≠2, comment 1).

Technique of fistulotomy and marsupialisation

In Anan et al. [16], povidone iodine was injected through the external opening to identify the internal opening. For intersphincteric fistulae, the entire tract was laid open using electrocautery over a fistula probe in the fistulotomy cohort, whilst in low trans-sphincteric fistulae, less than 30% of the EAS was divided. The laid open tract was subsequently curetted. In patients assigned to marsupialisation, the wound

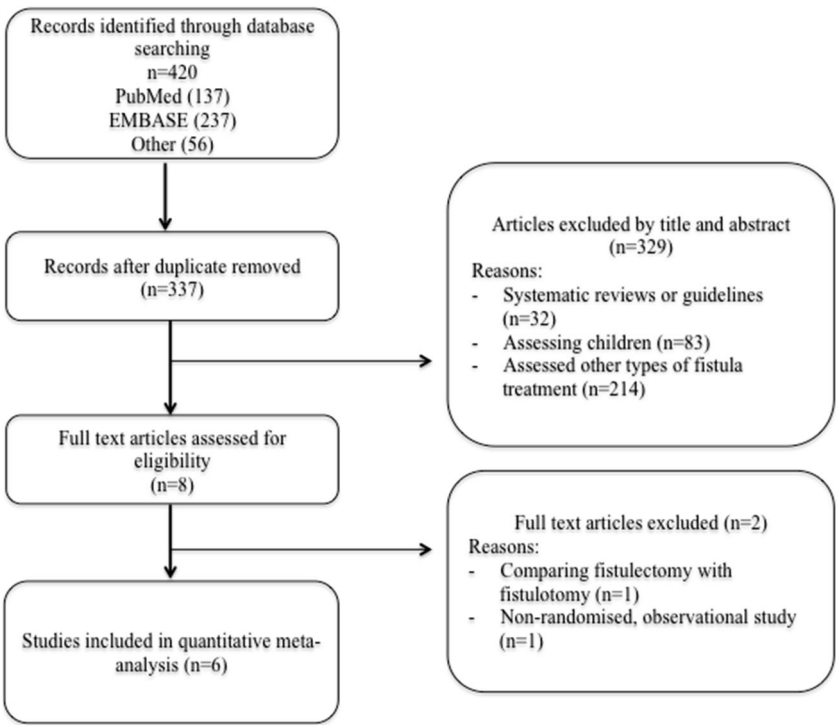

Fig. 1 PRISMA flowchart of search strategy

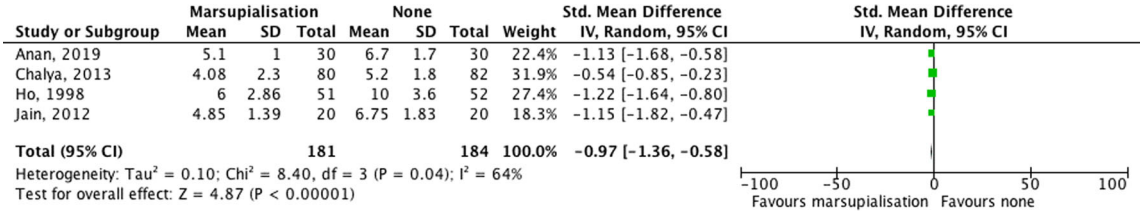

Fig. 2 Meta-analysis of time to complete healing between marsupialisation and no marsupialisation

edges were sutured to the fistula tract with absorbable interrupted 3-0 polyglactin sutures.

In Sahakitrungruang et al. [21], the fistula tracts were curetted following laying open, whilst in the marsupialisation cohort, the wound edges were sutured to the fistula tract using 4-0 Vicryl Rapide in a continuous fashion.

In Pescatori et al. [20], methylene blue was injected to aid identification of the internal opening (s), and the tract was curetted following laying open. In those randomised to marsupialisation, a continuous locking 3-0 Vicryl suture was employed. All wounds were packed with saline and iodine gauze for 48 h.

In Ho et al. [18], following laying open of the tract, the granulation tissue was curetted out. In patients randomised to fistulotomy without marsupialisation, a small amount of perianal skin was excised adjacent the laid open tract to prevent premature healing. Subsequently the wounds were packed with saline gauze for 24 h. In those assigned to marsupialisation, the wound edges were sutured to the laid open tract with interrupted polyglactin.

In Jain [19] and Chalya [17] et al., methylene blue was injected into the external opening to aid identification of the internal opening. In patients randomised to fistulotomy with marsupialisation, the tract was curetted following laying open, and the wound edges were sutured to the tract with interrupted 3-0 catgut sutures.

Risk of bias assessment

Computer-generated randomisation was only carried out in three studies [16, 17, 19] (Reviewer≠1, comment 1), whilst the studies by Chalya [17] and Jain [19] et al. were open-label with no allocation concealment. The study by Anan et al. [16] was single blinded, as patients were unaware of the interventions they underwent. Outcome assessors were also blinded as per the authors.

Further details are shown in the risk of bias summary (Supplementary Fig. 1).

Primary outcome

Time to complete healing

Data were available from 4 studies [16–19] totaling 365 patients. On random effects analysis, marsupialisation is associated with a significantly shorter time to complete healing compared with no marsupialisation (SMD − 0.97 weeks, 95% CI = − 1.36 to − 0.58, $p < 0.00001$; $Chi^2 = 8.40$, (df = 3), $p = 0.04$, $I^2 = 64\%$) (Fig. 2). However, there was a high level of between-study heterogeneity.

Secondary outcomes

Recurrence

Data were available from 5 studies [16–19, 21] totaling 415 patients. On random effects analysis, there is no difference between marsupialisation and omitting marsupialisation (RD − 0.00, 95% CI = − 0.02 to 0.02, $p = 0.72$; $Chi^2 = 1.08$, (df = 4), $p = 0.90$, $I^2 = 0\%$) (Fig. 3). There was no significant statistical heterogeneity observed.

Pain scores (VAS) at 24 h

Data were available from 2 studies [19, 20] totaling 86 patients. On random effects analysis, there is no difference in pain scores between marsupialisation and no marsupialisation (SMD − 0.03, 95% CI = − 0.56 to 0.50, $p = 0.91$; $Chi^2 = 1.56$,

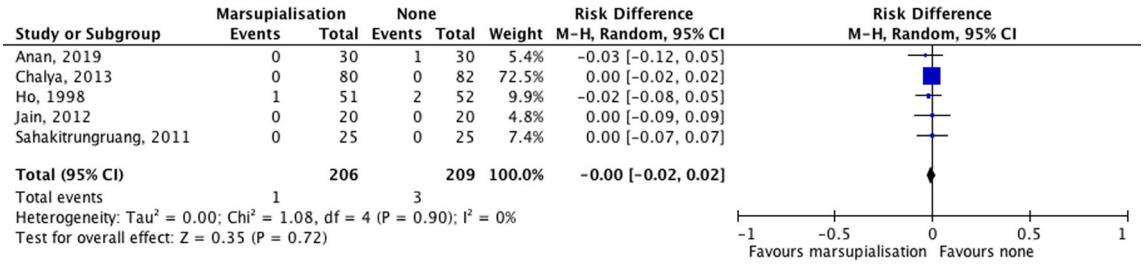

Fig. 3 Meta-analysis of recurrence between marsupialisation and no marsupialisation

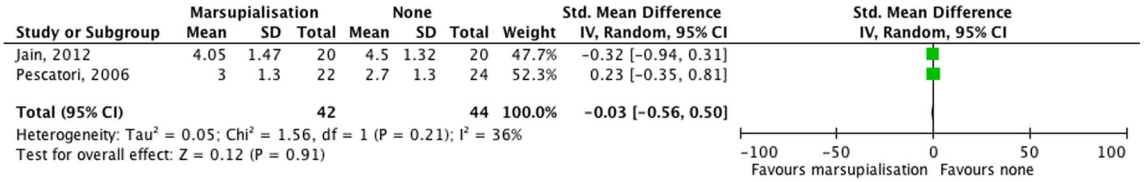

Fig. 4 Meta-analysis of pain scores at 24 hours between marsupialisation and no marsupialisation

(df = 1), $p = 0.21$, $I^2 = 36\%$) (Fig. 4). There was no significant between-study heterogeneity.

Incontinence

Data were available from all 6 studies [16–21] totaling 461 patients. On random effects analysis, there is no difference between marsupialisation and omitting marsupialisation (RD − 0.01, 95% CI = − 0.05 to 0.02, $p = 0.42$; $Chi^2 = 7.26$, (df = 5), $p = 0.20$, $I^2 = 31\%$) (Fig. 5). There was no observed significant heterogeneity.

Sensitivity analysis

After excluding complex/recurrent fistulae-in-ano (the study by Pescatori et al. [20]) and excluding fistulectomy procedures (Jain [19] and Chalya [17] et al.), the results for healing time, recurrence and incontinence prevailed, as shown below. Pain scores could not be evaluated due to insufficient data.

Time to complete healing (sensitivity analysis)

Data were available from 2 studies [16, 18] totaling 163 patients. On random effects analysis, marsupialisation is associated with a significantly shorter time to complete healing compared with no marsupialisation (SMD − 2.74 weeks, 95% CI = − 5.09 to − 0.39, $p = 0.02$; $Chi^2 = 10.68$, (df = 1), $p = 0.001$, $I^2 = 91\%$) (Supplementary Fig. 2). However, there was a high level of between-study heterogeneity.

Recurrence (sensitivity analysis)

Data were available from 3 studies [16, 18, 21] totaling 213 patients. On random effects analysis, there is no difference between marsupialisation and omitting marsupialisation (RD − 0.02, 95% CI = − 0.06 to 0.03, $p = 0.46$; $Chi^2 = 0.35$, (df = 2), $p = 0.84$, $I^2 = 0\%$) (Supplementary Fig. 3). There was no significant statistical heterogeneity observed.

Incontinence (sensitivity analysis)

Data were available from 3 studies [16, 18, 21] totaling 213 patients. On random effects analysis, there is no difference between marsupialisation and omitting marsupialisation (RD − 0.04, 95% CI = − 0.10 to 0.02, $p = 0.22$; $Chi^2 = 3.08$, (df = 2), $p = 0.21$, $I^2 = 35\%$) (Supplementary Fig. 4). There was no observed significant heterogeneity.

Discussion

The current systematic review and meta-analysis, capturing data from 6 randomised controlled trials with 461 patients, demonstrate that marsupialisation of fistula-in-ano wounds is associated with a decreased healing time, but no difference in recurrence, incontinence or pain scores at 24 h. On sensitivity analysis, focusing exclusively on fistulotomy wounds performed for simple fistula-in-ano, the results remained similar. Fistulectomy results in larger wounds than simple fistulotomy alone, consequently requiring longer healing time and therefore represents a confounding variable in the assessment of marsupialisation. Therefore, studies examining fistulectomy were excluded, and hence, the sensitivity analyses reflect purely fistulotomy wounds. However, our findings have to be interpreted with caution given that there was some heterogeneity among the included studies. For example, computer-generated randomisation was explicitly carried out in three studies [16, 17, 19] only, whilst allocation concealment was absent in the two open-label trials [17, 19]. These methodological discrepancies may have introduced bias in the

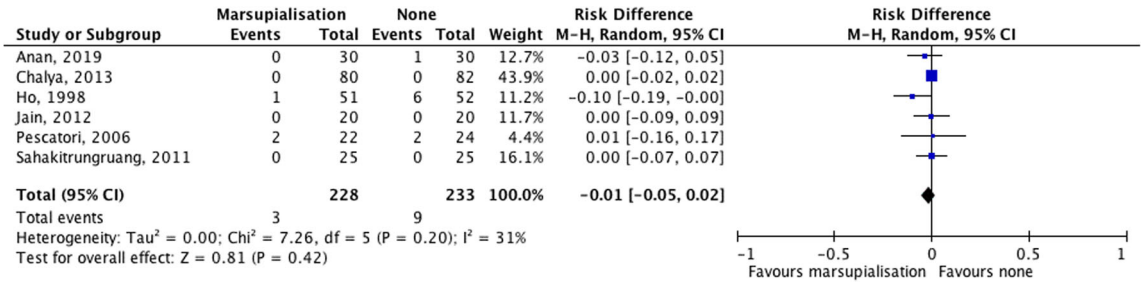

Fig. 5 Meta-analysis of incontinence between marsupialisation and no marsupialisation

observed findings (Reviewer≠1, comment 1). It is important to mention also that two studies [20, 21] employed a continuous absorbable suture for the marsupialisation wound, whilst the remaining four [16–19] used an interrupted absorbable suture. Continuous locking sutures may decrease the dead space underneath the peri-anal skin to a greater extent and hence result into a smaller wound with quicker healing (Reviewer≠2, comment 3). The use, type and duration of antibiotic prophylaxis were dissimilar across studies and may have affected surgical site infection rates and hence wound healing (Reviewer≠2, comment 3). In addition, the postoperative analgesic regimens differed across the trials and hence may have impacted the resultant pain scores.

The practice of marsupialisation remains extremely variable. Whilst the Association of Coloproctology of Great Britain and Ireland (ACPGBI) practice guidelines [22] recommend its use after fistulotomy to accelerate wound healing, the American guidelines [23] do not explicitly promote its adoption. Although fistulotomy is an effective therapeutic modality for the management of simple anorectal fistula, the resulting raw unepithelialised surface demands ongoing wound care and regular dressings and potentially repeated hospital visits for wound examination. Complete wound healing post fistulotomy is not typically achieved before 4 to 6 weeks postoperatively [24] and may even be delayed in the setting of infection. An ideal treatment for simple fistula-in-ano is one that eradicates the fistula without prolonged healing times, maintains continence and prevents fistula recurrence. No such treatment currently exists despite the wide armamentarium of surgical options. Attempts to accelerate the wound healing process after fistulotomy have led to the development of silicate-based dressings [25] as well as the application of topical sucralfate, a cytoprotective agent to anal wounds [26, 27]. However, none of these techniques has been universally adopted yet, and none was employed across the included trials (Reviewer≠1, comment 2).

Our findings demonstrate a shorter healing time associated with marsupialisation after fistulotomy (mean 5.55 vs. 8.35, weeks), which translates into potential cost savings and less patient inconvenience. No differences were observed with respect to recurrence or incontinence. This is unsurprising given that recurrence may be directly attributable to leaving unrecognised secondary fistulous tracts behind, which has no bearing on the technique of marsupialisation. With regard to incontinence, it is postulated that marsupialisation may result in less anal deformity and hence less incontinence. The lack of difference in the observed findings may be explained by dissimilar continence questionnaires employed by the authors. Furthermore, pain scores at 24 h were not significantly different between the 2 groups. However, data on pain scores were only available in 2 studies [19, 20] with a limited number of patients. More importantly, Pescatori et al. [20] used continuous locking sutures, whilst Jain et al. [19] used interrupted stitches.

Our study is not without limitations. Firstly, pain scores were only evaluated at 24 h postoperatively due to unavailable data regarding other time points. Secondly, we did not evaluate the effects of marsupialisation on wound sizes, quality of life scores or complication rates which are important parameters. Total costs of hospital or district health nurse visits for wound dressings were not formally evaluated in any studies (Reviewer≠2, comment 4). Ongoing RCTs (NCT04155905, NCT04215718) may help clarify these. In summary, marsupialisation of fistulotomy wounds for simple anal fistulae is associated with a shorter healing time but similar pain scores, incontinence and recurrence as omitting marsupialisation. We await the results of further high-quality RCTs before making firm recommendations about the adoption of marsupialisation for simple fistula-in-ano wounds.

Authors' contributions: Conceived and designed experiments: SMS
Performed the experiments: SMS, LOB
Analysed the data: SMS, LOB
Wrote the manuscript: All authors

Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

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