OXFORD

BJS Open, 2021, zrab091
DOI: 10.1093/bjsopen/zrab091
Systematic Review

Interventional treatments for prolapsing haemorrhoids: network meta-analysis

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Abstract

Background: Multiple treatments for early–moderate grade symptomatic haemorrhoids currently exist, each associated with their respective efficacy, complications, and risks. The aim of this study was to compare the relative clinical outcomes and effectiveness of interventional treatments for grade II–III haemorrhoids.

Methods: A systematic review was conducted according to PRISMA criteria for all the RCTs published between 1980 and 2020; manuscripts were identified using the MEDLINE, Embase, and CENTRAL databases. Inclusion criteria were RCTs comparing procedural interventions for grade II–III haemorrhoids. Primary outcomes of interest were: symptom recurrence at a minimum follow-up of 6 weeks, postprocedural pain measured on a visual analogue scale (VAS) on day 1, and postprocedural complications (bleeding, urinary retention, and bowel incontinence). After bias assessment and heterogeneity analysis, a Bayesian network meta-analysis was performed.

Results: Seventy-nine RCTs were identified, including 9232 patients. Fourteen different treatments were analysed in the network meta-analysis. Overall, there were 59 RCTs (73 per cent) judged as being at high risk of bias, and the greatest risk was in the domain measurement of outcome. Variable amounts of heterogeneity were detected in direct treatment comparisons, in particular for symptom recurrence and postprocedural pain. Recurrence of haemorrhoidal symptoms was reported by 54 studies, involving 7026 patients and 14 treatments. Closed haemorrhoidectomy had the lowest recurrence risk, followed by open haemorrhoidectomy, suture ligation with mucopexy, stapled haemorrhoidopexy, and Doppler-guided haemorrhoid artery ligation (DG-HAL) with mucopexy. Pain was reported in 34 studies involving 3812 patients and 11 treatments. Direct current electrotherapy, DG-HAL with mucopexy, and infrared coagulation yielded the lowest pain scores. Postprocedural bleeding was recorded in 46 studies involving 5696 patients and 14 treatments. Open haemorrhoidectomy had the greatest risk of postprocedural bleeding, followed by stapled haemorrhoidopexy and closed haemorrhoidectomy. Urinary retention was reported in 30 studies comparing 10 treatments involving 3116 participants. Open haemorrhoidectomy and stapled haemorrhoidopexy had significantly higher odds of urinary retention than rubber band ligation and DG-HAL with mucopexy. Nine studies reported bowel incontinence comparing five treatments involving 1269 participants. Open haemorrhoidectomy and stapled haemorrhoidopexy had the highest probability of bowel incontinence.

Conclusion: Open and closed haemorrhoidectomy, and stapled haemorrhoidopexy were associated with worse pain, and more postprocedural bleeding, urinary retention, and bowel incontinence, but had the lowest rates of symptom recurrence. The risks and benefits of each treatment should be discussed with patients before a decision is made.

Introduction

Haemorrhoids are common and affect up to 38.9 per cent of the adult population[1]. Patients typically experience symptoms such as perianal pain, bleeding after defaecation, discharge, and difficulties with perianal hygiene and prolapse, with a substantial impact on quality of life[2].

The anatomical degree of prolapse for haemorrhoids is based on Goligher's grading[3]. Grade I refers to non-prolapsing haemorrhoids that bleed only. Grade 2 haemorrhoids intermittently prolapse with spontaneous reduction, whereas grade 3 haemorrhoids require manual reduction. Grade IV haemorrhoids are considered most severe; they are permanently prolapsed externally and cannot be reduced manually. Although this grading is used routinely, the anatomical grade of severity does not necessarily correlate with patient-reported symptom severity[4].

The treatment of prolapsing haemorrhoids of grade II–III varies, ranging from office-based procedures to surgical excision, and the choice of intervention can depend on patient or surgeon preference. However, the treatment of choice for grade IV haemorrhoids usually involves a form of surgical excision, such as Milligan–Morgan (open) haemorrhoidectomy, or Ferguson (closed) haemorrhoidectomy. Other techniques such as Doppler-guided haemorrhoid artery ligation (DG-HAL) with mucopexy have also been shown to be effective for grade 4 haemorrhoids[5]. The decision regarding the treatment of haemorrhoids depends on patient or surgeon preference and the availability of resources[6]. This study

Received: January 20, 2021. **Accepted:** August 11, 2021

aimed to assess the available treatments for patients with prolapsing-grade haemorrhoids, excluding studies with permanently prolapsed grade IV haemorrhoids, as the latter are commonly treated with surgical excision, rather than less invasive procedures[5,6].

Given the number of procedures available, the use of a network meta-analysis (NMA) to pool the evidence presented in multiple RCTs simultaneously through direct and indirect comparisons could provide a comprehensive insight. RCTs usually compare the treatment efficacy of two treatments directly, resulting in difficulty in gauging each treatment's relative effectiveness and complication profiles when comparing numerous treatments. Therefore, this systematic review and NMA aimed to compare the clinical outcomes and effectiveness of interventional treatments for grade II–III haemorrhoids.

Methods

This systematic review and NMA was conducted in accordance with the PRISMA guidelines, with extension for network meta-analysis (NMA)[7,8].

Search strategy

The MEDLINE, Embase, and Cochrane Central Register of Clinical Trials (CENTRAL) were searched systematically using a comprehensive search strategy involving free text and Medical Subject Headings. The complete search string is included in the study protocol (*Appendix S1*). Articles were restricted to those published in the English language between 1 January 1980 and 15 September 2020. RCTs comparing interventional treatments for patients with grade II or III haemorrhoids were considered for inclusion. Studies that had participants with grade I haemorrhoids were also included as long as over 50 per cent of study participants had grade II or III haemorrhoids. Studies were excluded if more than 3 per cent of the total study population had grade IV haemorrhoids.

Only studies reporting on interventional treatments in an elective setting were included; studies documenting treatments for haemorrhoids in the emergency setting were excluded, as were those reporting on medical treatments for haemorrhoids.

Study selection and data collection

The RCTs for inclusion were identified by two review authors by independent screening of titles and abstracts. Full texts of potentially included studies were then sought and further selection for inclusion was undertaken independently by two review authors, based on the full text. Consensus among the review authors was required before inclusion of each study, and any discrepancies were adjudicated by a senior author.

The following data were extracted from each study independently by two review authors: study characteristics (first author, year of publication, and country), selection criteria (inclusion and exclusion criteria), participant characteristics (sample size, haemorrhoid grade), interventional treatments compared, and outcome measures. Any discrepancies in extracted data were resolved by discussion, and a final decision was taken by the senior author.

Outcomes of interest

The primary outcomes were symptom recurrence, postprocedural pain, and postprocedural complications. Symptom recurrence was defined according to the patient's self-reported symptoms at a minimum follow-up of 6 weeks after the procedure. Postprocedural pain was measured on day 1 using a visual analogue scale (VAS). Postprocedural complications, defined as any deviation from the normal postprocedural course, were also included in the outcomes. The complications analysed included postprocedural bleeding, urinary retention, and bowel incontinence. Secondary outcomes were repeat treatment, length of hospital stay and time to return to work or resumption of normal activity. Repeat treatment was defined as any additional treatment required within the postprocedure follow-up interval and included a repeat of the same treatment or a different treatment.

Bias assessment

The Cochrane Collaboration's risk-of-bias tool 2.0[9] was used to assess the risk of bias in included RCTs based on the following domains: randomization process, deviation from intended interventions, missing outcome data, measurement of outcome, and selection of reported result. For each of these risk domains, studies were categorized as having either a low, uncertain or high risk of bias. The overall risk of bias was calculated according to the algorithm's overall judgement.

Statistical analysis

An intention-to-treat Bayesian NMA with a non-informative prior was undertaken in R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria)[10].

For each outcome, a network plot of all treatments assessed was constructed to visually represent all direct comparisons between included interventional treatments. Nodes on the network plot were used to depict the number of participants receiving a particular treatment and the thickness of each connecting line correlated with the number of studies assessing a particular direct comparison. Interventional treatments assessed in only one study and not connected to at least two treatments through the network plot were excluded from the analysis of that outcome to minimize bias resulting from single-trial effects. Rubber band ligation (RBL) was used as the reference treatment in the network plot for all outcomes. Continuity corrections were applied to dichotomous (categorical) outcomes with no events, by adding an arbitrary constant of 1 to both the numerator and denominator of each treatment arm[11]. Where continuous data were presented as median and range or interquartile range, mean and standard deviation estimates were calculated[12,13]. If the standard deviation was not reported, it was calculated from the standard error, *P* value, confidence interval or interquartile range according to guidance in the *Cochrane Handbook for Systematic Reviews of Interventions*[14]. Standard deviations that could not be calculated were imputed using the largest value in other trials for that outcome. Categorical and continuous outcomes were reported as an odds ratio (OR) and mean difference (MD) respectively, with 95 per cent credible interval (CrI). Final results for each outcome were illustrated in a league table, showing OR or MD (with 95 per cent CrI) for each treatment comparison, surface under the cumulative ranking (SUCRA) curve, indicating each treatment ranking with its respective ranking probability, and forest plot, illustrating the OR (or MD) of each treatment relative to a reference treatment[15]. SUCRA values range from 0 to 100 per cent; higher values indicate a greater likelihood of a particular treatment being in a top rank, whereas lower values mean a particular treatment is more likely to be in a bottom rank[16]. A node-splitting analysis was conducted to assess for inconsistency between direct and indirect treatment comparisons in each network[17]. Heterogeneity owing to differences between studies within each direct treatment comparison was evaluated by the I^2

statistic; a value of more than 50 per cent was indicative of significant heterogeneity between the studies[18].

For each outcome, analyses were performed using both fixed- and random-effects NMA models. The goodness of fit of each model was assessed by means of leverage plots displaying the corresponding effective number of parameters, total residual deviance, and deviance information criterion (DIC)[19]. DIC values were compared and the model with the lower value (fewer outliers on visual examination of the leverage plot) was chosen. In most instances, a random-effects model was used, which assumes variation between studies owing to heterogeneity and generates a wider CrI.

An NMA relies on the assumption of transitivity, which refers to potential modifiers of the treatment effect being distributed equally across all included RCTs[20]. In the present NMA, the transitivity assumption was analysed by collecting and comparing data on potential modifiers of the outcomes such as participant age, sex, grade of haemorrhoids, geographical location of studies, and duration of follow-up, in each direct treatment comparison.

Sensitivity analyses were also undertaken, including only studies comparing treatments for patients with grade II and grade III haemorrhoids, recognizing that the initial treatment for grade I haemorrhoids is seldom surgical, and so studies including patients with grade 1 haemorrhoids were excluded.

Results

In total, 2367 articles were screened for relevance based on title and/or abstract. After full-text assessment, 79 RCTs[21–99] were included, with 9232 patients. Thirty-three full-text articles were excluded based on the inclusion of a significant number of participants with grades I and IV haemorrhoids (*Fig. 1*). *Table 1* provides a summary of the studies included in the NMA.

Risk-of-bias analysis

The risk of bias of included RCTs is summarized in *Fig. 2* and described for each study in *Appendix S2*. Bias was mostly attributable to lack of blinding among the outcome observers, in 52 RCTs (64 per cent). Overall, 59 trials (73 per cent) were judged as being at high risk of bias, and the domain showing the greatest risk was measurement of outcome.

Risk of heterogeneity and inconsistency

There were variable amounts of heterogeneity between studies within particular direct treatment comparisons for each outcome. For symptom recurrence, significant heterogeneity was detected among direct comparisons between RBL *versus* injection sclerotherapy (IJS) and Milligan–Morgan *versus* laser haemorrhoidectomy. Postprocedural pain was associated with significant heterogeneity among multiple direct treatment comparisons. There were few comparisons with significant heterogeneity for repeat treatment, duration of hospital stay, time off work, postprocedural bleeding, urinary retention, and bowel incontinence (*Appendix S3*). The node-splitting analysis revealed few instances of inconsistency in the overall network. For symptom recurrence, it revealed an overall consistent profile except for two instances of inconsistency in the network, which were mainly attributable to direct comparisons between laser haemorrhoidectomy *versus* open haemorrhoidectomy and laser haemorrhoidectomy *versus* RBL. For

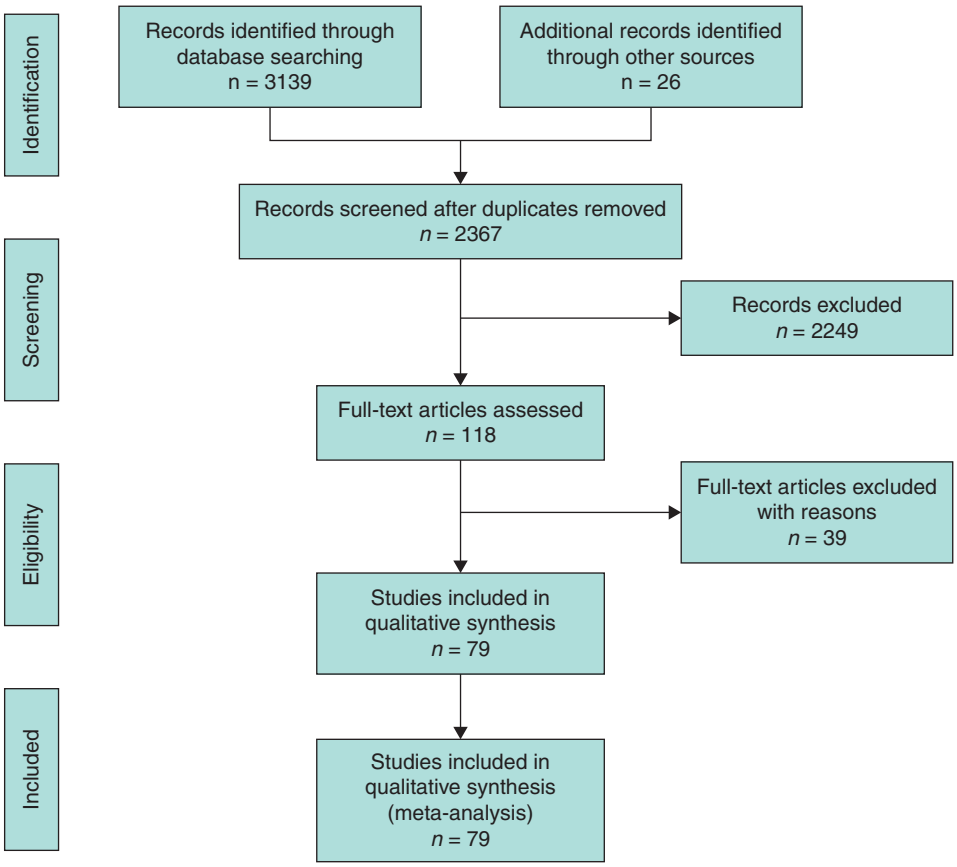

Fig. 1 PRISMA flow diagram showing selection of articles for review

Table 1 Summary of included studies

Reference	Treatments compared	Haemorrhoid grade			Total
		I	II	III	
Abiodun *et al.* (2020)[21]	RBL *versus* IJS		25	35	60
Ahmad *et al.* (2011)[22]	DG-HAL *versus* IRC		123	122	245
Aigner *et al.* (2016)[23]	DG-HAL *versus* SL-M			40	40
Ali *et al.* (2005)[24]	RBL *versus* MM		50	50	100
Ambrose *et al.* (1983)[25]	IRC *versus* RBL	60	195		255
Ambrose *et al.* (1985)[26]	IRC *versus* IJS	43	92		135
Ammaturo *et al.* (2012)[27]	SH *versus* MM			79	79
Arbman *et al.* (2000)[28]	MM *versus* FH		21	55	76
Arslani *et al.* (2012)[29]	SH *versus* LigaH^{TM}			98	98
Ashgar Khan *et al.* (2013)[30]	MM *versus* RBL		60	60	120
Awad *et al.* (2012)[31]	RBL *versus* IJS		66	52	118
Brown *et al.* (2016)[32]	DG-HAL *versus* RBL		207	128	335
Cestaro *et al.* (2013)[33]	RBL *versus* IJS		36	36	72
Cheng *et al.* (1981)[34]	IJS *versus* RBL *versus* MAD *versus* MM		120		120
Chung *et al.* (2005)[35]	HarS *versus* SH			88	88
De Nardi *et al.* (2014)[36]	DG-HAL *versus* MM			50	50
Elshazly *et al.* (2015)[37]	MM *versus* SL-M		138	62	200
Filgate *et al.* (2019)[38]	HET *versus* RBL		30		30
Filingeri *et al.* (2012)[39]	RBL *versus* CHR		90		90
Filingeri *et al.* (2013)[40]	RFC *versus* CHR		30		30
Gagloo *et al.* (2013)[41]	RBL *versus* MM		62	38	100
Gartell *et al.* (1985)[42]	RBL *versus* IJS	67	111	40	218
Giamundo *et al.* (2011)[43]	DG-HAL *versus* RBL		39	21	60
Greca *et al.* (1981)[44]	RBL *versus* IJS	7	67	8	82
Gupta (2003)[45]	RFC *versus* MM				n.r.
Gupta (2003)[46]	RBL *versus* IRC		100		100
Gupta (2004)[47]	RFC *versus* RBL		80		80
Gupta *et al.* (2009)[48]	SL-M *versus* RFC/SL-M			128	128
Gupta *et al.* (2011)[49]	SL-M *versus* DG-HAL			48	48
Hetzer *et al.* (2002)[50]	SH *versus* FH		12	28	40
Hinton *et al.* (1990)[51]	DCV *versus* BPC			50	50
Huang *et al.* (2007)[52]	SH *versus* FH			596	596
Infantino *et al.* (2012)[53]	SH *versus* DG-HAL			169	169
Izadpanah and Hosseini (2005)[54]	FH *versus* DCV	63	246	99	408
Jamjoom and Jamal (1991)[55]	RBL *versus* IJS *versus* CRY		848		848
Jensen *et al.* (1997)[56]	BPC *versus* HET		32	49	81
Jutabha *et al.* (2009)[57]	RBL *versus* BPC		16	29	45
Kairaluoma *et al.* (2003)[58]	SH *versus* MM			60	60
Kanellos *et al.* (2003)[59]	RBL *versus* IJS *versus* RBL-IJS		243		243
Khalil *et al.* (2000)[60]	FH *versus* SH			40	40
Khan *et al.* (2001)[61]	MM *versus* HarS		15	15	30
Khan and Malik (2006)[62]	IJS *versus* BPC	51	51		102
Kim *et al.* (2014)[63]	SH *versus* MM			122	122
Lau *et al.* (2004)[64]	MM *versus* SH		13	12	25
Leardi *et al.* (2016)[65]	DG-HAL *versus* SH			100	100
Lehur *et al.* (2016)[66]	DG-HAL *versus* SH		91	302	393
Leung *et al.* (2017)[67]	TST *versus* DG-HAL		40	40	80
Lewis *et al.* (1983)[68]	MM *versus* MAD *versus* RBL *versus* CRY		46	66	112
Liu *et al.* (2019)[69]	RBL *versus* RBL-IJS		160	140	300
Marques *et al.* (2006)[70]	RBL *versus* IRC	46	48		94
Mikuni *et al.* (2002)[71]	MM *versus* SOH			34	34
Murie *et al.* (1980)[72]	FH *versus* RBL		44	43	87
Naderan *et al.* (2017)[73]	LASER *versus* MM		23	27	50
Nasir *et al.* (2017)[74]	RBL *versus* IJS		42	44	86
Nikooiyan *et al.* (2016)[75]	DCV *versus* FH				n.r.
Nikshoar *et al.* (2018)[76]	IRC *versus* FH			40	40
Nyström *et al.* (2010)[77]	SH *versus* MM			178	178
Parveen *et al.* (2019)[78]	IJS *versus* RBL	26	64		90
Poen *et al.* (2000)[79]	RBL *versus* IRC	89	35	9	133
Poskus *et al.* (2020)[80]	LASER *versus* FH *versus* SL-M		27	94	121
Quah and Seow-Choen (2004)[81]	MM *versus* BPC				n.r.
Randall *et al.* (1994)[82]	DCV *versus* BPC		30	58	88
Ricci *et al.* (2008)[83]	IRC *versus* RBL	12	30	6	48
Rowsell *et al.* (2000)[84]	FH *versus* SH			22	22
Saeed *et al.* (2017)[85]	MM *versus* RBL		60	80	140
Schuurman *et al.* (2012)[86]	SL-M *versus* DG-HAL		36	37	73
Senagore *et al.* (1993)[87]	LASER *versus* MM			86	86
Senagore *et al.* (2004)[88]	SH *versus* FH			146	146
Shabahang *et al.* (2019)[89]	MM *versus* LASER		54	26	80

(continued)

Table 1. (continued)

Reference	Treatments compared	Haemorrhoid grade			Total
		I	II	III	
Shanmugaiah and Selvam (2020)[90]	RBL *versus* IJS		72		72
Shanmugam *et al.* (2010)[91]	RBL *versus* SH		60		60
Templeton *et al.* (1983)[92]	IRC *versus* RBL	137	82	55	274
Tsunoda *et al.* (2017)[93]	DG-HAL *versus* HarS			41	41
Van de Stadt *et al.* (2005)[94]	MM *versus* SH		20	20	40
Varma *et al.* (1991)[95]	IJS *versus* BPC				n.r.
Walker *et al.* (1990)[96]	IRC *versus* IJS	165	87	78	330
Wilson *et al.* (2002)[97]	MM *versus* SH			89	89
Yang *et al.* (1993)[98]	DCV *versus* BPC	25	20	5	50
Zhai *et al.* (2016)[99]	SH *versus* DG-HAL			100	100

RBL, rubber band ligation; IJS, injection sclerotherapy; DG-HAL, Doppler-guided haemorrhoid artery ligation with mucopexy; SL-M, suture ligation with mucopexy; MM, Milligan–Morgan (open) haemorrhoidectomy; IRC, infrared coagulation; SH, stapled haemorrhoidopexy; FH, Ferguson (closed) haemorrhoidectomy; LigaH, LigaSure™ haemorrhoidectomy; MAD, maximal anal dilatation; HarS: Harmonic® scalpel haemorrhoidectomy; HET, haemorrhoid energy therapy; CHR, combined haemorrhoidal radiocoagulation; RFC, radiofrequency coagulation; n.r., not reported; DCV, direct current electrotherapy; BPC, bipolar coagulation; CRY, cryotherapy; RBL-IJS, combined rubber band ligation and injection sclerotherapy; TST, tissue-selecting technique; SOH, semi-open haemorrhoidectomy; LASER, laser haemorrhoidectomy.

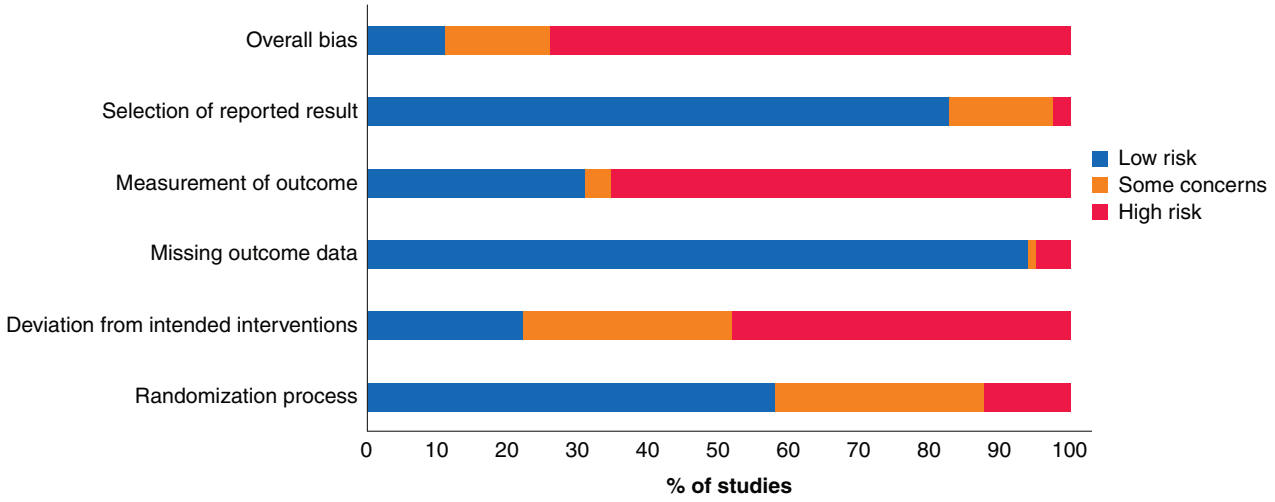

Fig. 2 Cochrane risk-of-bias 2.0 summary chart

the repeat treatment outcome, the node-splitting analysis revealed inconsistencies in the network that were attributable to direct comparisons between bipolar coagulation (BPC) *versus* infrared coagulation (IRC) and BPC *versus* open haemorrhoidectomy.

Comparison of procedural treatments

The following elective interventions and procedures were identified for the treatment of predominantly grade II and/or III haemorrhoids: open haemorrhoidectomy performed with a scalpel, conventional scissors or diathermy; closed haemorrhoidectomy performed with a scalpel, conventional scissors or diathermy; stapled haemorrhoidectomy (SH), haemorrhoidopexy or the Longo procedure for prolapsed haemorrhoids; transanal haemorrhoid dearterialization with mucopexy or DG-HAL with mucopexy or performed without Doppler; haemorrhoidectomy using a radiofrequency device; haemorrhoidectomy using a LigaSure™ device (Medtronic, Minneapolis, MN, USA); Harmonic® (Johnson and Johnson, Raritan, NJ, USA) or ultrasonic scalpel haemorrhoidectomy; laser haemorrhoidectomy with a Nd : YAG or carbon dioxide laser; suture ligation or mucopexy on its own; RBL; IJS; IRC Bipolar Coagulation; direct current electrotherapy (DCV) at 16 or 30 mA; semi-open haemorrhoidectomy; cryotherapy; and use of a heater probe[21–99].

The league tables, SUCRA plot, and forest plot for all comparisons of interventional treatments for each of the outcomes are shown in *Table 2* and *Appendix S4*.

Analysis of transitivity

There was variation in the grade of haemorrhoids included in the treatment comparisons across the studies. Treatment comparisons in patients with grade 1 haemorrhoids also varied, and included RBL, IRC, IJS, BPC, and DCV. Other studies contained a varying proportion of patients with grade II and III haemorrhoids. The duration of follow-up ranged from 6 weeks to 5 years. Participant age and the proportion of female participants did not vary across the included studies. However, the geographical location of the studies was diverse, with most conducted in Europe. Study characteristics are summarized in *Fig. 3*.

Primary outcomes

Symptom recurrence

Fifty-four studies comparing 14 treatments across 7026 participants were analysed in the network, with 29 unique direct comparisons (*Figs 4* and *S1*). A random-effects model was performed based on the lower DIC statistic. Compared with RBL, closed haemorrhoidectomy (OR 0.16, 95 per cent CrI 0.04 to 0.68), suture

Table 2 Overall summary of surface under cumulative ranking scores across outcomes

	SUCRA score							
	Recurrence	Pain on visual analogue scale	Repeat treatment	Prolonged hospital stay	Time off work	Postprocedural bleeding	Urinary retention	Bowel incontinence
BPC	0.55	–	–	–	–	0.43	–	–
CRY	0.38	–	–	–	–	–	–	–
DCV	0.40	–	–	–	–	0.92	–	–
DG-HAL	0.59	0.78	0.56	0.79	0.62	0.17	0.29	0.70
FH	0.92*	0.05	–	0.17	0.34	0.39	0.48	–
HarS		0.24	–	0.75	0.26	0.15	0.55	–
IJS	0.14	–	0.15	–	–	0.75	0.71	–
IRC	0.21	0.92*	0.13	0.59	–	0.68	0.74	–
LASER	0.26	0.42	0.00	0.40	0.63	0.64	0.71	–
LigaH	–	0.53	–	–	–	–	–	–
MM	0.85	0.09	0.93*	0.35	0.19	0.22	0.18	0.23
RBL	0.34	0.47	0.45	0.80*	0.93*	0.71	0.77*	0.83*
RBL-IJS	0.63	–	0.31	–	–	0.93*	–	–
RFC	0.17	0.77	–	–	–	0.30	–	–
SH	0.69	0.52	0.76	0.80*	0.64	0.24	0.12	0.05
SL-M	0.86	0.71	0.88	0.11	0.20	0.46	0.46	0.69

The higher the SUCRA score, the lower the likelihood of that outcome. *Best intervention for that outcome. BPC, bipolar coagulation; CRY, cryotherapy; DCV, direct current electrotherapy; DG-HAL, Doppler-guided haemorrhoid artery ligation with mucopexy; FH, Ferguson (closed) haemorrhoidectomy; HarS, Harmonic® scalpel haemorrhoidectomy; IJS, injection sclerotherapy; IRC, infrared coagulation; LASER, laser haemorrhoidectomy; LigaH, LigaSure™ haemorrhoidectomy; MM, Milligan–Morgan (open) haemorrhoidectomy; RBL, rubber band ligation; RBL-IJS, combined rubber band ligation and injection sclerotherapy; RFC, radiofrequency coagulation; SH, stapled haemorrhoidopexy; SL-M, suture ligation with mucopexy.

ligation with mucopexy (OR 0.24, 0.08 to 0.74), open haemorrhoidectomy (OR 0.27, 0.12 to 0.58), and SH (OR 0.41, 0.18 to 0.98) showed a significantly decreased odds of symptom recurrence (*Figs 5* and *S1*). The highest SUCRA scores, representing treatments associated with the least symptom recurrence, were 0.93 (closed haemorrhoidectomy), 0.86 (suture ligation and mucopexy), and 0.85 (open haemorrhoidectomy). IJS ranked as the treatment associated with the most symptom recurrence, with a SUCRA score of 0.14 (*Table 2*).

Postprocedural pain

Thirty-four studies comparing 11 treatments across 3812 participants were analysed for pain using a VAS on day 1 after operation. A random-effects model was chosen based on the lower DIC statistic. Compared with RBL, open (MD 1.64, 95 per cent CrI 0.15 to 3.04) and closed (MD 1.97, 0.28 to 3.58) haemorrhoidectomy were associated with significantly more postprocedural pain. There were no significant differences in postprocedural pain on the VAS in comparisons between the eight remaining treatment modalities, which were IRC, DG-HAL, radiofrequency coagulation, suture ligation with mucopexy, LigaSure™ haemorrhoidectomy, SH, and laser haemorrhoidectomy (*Fig. S2*). The highest SUCRA scores, representing the least painful treatments, were 0.92 (IRC), 0.78 (DG-HAL), and 0.77 (radiofrequency coagulation). Closed haemorrhoidectomy ranked as the most painful treatment, with a SUCRA score of 0.05 (*Table 2*).

Postprocedural bleeding

Forty-six studies reported post-procedural bleeding, in which 14 treatments were compared across 5696 participants. A random-effects model was used based on the lower DIC statistic. Compared with RBL, open haemorrhoidectomy (OR 3.66, 95 per cent CrI 1.79 to 7.00), SH (OR 4.53, 1.46 to 11.56), and DG-HAL (OR 5.82, 1.43 to 17.02) were associated with a significantly higher odds of postprocedural bleeding (*Fig. S3*). The highest SUCRA scores, reflecting the lowest postprocedural bleeding rates, were 0.93 (RBL and IJS combined), 0.92 (DCV), and 0.75 (IJS). Harmonic® scalpel haemorrhoidectomy ranked as the treatment reflecting the highest rate of postprocedural bleeding, with a SUCRA score of 0.15 (*Table 2*).

Urinary retention

Thirty studies reported urinary retention, comparing 10 treatments across 3116 participants. A random-effects model was used based on the lower DIC statistic. Compared with RBL, DG-HAL (OR 6.73, 95 per cent CrI 1.09 to 22.99), open haemorrhoidectomy (OR 7.71, 2.37 to 19.20), and SH (OR 9.56, 2.13 to 28.17) were associated with a significantly higher odds of urinary retention (*Fig. S4*). The highest SUCRA scores, reflecting treatments least likely to result in urinary retention, were 0.77 (RBL) and 0.74 (IRC). SH ranked as being most likely to result in urinary retention, with a SUCRA score of 0.12 (*Table 2*).

Bowel incontinence

Five treatments were compared among nine studies with 1269 patients. A fixed-effects model was used based on the lower DIC statistic. Compared with RBL, open haemorrhoidectomy (OR 4.42, 95 per cent CrI 1.04 to 32.42) and SH (OR 6.96, 1.30 to 58.49) were significantly more likely to result in bowel incontinence. SH also resulted in significantly more bowel incontinence than DG-HAL (OR 4.43, 1.66 to 12.80) or suture mucopexy (OR 4.34, 1.33 to 15.72) (*Fig. S5*). The lowest SUCRA scores, reflecting the treatments most likely to result in bowel incontinence, were 0.05 (SH) and 0.23 (open haemorrhoidectomy) (*Table 2*).

Secondary outcomes

Appendix S4 shows the network plot, league table, SUCRA plot, and SUCRA table for all secondary outcomes.

Repeat treatment

Eighteen studies compared seven different treatments involving 2819 participants. A random-effects model was used based on the lower DIC statistic. Compared with RBL, open haemorrhoidectomy was associated with a significantly lower odds of repeat treatment (OR 0.12, 95 per cent CrI 0.01 to 0.48), whereas bipolar

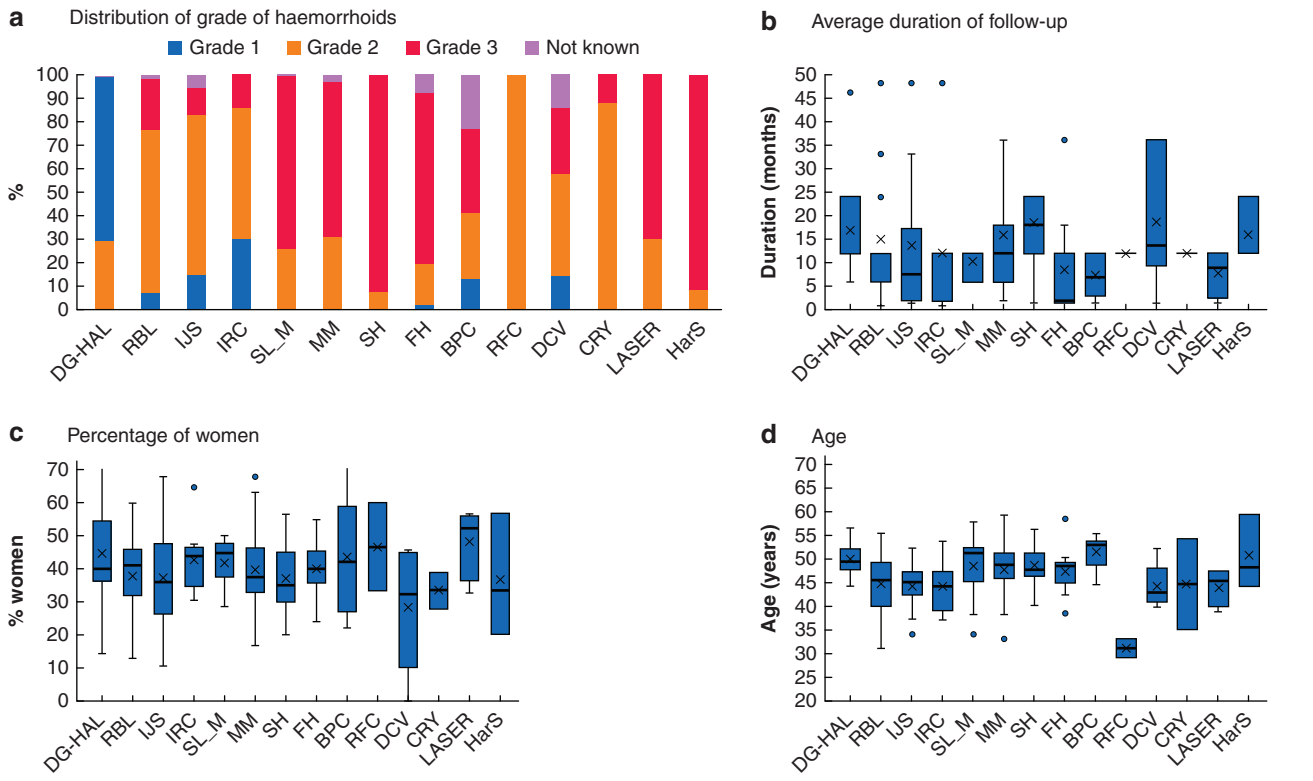

Fig. 3 Analysis of transitivity across included treatments

a Distribution of grade of haemorrhoids, **b** average duration of follow-up, **c** percentage of women, and **d** average age distribution of participants. DG-HAL, Doppler-guided haemorrhoid artery ligation with mucopexy; RBL, rubber band ligation; IJS, injection sclerotherapy; IRC, infrared coagulation; SL-M, suture ligation with mucopexy; MM, Milligan–Morgan (open) haemorrhoidectomy; SH, stapled haemorrhoidopexy; FH, Ferguson (closed) haemorrhoidectomy; BPC, bipolar coagulation; RFC, radiofrequency coagulation; DCV, direct current electrotherapy; CRY, cryotherapy; LASER, laser haemorrhoidectomy; HarS, Harmonic® scalpel haemorrhoidectomy. In **b–d**, Median (crosses), median values (bold lines), i.q.r. (boxes), and range excluding outliers (circles) are shown.

coagulation (OR 39.47, 1.09 to 228.61) and DCV (OR 62.61, 1.11 to 363.35) were associated with a significantly higher odds of repeat treatment (*Fig. S6*). The lowest SUCRA scores, reflecting treatments most likely to result in repeat treatment, were IRC (0.13) and IJS (0.15). The highest SUCRA scores reflecting treatments least likely to result in repeat treatment were 0.99 (open haemorrhoidectomy) and 0.81 (SH) (*Table 2*).

Duration of hospital stay

Twenty-one studies reported duration of inpatient hospital admission, with 10 treatment comparisons and 2907 participants. The mean length of stay across the network was 1.6 days. A random-effects model was used based on the lower DIC statistic. Compared with RBL, closed haemorrhoidectomy (MD 1.20, 95 per cent CrI 0.32 to 2.09) and suture ligation with mucopexy (MD 1.41, 0.04 to 2.80) were associated with a significantly longer hospital admission (*Fig. S7*). The highest SUCRA scores, representing treatments with the shortest hospital admission, were 0.80 (RBL and SH) and 0.79 (DG-HAL). Closed haemorrhoidectomy ranked as the treatment associated with the longest hospital admission, with a SUCRA score of 0.17 (*Table 2*).

Time off work

Eighteen studies reported time off work, comparing nine treatments with a total of 2103 participants. The mean time off work across the network was 14.7 days. A random-effects model was used based on the lower DIC statistic. Compared with RBL, closed haemorrhoidectomy (MD 13.24, 95 per cent CrI 0.78 to 26.21), Harmonic® scalpel haemorrhoidectomy (MD 15.79, 1.47 to 30.34), open haemorrhoidectomy (MD 15.36, 4.35 to 26.64), and bipolar coagulation (MD 20.05, 0.72 to 39.73) were associated with significantly longer time off work (*Fig. S8*). The highest SUCRA score, reflecting the treatment associated with the least time off work, was 0.93 (RBL). Open haemorrhoidectomy ranked as the treatment associated with the most time off work, with a SUCRA score of 0.19 (*Table 2*).

Sensitivity analysis

A sensitivity analysis of symptom recurrence was analysed for 45 studies with 5337 participants comparing 14 treatments. A random-effects model was chosen based on the lower DIC value. Overall, there was no significant difference in the results compared with the initial analysis (*Fig. S9*). A sensitivity analysis was conducted for postprocedural bleeding, in which 38 studies compared 14 treatments, involving 4482 participants. A fixed-effects model was chosen based on the lower DIC value. Overall, the results of the sensitivity analysis showed no significant difference compared with the main analysis (*Fig. S10*). No studies reporting on postprocedural pain on the VAS, urinary retention, bowel incontinence, repeat treatment, duration of hospital stay or time off work were omitted as none included grade I haemorrhoids.

Discussion

This systematic review and NMA compared treatment modalities ranging from minimally invasive, clinic-based procedures to excisional therapy requiring anaesthesia for prolapsing haemorrhoids.

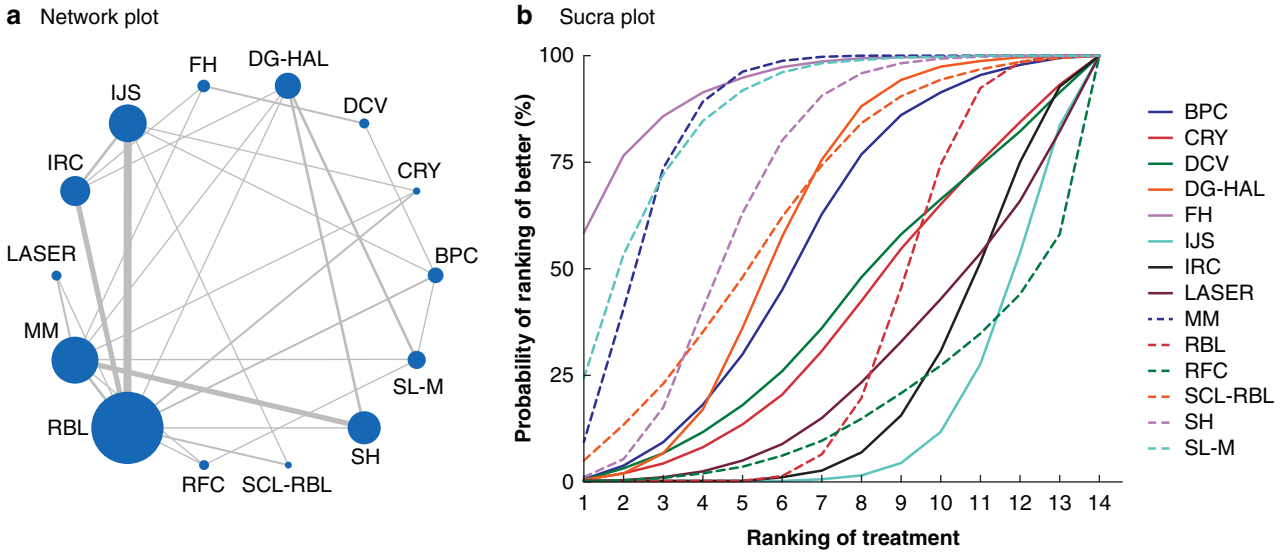

Fig. 4 Network plot and surface under cumulative ranking curves for recurrence

a Network plot of studies analysed for the outcome recurrence. The nodes represent the number of participants receiving each treatment, and the line thickness represents the number of studies assessing each direct treatment or procedure comparison. **b** Surface under cumulative ranking (SUCRA) plot and treatments. Higher rankings are associated with smaller outcome values; BPC, bipolar coagulation; CRY, cryotherapy; DCV, direct current electrotherapy; DG-HAL, Doppler-guided haemorrhoid artery ligation with mucopexy; FH, Ferguson (closed) haemorrhoidectomy; IJS, injection sclerotherapy; IRC, infrared coagulation; LASER, laser haemorrhoidectomy; MM, Milligan–Morgan (open) haemorrhoidectomy; RBL, rubber band ligation; RFC, radiofrequency coagulation; SCL-RBL, combined injection sclerotherapy and rubber band ligation; SH, stapled haemorrhoidopexy; SL-M, suture ligation with mucopexy.

Treatment

Comparator	FH	SL-M	MM	SM	SCL-RBL	DG-HAL	BPC	DCV	CRY	RBL	LASER	IRC	RFC	IJS
FH		1.48 (0.27, 7.90)	1.64 (0.40, 6.77)	2.56 (0.56, 11.60)	2.95 (0.46, 17.67)	3.25 (0.68, 14.95)	3.63 (0.79, 16.15)	5.24 (1.52, 18.13)*	5.60 (0.89, 34.57)	6.20 (1.47, 25.73)*	7.78 (1.27, 48.73)*	8.18 (1.87, 36.08)*	11.19 (1.42, 87.60)*	9.66 (2.12, 42.77)*
SL-M	0.68 (0.13, 3.67)		1.11 (0.36, 3.55)	1.73 (0.55, 5.76)	1.98 (0.40, 9.97)	2.17 (0.77, 6.43)	2.46 (0.67, 9.16)	3.55 (0.63, 20.78)	3.80 (0.75, 19.23)	4.20 (1.36, 13.11)*	5.28 (1.07, 27.20)*	5.50 (1.67, 19.11)*	7.50 (1.43, 44.33)*	6.51 (1.94, 22.18)*
MM	0.61 (0.15, 2.53)	0.90 (0.28, 2.76)		1.56 (0.77, 3.16)	1.77 (0.45, 6.89)	1.96 (0.80, 4.82)	2.22 (0.64, 7.30)	3.21 (0.66, 15.15)	3.40 (0.88, 13.22	3.76 (1.74, 8.14)*	4.73 (1.40, 16.67)*	4.94 (1.98, 12.62)*	6.74 (1.36, 35.75)*	5.83 (2.34, 14.47)*
SH	0.39 (009, 1.77)	0.58 (0.17, 1.81)	0.64 (0.32, 1.29)		1.14 (0.27, 4.70)	1.26 0.54, 2.91)	1.43 (0.36, 5.02)	2.05 (0.39, 10.23)	2.19 (0.52, 9.27)	2.41 (1.02, 5.71)*	3.04 (0.78, 12.25)	3.18 (1.19, 8.61)*	4.33 (0.81, 24.21)	3.76 (1.36, 10.08)*
SCL-TBL	0.34 (0.06, 2.19)	0.50 (0.10, 2.50)	0.56 (0.15, 2.23)	0.88 (0.21, 3.68)		1.10 (0.27, 4.57)	1.24 (0.27, 5.88)	1.80 (0.27, 11.88)	1.92 (0.37, 10..04)	2.12 (0.69, 6.65)	2.64 (0.50, 15.21)	2.78 (0.80, 10.09)	3.84 (0.54, 27.35)	3.28 (1.06, 10.73)*
DG-HAL	0.31 (0.07, 1.48)	0.46 (0.16, 1.30)	0.51 (0.21, 1.25)	0.80 (0.34, 1.85)	0.91 (0.22, 3.71)		1.13 (0.31, 3.90)	1.63 (0.31, 8.35)	1.74 (0.41, 7.34)	1.92 (0.81, 4.53)	2.43 (0.58, 10.34)	2.53 (0.98, 6.61)	3.43 (0.65, 19.66)	2.98 (1.12, 7.93)*
BPC	0.28 (0.06, 1.26)	0.41 (0.11, 1.50)	0.45 (0.14, 1.56)	0.70 (0.20, 2.60)	0.80 (0.71, 3.75)	0.88 (0.26, 3.20)		1.44 (0.36, 5.85)	1.54 (0.31, 7.34)	1.69 (0.59, 5.08)	2.14 (0.43, 11.41)	2.24 (0.69, 7.44)	3.07 (0.50, 19.82)	2.63 (0.85, 8.38)
DCV	0.19 (0.06, 0.66)*	0.28 (0.05, 1.59)	0.31 (0.07, 1.51)	0.49 (0.10, 2.59)	0.56 (0.08, 3.67)	0.61 (0.12, 3.22)	0.70 (0.17, 2.78)		1.07 (0.16, 7.44)	1.18 (0.26, 5.50)	1.49 (0.22, 10.32)	1.56 (0.32, 7.73)	2.12 (0.26, 18.35)	1.83 (0.38, 8.78)
CRY	0.18 (0.03, 1.13)	0.26 (0.05, 1.33)	0.29 (0.08, 1.13)	0.46 (0.11, 1.92)	0.52 (0.10, 2.72)	0.57 (0.14, 2.45)	0.65 (0.13, 3.22)	0.93 (0.13, 6.42)		1.10 (0.33, 3.85)	1.39 (0.25, 7.94)	1.45 (0.38, 5.71)	1.97 (0.38, 15.21)	1.70 (0.48, 6.35)
RBL	0.16 (0.04, 0.68)*	0.24 (0.08, 0.58)*	0.27 (0.12, 0.58)*	0.41 (0.18, 0.98)*	0.47 (0.15, 1.44)	0.52 (0.22, 1.24)	0.59 (0.20, 1.69)	0.85 (0.18, 3.85)	0.91 (0.26, 3.04)		1.26 (0.35, 4.61)	1.31 (0.72, 2.45)	1.79 (0.38, 9.13)	1.56 (0.90, 2.67)
LASER	0.13 (0.02, 0.79)*	0.19 (0.04, 0.93)*	0.21 (0.06, 0.71)*	0.33 (0.08, 1.27)	0.38 (0.07, 2.02)	0.41 (0.10, 1.72)	0.47 (0.09, 2.33)	0.67 (0.10, 4.50)	0.72 (0.13, 4.04)	0.80 (0.22, 2.84)		1.05 (0.25, 4.19)	1.42 (0.20, 10.56)	1.24 (0.30, 4.83)
IRC	0.12 (0.03, 0.53)*	0.18 (0.05, 0.60)*	0.20 (0.08, 0.50)*	0.31 (0.12, 0.84)*	0.36 (0.10, 1.25)	0.40 (0.15, 1.02)	0.45 (0.13, 1.44)	0.64 (0.13, 3.12)	0.69 (0.18, 2.62)	0.76 (0.41, 1.39	0.96 (0.24, 3.92)		1.37 (0.26, 7.66)	1.88 (0.57, 2.36)
RFC	0.9 (0.01, 070)*	0.13 (0.02, 0.70)*	0.15 (0.03, 0.74)*	0.23 (0.04, 1.23)	0.26 (0.04, 1.86)	0.29 (0.05, 1.54)	0.33 (0.05, 2.01)	0.47 (0.05, 3.89)	0.51 (0.07, 3.51)	0.56 (0.11, 2.63)	0.70 (0.09, 5.00)	0.73 (0.13, 3.82)		0.87 (0.16, 4.43)
IJS	0.10 (0.02, 0.47)*	0.15 (0.05, 0.51)*	0.17 (0.07, 0.43)*	0.27 (0.10, 0.74)*	0.30 (0.09, 0.97)*	0.34 (0.13, 0.89)*	0.38 (0.12, 1.17)	0.55 (0.11, 2.64)	0.59 (0.16, 2.09)	0.64 (0.37, 1.11)	0.81 (0.21, 3.29)	0.85 (0.42, 1.74)	1.16 (0.23, 6.41)	

Fig. 5 League table of treatment comparisons for recurrence

Numbers in each cell represent the odds ratio (95 per cent credible interval) for recurrence between the procedure specified in the column *versus* that specified in the row. FH, Ferguson (closed) haemorrhoidectomy; SL-M, suture ligation with mucopexy ; MM, Milligan–Morgan (open) haemorrhoidectomy; SH, stapled haemorrhoidopexy; SCL-RBL, combined injection sclerotherapy and rubber band ligation; DG-HAL, Doppler-guided haemorrhoid artery ligation with mucopexy; BPC, bipolar coagulation; DCV, direct current electrotherapy; CRY, cryotherapy; RBL, rubber band ligation; LASER, laser haemorrhoidectomy; IRC, infrared coagulation; RFC, radiofrequency coagulation; IJS, injection sclerotherapy. *Statistically significant. Greater intensity of shading reflects the greater the effect size.

The key findings were that for grades II and III haemorrhoids, which are not prolapsed permanently, conservative clinic-based procedures have a greater odds of symptom recurrence, and lower odds of pain and postprocedural complications than excisional treatments.

This study allowed simultaneous comparisons of the clinical outcomes and effectiveness of a multitude of treatments for grade II–III haemorrhoids. An NMA was appropriate to answer a question of this nature, where multiple outcomes were analysed and common treatments were compared through direct and indirect comparisons across the included population[100]. The present study presents evidence for what is commonly observed in clinical practice: excisional therapies are typically preferred after more conservative clinic-based procedures have not proved

successful[5]. The ranking of treatments based on their complication profile confirms that significant postprocedural complications, such as bleeding, urinary retention, and bowel incontinence, are much more common after excisional compared with non-excisional therapy. This study has also highlighted differences in treatment outcomes such as postprocedural pain scores measured on a VAS, time off work, and duration of hospital stay; excisional treatments, which are more invasive, were found to have higher complication rates.

There were some differences in the distribution of grades across treatments compared, which may have affected transitivity assumptions. In the clinical setting, participants could be offered any of the treatments, but the choice of procedure in clinical practice depends on both patient and surgeon factors. Nonetheless, the treatments compared in this study are broadly applicable to the study population. This was confirmed by the sensitivity analysis that excluded grade I haemorrhoids, and resulted in either no studies being omitted or did not result in a significant change to the outcome of interest. Other factors affecting the outcomes included variation in the duration of follow-up among the analysed studies. The minimum 6-week postprocedure follow-up for symptom recurrence likely led to significant heterogeneity, particularly resulting from studies reporting on longer durations of follow-up for this outcome. There was also a noticeable trend that older studies reported non-surgical treatments, whereas newer studies compared surgical treatments that were introduced more recently. Older studies reported postprocedural pain on a VAS less often and used categorical scales instead. In addition, postprocedural pain comparisons were based only on day 1 scores, owing to the lack of data on pain for other days. Pain scores may vary over several days after the procedure and this should be considered when interpreting data on this outcome. The Cochrane Collaboration's risk-of-bias tool 2.0 was used to assess study quality, and overall found it to be adequate, except for measurement of blinding of both participants and personnel (risk of bias due to deviation from intended interventions) and outcome assessors (risk of bias in measurement of outcome).

The findings of the present NMA are similar to those of a previously reported NMA[101] of grade III–IV haemorrhoids, which concluded that open and closed haemorrhoidectomy and SH are associated with worse postprocedural pain, bleeding, urinary retention, and bowel incontinence than other non-surgical treatments, but have the advantage of lower rates of symptom recurrence. These results are concordant with a previous meta-analysis[102] comparing conventional with stapled haemorrhoidectomy, which showed the stapled procedure to have better outcomes with regard to operating time, postprocedural pain, duration of hospital stay, and time to return to work, but resulted in a higher recurrence risk. Similarly, a previous meta-analysis[103] that compared DG-HAL with SH showed no differences between the two treatments in terms of postprocedural complications and recurrence of haemorrhoids. The present study also had equivalent results to an earlier meta-analysis[104] comparing conservative treatment options for haemorrhoids, where IJS and IRC were more likely to require further therapy than RBL, but were less painful. A number of studies[23,37,48,49,80,99] reported the use of suture ligation or suture mucopexy for the treatment of prolapsing haemorrhoids. Using NMA, it was documented that suture ligation results in relatively lower odds of symptom recurrence than RBL. However, the included studies in this NMA comparing suture ligation are limited in number and quality, and further studies comparing suture ligation with stapled and excisional (open and closed) haemorrhoidectomy are warranted for grade II–III haemorrhoids.

The limitations of this NMA include the presence of a small number of grade 1 haemorrhoids in studies that compared conservative treatments, such as RBL and IJS. However, the findings of the sensitivity analysis showed that this did not affect the overall results. The inclusion range of the literature also dates back 30 years, which may affect the quality of studies. It was deemed necessary to include older publications, as studies comparing conservative treatments frequently date from older periods, and newer surgical treatments have been published more recently. Other limitations include heterogeneity in the duration of follow-up. Some studies reported follow-up as short as 6 weeks, whereas others had a follow-up of over 2 years, which may have contributed to heterogeneity in the recurrence outcome. Further limitations of an NMA include inconsistencies between direct and indirect comparisons. Although there were few instances of inconsistency in the outcomes measured, the failure to detect inconsistency does not imply consistency. The amount of evidence a treatment carries and the number of available comparisons between treatments determines the diversity and strength of an NMA[105]. A major imbalance between the quantity of evidence and treatments available for comparison may affect the power and reliability of the NMA[100]. Some treatment comparisons were informed by several RCTs, whereas others were sparsely informed. In the present NMA, treatments analysed in only one study were excluded from the network of that outcome to remove sparsely informed trials and obscure treatments that are not commonly used. The present NMA could not distinguish differences in outcomes between a number of excisional surgical techniques owing to the small number of relevant trials in each network. There was also an inadequate number of studies to reach statistical significance when LigaSure™ and Harmonic® scalpel haemorrhoidectomy were compared with other treatments in this NMA.

Further studies comparing treatments for haemorrhoids should assess treatment effectiveness according to standardized and validated patient-reported outcome measures (PROMs)[2,106]. The use of a PROM such as a haemorrhoid symptom severity score or a health-related quality-of-life scale may provide valuable information about the symptomatic burden of disease and is a useful measure for assessing the recurrence of haemorrhoidal symptoms. Many older studies did not use a PROM for haemorrhoid symptom recurrence; such an assessment is important and necessary for a disease such as haemorrhoids, as some symptoms may persist even though the patient may be unconcerned[2]. Future clinical trials should consider reporting outcomes against a haemorrhoid core outcome set with regard to symptoms, complications, and patient satisfaction[106]. A method of standardized reporting of outcomes will enable more reliable comparison of outcomes in meta-analyses. Finally, further higher-quality RCTs are needed to compare interventional treatments for haemorrhoids, particularly in terms of blinding of participants, personnel, and outcome assessors.

A range of treatments is available for grade II–III haemorrhoids, each with its benefits and complication profiles. Conservative, clinic-based procedures are associated with a higher rate of symptom recurrence, but should be considered initially as they carry a lower risk of complications. If they are not successful in resolving symptoms, more invasive treatments with a much greater risk of complications should be offered. The benefits and risks of each treatment should be discussed with the patient before a treatment decision is made.

Disclosure. The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

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