Stapled Haemorrhoidectomy (Haemorrhoidopexy)

for the Treatment of Haemorrhoids

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1 Definition of terms and list of abbreviations

1.1 Glossary of terms

Anastomosis	Surgical connection
Anoderm	Lining of the anal canal immediately inferior to the dentate line and extending for about 1.5 cm to the anal verge
Day case surgery	Surgery with hospital stay less than 24 hours
Dentate line	A ring of tissue on top of the anal canal which separates the anus from the rectum.
Disutility	The reduction in utility compared to a healthy population
Everting	Turning out the prolapsed haemorrhoidal tissue and taking it toward the lumen of the anal canal for resection during haemorrhoidectomy
Obturator	The central removable core of the staple gun's circular anal dilator which allows easy insertion of the tip into the anal canal and easy visibility of the anal canal during haemorrhoidopexy. The Obturator is also used to push the prolapsed haemorrhoidal tissue back and lift it into place
PPH01	First package for PPH produced by Ethicon Endo-Surgery (Johnson & Johnson) discontinued in 2004
PPH03	Second package for PPH produced by Ethicon Endo-Surgery (Johnson & Johnson) in 2004
Pre-medication	Drugs, usually sedatives and/or analgesics, given several hours prior to anaesthesia/surgery.
Pruritis	Itching
STRAM kit	An adaptor produced by Tyco to convert their stapler to be suitable to perform SH
Submucosal	Layer of tissue below the mucus membrane
Submucosal anastomosis	The surgical connection of connective tissue that lies below the mucous membrane of the anal canal; connects the submucosal tissue of the proximal and distal parts of the anal canal above the dentate line once the prolapsed haemorrhoidal tissue is resected
Utility	A measure of the strength of an individual's preference for a given health state or outcome. Utilities assign numerical values on a scale from 0 (death) to 1 (optimal or 'perfect' health), and provide a single number that summarises health-related quality of life.

1.2 List of abbreviations

AIDS	Acquired immunodeficiency syndrome
BP	Bodily pain
CAD	Circular anal dilator
CDSR	Cochrane Database of Systematic Reviews
CEAC	Cost-effectiveness acceptability curve
CENTRAL	Cochrane Central Register of Controlled Trials
CH	Conventional haemorrhoidectomy
CHE	Centre for Health Economics
CI	Confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CRD	Centre for Reviews and Disseminations
DARE	Database of Abstract of Reviews of Effects
EE-S	Ethicon Endo-Surgery (Johnson & Johnson)
EQ-5D	EuroQoL - 5 dimensions
EVPI	Expected value of perfection information
GH	General health perception (SF-36)
GA	General anaesthetic
HCS33	First stapler to be produced by Ethicon Endo-Surgery
HES	Hospital Episode Statistics
HIV	Human immunodeficiency virus
HLB	Hospital Leopold Bellan
HODaR	Health Outcomes Data Repository
HRQoL	Health related quality of life
HTA	Health Technology Assessment
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
ICER	Incremental cost-effectiveness ratio
IQR	Interquartile range
M&M	Milligan-Morgan
MeSH	Medical subject headings in the MEDLINE thesaurus
N/A	Not applicable
NHS	National Health System in England and Wales
NICE	National Institute for Health and Clinical Excellence

NLH	National Library for Health
NRR	National Research Register
OLS	Ordinary least squares
OPCS	Office of Populations Census and Surveys
OR	Odds ratio
PF	Physical function (SF-36)
PPH	Procedure for Prolapse and Haemorrhoids
QALY	Quality adjusted life year
QoL	Quality of Life
RA	Regional anaesthetic
RBL	Rubber band ligation
RCT	Randomised controlled trial
RevMan	Review Manager
RP	Role physical (SF-36)
SCI	Science Citation Index
SD	Standard deviation
SE	Standard Error
SF-36	Short form 36
SF-36BP	SF-36 Bodily Pain
SH	Stapled haemorrhoidopexy
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turning Research Into Practice
TTO	Time Trade Off
UK	United Kingdom
VAS	Visual analogue scale
WMD	Weighted mean difference

2 Executive summary

2.1 Background

Haemorrhoids are inflammation or prolapse of the vascular tissues of the anal canal; they affect people of any age and gender, and most commonly occur between the ages of 45 and 65 years. Symptoms include rectal bleeding, pain, irritation, and mucous discharge. Treatments include conservative management; non-excisional interventions; and surgical haemorrhoidectomy. Haemorrhoidectomy is typically used when conservative management or non-excisional interventions fail. Approximately 8,000 haemorrhoidectomies were performed in England in 2004/5. A range of techniques are used including Milligan-Morgan, Ferguson, Parks, Fansler-Arnold and Fansler-Anderson; Milligan-Morgan is most commonly used in the UK. In 1998, Longo introduced a procedure called stapled haemorrhoidopexy, which involves stapling haemorrhoids into their original position, and excising excess haemorrhoidal tissue.

2.2 Objectives

To determine the safety, clinical effectiveness and cost-effectiveness of circular stapled haemorrhoidectomy (SH) for the treatment of haemorrhoids.

2.3 Methods

We conducted a systematic review of the clinical and cost-effectiveness literature. Twenty six electronic databases and internet resources were searched from inception to July 2006. Randomised controlled trials (RCTs) with 20 or more participants; comparing SH with any conventional haemorrhoidectomy (CH) technique; in people of any age with prolapsing haemorrhoids, for whom surgery is considered a relevant option were used to evaluate clinical effectiveness. The main outcomes were pain, bleeding, prolapse and reintervention rate. An economic model of the surgical treatment of haemorrhoids was developed.

2.4 Results

The clinical effectiveness review included 27 RCTs (n=2279; 1137 SH; 1142 CH). All had some methodological flaws; only two reported recruiting patients with II, III and IV degree haemorrhoids, and 37% reported using an appropriate method of randomisation and/or allocation concealment.

In the early post-operative period 95% of trials reported less pain following SH and analysis of the data revealed that by day 21 the pain reported following SH and CH was minimal, with little difference between the two techniques. Residual prolapse was more common after SH (OR 3.38; 95% CI: 1.00, 11.47; p=0.05; 9 RCTs: results of a sensitivity analysis). There was no difference between SH and CH in the incidence of bleeding or post-operative complications. SH resulted in shorter operating times, hospital stay, time to first bowel movement, and time to normal activity.

In the short-term (>6 weeks to <1 year) prolapse was more common after SH (OR 4.68; 95% CI: 1.11, 19.71; p=0.04; 6 RCTs). There was no difference in the number of patients complaining of pain between SH and CH. Significantly fewer wounds remained unhealed at 6 weeks after SH (OR 0.08; 95% CI: 0.03, 0.19; p<0.001; 9 RCTs).

In the long-term (1 year and beyond) there was a significantly higher rate of prolapse after SH (OR 4.34; 95% CI: 1.67, 11.28; p=0.003; 12 RCTs). There was no difference in the number of patients experiencing pain, or the incidence of bleeding, between SH and CH.

There was no difference in the total number of reinterventions, or reinterventions for pain, bleeding or complications, between SH and CH. A significantly greater number of reinterventions were undertaken after SH for prolapse at 12 months or longer (OR 6.78; 95% CI: 2.00, 23.00; p=0.002; 6 RCTs).

Overall, there was no statistically significant difference in the rate of complications between SH and CH.

In the economic assessment it was found that, on average, CH dominates SH. However, CH and SH had very similar costs and QALYs. On average the difference in costs between the procedures was £19 and the difference in QALY was -0.001, favouring CH, over 3 years.

In terms of costs, the additional cost of the staple gun was largely offset by savings in operating time and hospital stay. In terms of QALYs, the superior quality of life due to lower pain levels in the early post-operative period with SH, were offset by the higher rate of symptoms over the follow-up period, as compared with CH. The results are very sensitive to modelling assumptions, particularly the valuation of utility in the early post-operative period.

The probabilistic sensitivity analysis showed that, at a threshold ICER of between £20,000 and £30,000 per QALY, SH had a 45% probability of being cost-effective.

2.5 Limitations and uncertainties

No large, high quality RCTs conducted in a representative population were located. There were limited data relating to recurrence and reintervention rates in the long-term. There is currently no evidence relating to the efficacy of the PPH03 stapling gun (Endo Ethicon-Surgery), or the Autosuture staple gun with the STRAM kit adaptor (Tyco Healthcare). Insufficient data were available for subgroups of patients: with different degrees of pre-surgery haemorrhoids; undergoing surgery as a day case procedure; and co-morbid conditions, to assess the impact of these factors on outcomes. The main limitation of the economic study is the lack of directly observed utility data in the early post-operative period.

2.6 Conclusions

- SH was associated with less pain in the immediate post-operative period, but a higher rate of residual prolapse, prolapse in the longer term and reintervention for prolapse.
- There was no clear difference in the rate or type of complications associated with the two techniques.

- The absolute and relative rates of recurrence and reintervention for SH and CH, are still uncertain.
- CH and SH had very similar costs and QALYs; the cost of the staple gun being offset by savings in hospital stay. Should this price of the gun change, the conclusions of the economic analysis may change.
- Some training may be required in the use of the staple gun; this is not expected to have major resource implications for the NHS.
- Given the currently available clinical evidence and the results of the economic analysis, the decision as to whether SH or CH is conducted could primarily be based upon the priorities and preferences of the patient and surgeon.

2.7 Recommendations for research

- An adequately powered, good quality RCT comparing SH with CH, recruiting patients with II, III and IV degree haemorrhoids, and having a minimum follow-up period of five years to ensure an adequate evaluation of the reintervention rate.
- A prospective register of patients undergoing initial haemorrhoidal surgery, with follow-up to determine the rate of surgical and non-surgical reinterventions.
- Evaluation of the effectiveness of SH in patients with IV degree haemorrhoids and patients with co-morbid conditions.
- A review of all treatments for haemorrhoids (conservative, non-surgical and surgical) investigating and comparing reintervention rates.
- Research into utilities up to six months post-operatively.
- Exploration of the trade-offs of patients for short-term pain versus long term outcomes through a discrete choice experiment.
- Exploration of the ability of SH to reduce hospital stays, by shortening inpatient admissions or increasing the proportion of day cases, in a real practice setting.

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3 Background

3.1 Description of health problem

3.1.1 Definition of haemorrhoids

Haemorrhoidal tissue is a normal component of the anal canal in any healthy individual. It is composed predominantly of vascular tissue, supported by smooth muscle and connective tissue.[1] The main haemorrhoidal cushions lie at the left lateral, right antero-lateral and right postero-lateral portions of the anal canal,[2] and function as a compressible lining which allows the anus to close completely.[2] The term haemorrhoid (or pile) is usually used to describe the enlargement of the vascular tissues, which become inflamed or prolapsed.[1] Haemorrhoids result from the hypertrophy of the haemorrhoidal plexus and pathological changes in the anal cushions.[3, 4]

3.1.2 Epidemiology

Haemorrhoidal disease affects people of any age and gender, but its true prevalence has not been well documented.[5, 6] The reported prevalence of haemorrhoids varies widely depending on the study population and the methods and definition used;[7, 8] it is estimated to be between 4.4% and 24.5%.[7, 9] However, this may be an underestimate, as many patients may have the disease but not consult a physician.[6, 9, 10]

Haemorrhoids most commonly occur between the ages of 45 and 65 years.[9] The risk of haemorrhoids increases in men until the age of 60 years, and then declines.[7] In women haemorrhoids are most common during the child-bearing years,[7] with between 13% and 30% of women experiencing some degree of haemorrhoids following childbirth.[11] While it is thought that there is a higher rate of haemorrhoids in men [9], some studies have reported a similar rate in men and women,[7] or a lower rate in men.[8, 12] In 2004/5, the mean age of people undergoing haemorrhoidectomies in England was 53 years, and 53% of admissions were men.[13]

3.1.3 Aetiology and pathogenesis

The main cause of haemorrhoids is unknown,[14] but there is a well-recognised association with fibre intake, constipation, prolonged straining,[15] and hormonal changes and straining associated with constipation during pregnancy.[4] Straining, and the passage of constipated stools, result in engorgement of the vascular tissues, which if prolonged, may result in the fragmentation of the connective tissue and subsequent haemorrhoidal prolapse. The prolapsed cushion is thought to have impaired venous return, causing dilation of the plexus and venous stasis, and inflammation occurs with erosion of the lining epithelium, resulting in bleeding.[4]

There is some evidence to suggest that vascular dilatation and an increased arterial inflow contributes to the development of haemorrhoids, rather than being a consequence of haemorrhoid development.[16] Haemorrhoids have also been associated with chronic diarrhoea.[15]

If haemorrhoids develop during pregnancy, it tends to be in the third trimester.[17] Management should be as conservative as possible to avoid risks to the foetus,[17] with surgery only undertaken for intractable disease, and delayed until the foetus is viable.[4] Performing the procedure under local anaesthetic is considered to be the safest option.[17]

3.1.4 Classification of haemorrhoids

Haemorrhoids can be internal or external according to their position relative to the dentate line. The dentate line lies approximately 2 cm from the anal verge and demarcates the transition from the upper anal canal, lined with columner epithelium, to the lower anal canal, lined with sensate squamous epithelium.[4] Internal haemorrhoids originate from the internal haemorrhoidal venous plexus of the anal canal above the dentate line, and external haemorrhoids originate from the external haemorrhoidal plexus below the dentate line.[2, 4] Although this division is anatomical, rather than functional, it has implications for surgical treatment. This review focuses on the management of internal haemorrhoids.

Internal haemorrhoids are frequently classified into four categories depending on the degree of prolapse (Table 3.1).[4] Haas *et al* (1983) reported that about 25% of haemorrhoids were grade III or IV.[18]

Table 3.1: Classification of internal haemorrhoids[4]

Classification by severity	Characteristics	Treatment
I degree	Small, bleed at defecation but no prolapse	Attention to bowel habit and avoidance of straining on defaecation
II degree	Bleed and prolapse from anus at defaecation but reduce spontaneously	Initial treatment is usually rubber band ligation or injection sclerotherapy. Where these interventions fail, surgery may be considered.
III degree	Bleed, mucous discharge, prolapse but can be manually reduced	Haemorrhoidectomy
IV degree	Bleed, mucous discharge, prolapse that cannot be manually reduced	Haemorrhoidectomy

This classification is of practical benefit as it is useful in determining treatment. It does however, omit patients with internal haemorrhoids suffering from anal discomfort or soiling, or claiming a large cutaneous component, but having no prolapse or bleeding.[14] Lunniss and Mann have proposed a new classification by combining prolapse and bleeding with other symptoms,[19] but their classification is more complicated and perhaps more difficult for routine use in clinical management. It is not used generally and has not been used in this report.[14]

3.1.5 Clinical presentation

The symptoms associated with enlarged internal haemorrhoids include rectal bleeding, perianal pain, discomfort, mucous discharge and perianal itching or irritation (referred to as pruritis and usually caused by discharge).[3, 4, 6, 14, 20] First degree haemorrhoids may present with only bleeding. An increase in the degree of haemorrhoids may increase the probability of other symptoms being present.[14]

Rectal bleeding appears to be the most common symptom associated with haemorrhoids.[5] Haemorrhoidal bleeding is bright red and usually noticed on wiping or in the toilet bowl.[4] In some patients the predominant clinical presentation is prolapse where a mass is protruding through the anus usually following a bowel action. In the early stages of the disease the prolapse is typically small and reduces spontaneously, but over time this may become larger and result in a persistent mass.[5] This may lead to leakage of mucus which causes perianal irritation and discomfort.[21]

The epithelium covering the haemorrhoids is derived from the anoderm in the lower half of the anal canal and is sensitive to pain, whereas that of the upper half is derived from the rectal epithelium and is relatively insensitive.[1] Therefore internal haemorrhoids are not commonly associated with anal pain unless they become thrombosed, strangulated or acutely prolapsed.[5] Soiling may occur with third and fourth degree haemorrhoids as a result of impaired continence.[4] Haemorrhoids are frequently associated with anal skin tags, which may lead to difficulty with perianal hygiene.[22]

3.1.6 Significance for NHS

In England in 2004/5, approximately 23,000 haemorrhoidal procedures were performed as hospital daycase or inpatient admissions, of which about 8,000 were excisional surgery.[13]

3.2 Current service provision

3.2.1 Management of disease

Patients with no bleeding or prolapse or with infrequent symptoms may not require any therapy.[5] For those that do require some form of management, the treatment of haemorrhoids can be classified as: conservative management; non-excisional interventions; and surgical haemorrhoidectomy.[4, 6] The choice of treatment will depend on the severity and frequency of symptoms.[5]

3.2.1.1 Conservative management

Conservative management is the approach used when the symptoms are minor and do not interrupt the patient's normal activities. This includes attention to bowel habit and changes in diet and lifestyle, with fibre intake being the most common recommendation.[5] Although there is no conclusive evidence on the beneficial effect of fibre supplements, it is suggested that increasing fibre intake to soften stool combined with laxatives to relieve constipation will reduce straining.[2, 4] A range of ointments are available that contain local anaesthetics, mild astringents, or steroids, providing short-term relief from discomfort and irritation However, these do not deal with the underlying problem, and continued use can cause eczema and sensitisation of the endoderm, and rectal absorption can lead to systemic side effects.[4]

3.2.1.2 Non-excisional interventions

Non-excisional interventions are generally used when haemorrhoidal symptoms do not respond to conservative management or when the symptoms on initial presentation would indicate that conservative management alone is unsuitable. Non-excisional interventions include rubber band ligation (RBL), injection sclerotherapy, cryotherapy, infrared coagulation, laser therapy and diathermy coagulation.[6] Assessment of these interventions is beyond the scope of this review; further information can be found elsewhere.[4, 14, 17, 20, 23]

3.2.1.3 Surgical interventions

If a non-excisional intervention fails to control symptoms, patients may be considered for surgical haemorrhoidectomy.[6] Third and fourth degree haemorrhoids are often treated by surgical intervention,[6] however, surgery is also considered for second degree haemorrhoids which have not responded to non-excisional interventions.[6] Surgery can be performed as a day case, with suitability for a day case procedure being judged by social factors, age, body mass index, and comorbidity.[24]

The two most commonly conducted surgical techniques are the open (Milligan-Morgan) and closed (Ferguson) haemorrhoidectomy.[14] These are surgical procedures using scalpel, diathermy or laser.[6] Milligan-Morgan is the most frequently used

technique in the UK.[25] This involves grasping and everting the haemorrhoid and ligating the vascular pedicle. The wounds left open to granulate, separated by bridges of skin and mucosa.[4] The Milligan-Morgan procedure is thought to be relatively safe and effective for managing advanced haemorrhoidal disease; however because the anodermal wounds are left open, healing is delayed and may cause considerable discomfort and prolonged morbidity after the operation.[22]

The Ferguson technique is a modified version of the Milligan-Morgan technique, where excision and ligation are performed with the haemorrhoid in its anatomical position, and the wound closed using a continuous suture in an attempt to promote wound healing. This technique is more frequently used in the USA.[4]

Parks submucosal haemorrhoidectomy is another technique that uses intra-anal incisions directly over each haemorrhoid, with anodermal flaps raised to either side of each incision and the underlying haemorrhoidal tissue excised. The flaps are loosely sutured together at the conclusion of the operation. No anoderm is excised along with the haemorrhoidal tissue during this technique.[26, 27]

LigaSure, is a haemostatic system that permanently seals blood vessels by transforming the collagen and elastin within vessels walls (Tyco Healthcare, Gosport, UK).[28] The LigaSure device is applied across the base of the haemorrhoid until coagulation of the tissue is complete; the haemorrhoid is then excised along the coagulated strip of tissue.[29] This method therefore differs from the open technique in that the wound is sealed, and from the closed technique in that sutures are not used to seal the wound.

There is currently no consensus as to which intervention is 'best practice'. All surgical haemorrhoidectomies (collectively referred to as conventional haemorrhoidectomy (CH)) methods are subject to adaptations, resulting in a wide variation in the surgical techniques used to treat haemorrhoids between countries, institutions and even surgeons within the same institution.

A range of post-operative complications pain are associated with CH. Short term complications include, urinary retention,[4, 26] bleeding,[4, 26, 30-32] and perianal sepsis.[4]

Long-term complications include anal fissure,[30] anal stenosis,[26, 30, 31, 33, 34] incontinence,[4, 26] anal fistula, external haemorrhoidal thrombosis,[30] and the recurrence of haemorrhoidal symptoms.[35, 36]

3.3 Description of technology under assessment

Stapled haemorrhoidopexy (SH) is a new alternative to CH introduced by Longo in 1998.[37] The original technique involved stapling haemorrhoids into their original position, and leaving the haemorrhoidal tissue to shrivel over time. Residual haemorrhoidal tissue, however, is prone to thrombosis and infection. Pain, bleeding and discharge can also recur.[38] Therefore the technique was modified so that haemorrhoidal tissue was repositioned and excess prolapsing tissue excised.[38] Several terms are synonymous with SH, including: PPH: Procedure for Prolapse and Haemorrhoids; stapled mucosectomy; stapled prolapsectomy; and stapled haemorrhoidectomy.

During SH, a stapling device is passed into the anal canal, which simultaneously excises excess prolapse and creates a submucosal anastomosis and a closed wound high in the anorectum.[6] The insertion of the anal dilator causes the reduction of the prolapse of the anoderm and parts of the anal mucous membrane. The prolapsed mucous membrane falls into the lumen of the anal dilator once the obturator is removed. As the anal dilator is transparent, the dentate line can be visualised.[39] A purse string suture is placed 4cm to 6 cm from the anal verge, proximal to the dentate line.[25, 39]

The pursestring suture and its correct placement is thought to control the volume of tissue drawn into the centre of the stapler chamber. Incorrect placement of the suture can lead to problems such as: an incomplete excision of excess tissue; the inclusion of perirectal fat; or a staple line too close to the dentate line, which may increase pain and the risk of anal stenosis.[40] Once the purse-string suture is in place, the circular stapler is introduced to the anus. The stapler is opened to its maximum position, and the head positioned proximal to the suture. The suture is tied with a closing knot and the ends pulled through the lateral holes of the stapler. It is knotted externally or fixed using a clamp, and tightened onto the shaft.[39] The entire casing of the stapler is

introduced into the anal canal, and moderate traction put on the purse-string to draw the prolapsed mucous membrane into the casing of the stapler. The instrument is then tightened and fired to staple the prolapse. When the gun is fired, a double row of titanium staples are released and a knife within the head of the gun excises the excess rectal mucosa.[25] The stapler is kept closed for approximately 20 seconds after firing to help promote haemostasis. The staple line should be examined and absorbable sutures used if bleeding from the staple line occurs.[39] Most of the staples used to create the anastomosis fall out after a few weeks, but some are retained and incorporated into the scar tissue, usually without any adverse effects. The procedure is described in detail and illustrated by Corman (2003).[41]

One advantage of SH is the lack of anal wounds.[42] Also stapled haemorrhoidopexy aims to resect only rectal mucosa. However some studies have reported circular muscle, myentric plexus, longitudinal muscle,[43, 44] and squamous epithelium, in the excised tissue.[44] This is thought to be due to the pursestring suture being placed too low or too deep, and may become less common with increased experience conducting SH.[44] It is recommended that the stapler should not be used where the combined tissue thickness is <1.0mm or >2.5mm, as an inadequate mucosal repair and inadequate haemostasis may result. Also, the internal diameter of the rectum must be sufficient to accommodate the instrument and accessories, precluding its use in anal stenosis.

A range of post-operative complications are associated with SH. Many are the same as CH: urinary retention,[4, 42] bleeding,[3, 4, 30, 42] perianal sepsis,[3, 42] anal fissure, incontinence,[4] anal fistula, external haemorrhoidal thrombosis,[30, 42] and the recurrence of haemorrhoidal symptoms. There is also a risk of sphincter damage,[30, 42] anastomotic stricture, the equivalent of anal stricture sometimes experienced after CH,[30, 42, 45] rectal obstruction,[46] proctitis,[47] and perirectal haemotoma.[48] SH is thought to be more commonly associated with pelvic/perianal sepsis,[3, 4, 42, 49-53] rectal perforation,[54, 55] and rectovaginal fistula;[3, 42] but may reduce the incidence of incontinence[42]:

- Pelvic sepsis is likely to occur after full thickness rectal injury, and may be a result of the incorporation of gas producing organisms in perianal space during the anastomosis, subcutaneous necrosis, or rectovaginal fistula.[42]

- Rectovaginal fistula/rectal perforation occur as a result of trapping the vaginal wall in the staple line. There is also a risk of entrapping a peritoneocele or enterocele in the purse string, particularly in women who have had a hysterectomy.[42]
- Injuries to the internal anal sphincter can be a result of a full thickness excision to the rectal wall, or stretching anal sphincter by the stapler head.[25] During SH, anal stenosis may be avoided by the use of a larger sized stapler, and the avoidance of the use of a narrow stapler in people with narrow anal canal, who should undergo an alternative intervention.[42]
- The risk of incontinence is thought to be reduced with SH, as the venous cushions are left intact, as opposed to healing with scar tissue production as after CH.[42]

Compared with CH, SH is thought to cause less post-operative pain[3] and bleeding, reduce operative time and length of hospital stay and allow a shorter convalescence. The reduction in the degree of post-operative pain may be the main reason why SH is fairly common in Europe.[56] The safety and clinical effectiveness of this technique, particularly in the long-term (recurrence and incontinence), and its cost-effectiveness, need to be appraised.[4, 11]

3.3.1 Device development

The first attempts at treating haemorrhoids using a stapling gun were undertaken using linear staplers.[57-59] These staplers were designed for use during other gastrointestinal operations, and there was difficulty gaining access to the anal canal.[60] As a result of these early attempts, adapters for linear staplers and circular staplers were developed. Tyco Healthcare produced an adaptor for their Autosuture instrument called the STRAM KIT. In contrast, Ethicon Endo-Surgery (EE-S; Johnson & Johnson) developed a circular stapler specifically for haemorrhoidopexy. The first of these was the HCS33 stapler in 1999 which came as part of the PPH01 pack. PPH01 was replaced in 2004 by PPH03, which differed by its ability to adjust the closed staple height down to 0.75 mm, rather than 1 mm, and the provision of clear plastic accessories to assist visualisation of the staple line.

3.3.2 Current usage in the NHS

It is thought that approximately 1500 SHs were conducted in the UK between 1998 and 2002.[25]

3.3.3 Anticipated costs associated with intervention

Several studies have compared the cost of SH and CH.[43, 61, 62] Ho *et al* (2000)[61] and Kirsch *et al* (2001)[62] found that SH is more expensive than conventional surgery. Wilson *et al* (2002)[43] however, found SH to be less expensive than CH due to reduced operating time and length of hospital stay. They also suggested that patients undergoing SH may return to work earlier than CH.[43]

The mean cost of an inpatient elective anal surgery was £1,127 and varied between £900 and £1,425 in 2005/06 in NHS hospitals, based on an intermediate anal procedure cost without complications. The associated length of stay was 1.51 days on average.[63] If performed as a day case procedure, based on an intermediate anal procedure cost without complications, the mean cost was £750 and varied between £554 and £937.[63] The SH operation is associated with higher equipment costs since it includes the cost of a staple gun which is approximately £420 per case.[64] However, Farinetti *et al* (2000)[65] found that on average the SH operation was associated with a shorter operation time than CH which offset the higher equipment costs associated with this procedure. The cost of the hospital stay contributes to the total cost of the operation. If it can be successfully performed as a day case procedure rather than as an inpatient procedure, there may be potential for offsetting cost savings.

3.3.4 Important subgroups of patients with reference to SH

Comorbid conditions

Certain co-morbid conditions have been identified that require a modification in the treatment of haemorrhoids. The success of SH and CH may be reduced, or in some cases contra-indicated, with the presence of conditions such as Crohn's disease, HIV, IBD and IBS, acute inflammatory episodes of the large bowel, and incontinence.[4, 17, 20] Treatment should be undertaken once perianal sepsis and inflammation are controlled,

and surgery conducted on a selective basis with antibiotic cover.[4] People with HIV, particularly those with AIDS, should preferably be treated conservatively, due to the risk of septic complications, and the potential for delayed wound healing.[4] A conservative approach to the management of haemorrhoids in patients with chronic liver disease or cirrhosis has been advised, due to portal hypertension, associated rectal varices, impaired coagulation and poor nutritional status.[17]

Different degrees of haemorrhoids prior to surgery

Patients may respond differently to haemorrhoidal surgery depending on the severity of their disease. There is some controversy as to the suitability of SH in those with IV degree haemorrhoids, with some thinking that SH may be more suitable for the treatment of third degree haemorrhoids.[64] The reasons highlighted for not using SH on people with IV degree haemorrhoids have been: the difficulty gaining access to the anal canal;[25] difficult placement of the pursestring suture;[66] excess tissue to be excised being too bulky to fit into the housing of the staple gun;[25] incomplete mucosal resection resulting in residual prolapse.[66] However, evidence to support these views has been lacking.

Patients undergoing a first or repeated surgery

Success of surgery may differ depending on whether a patient is undergoing a first or a repeated surgery and the type of previous operation. Recurrent haemorrhoidal symptoms may be less severe than the original symptoms, probably due to the removal of haemorrhoidal tissue. The majority of the patients with recurrent symptoms will respond to conservative or non-surgical therapies, however, if the symptoms are not controlled by these therapies, re-operation will need to be considered. It is unclear how suitable SH is as a repeat procedure, and whether the efficacy of SH will differ when undertaken as the repeated operation following SH or CH.

Day case vs in-patient surgery and use of local, regional or general anaesthesia

Both SH and CH can be, and are, conducted as day cases. Length of hospital stay may be dependent on several factors including the time the study was conducted, type of anaesthesia and the type of procedure used. Older studies may use general anaesthesia more frequently, and report longer hospital stays. SH may be more suitable for local and regional anaesthesia and day case procedures as there are no open wounds on the anoderm, the sensitive part of the anus, and therefore pain may be expected to be less. However, some argue that the wounds left by CH can be infiltrated with local anaesthetic and therefore negate any difference in relation to this. These are important issues as type of anaesthesia and length of hospital stay may have significant impact on surgical costs and outcomes.

4 Definition of decision problem

4.1 Decision problem

The potential reduction in operating time, hospital stay, time to return to work and post-operative pain, makes SH seem an attractive alternative to CH for the treatment of internal haemorrhoids. However, uncertainties over the incidence of complications; recurrence of haemorrhoidal symptoms; and the requirement for reintervention in the longer-term, together with uncertainty over the cost-effectiveness of SH relative to CH at present precludes a recommendation for the introduction of SH across the NHS.

To investigate these uncertainties and attempt to inform practice, a systematic review of the clinical evidence is required. The evidence reviewed should be from randomised controlled trials (RCTs) that compare SH with CH, in people of any age with prolapsing haemorrhoids for whom surgery is considered a viable option. Prolapse, pain, bleeding and reintervention rates should be considered the main outcomes. Other outcomes evaluated should include operating time, duration of hospital stay, wound healing, time to first bowel movement, and complications. Subgroups of interest include patients with IV degree haemorrhoids; comorbid conditions; and undergoing repeat procedures

An economic evaluation is required that considers the clinical and cost outcomes from the NHS and Personal Social Services Perspective. Attempts should be made to identify not only subgroups of individuals, but also conditions and settings of care (e.g. in-patient or day case procedure; general or local anaesthesia), where the technology is particularly clinically and cost-effective or contra-indicated.

4.2 Overall aims and objectives of assessment

The aim of this review is to determine the safety, clinical effectiveness and cost-effectiveness of circular SH for the treatment of haemorrhoids.

5 Assessment of Clinical Effectiveness

5.1 Methods for Reviewing Clinical Effectiveness

5.1.1 Search strategy

5.1.1.1 Resources Searched

The following resources were searched in order to retrieve papers relating to SH. No language or date restrictions were applied. However, SH was introduced in 1998, therefore trials evaluating this technology would not be located prior to this date. A range of free-text terms and subject headings were used to provide a focused strategy, and a variety of search strategies were used (details of the search strategies used are presented in Appendix 10.1):

Databases of Systematic Reviews

Cochrane Database of Systematic Reviews (CDSR) (Cochrane Library: http://www.library.nhs.uk/)
Database of Abstracts of Reviews of Effects (DARE) (CRD Internal Database)

Health/Medical Related Databases

BIOSIS (EDINA: discontinued 31/07/06)
CENTRAL (Cochrane Central Register of Controlled Trials) (Cochrane Library: http://www.library.nhs.uk/)
Cumulative Index to Nursing and Allied Health Literature (CINAHL) (OvidWeb: http://gateway.ovid.com/athens)
EMBASE (OvidWeb: http://gateway.ovid.com/athens)
Health Technology Assessment Database (HTA) (CRD Internal Database)
MEDLINE (OvidWeb: http://gateway.ovid.com/athens)
MEDLINE In Process and other non-indexed citations (OvidWeb: http://gateway.ovid.com/athens)
Science Citation Index (SCI) (Web of Knowledge: http://wos.mimas.ac.uk/)

Databases of Conference Proceedings

ISI Proceedings: science and technology (Web of Knowledge: http://wos.mimas.ac.uk/)

Zetoc Conferences (MIMAS: http://zetoc.mimas.ac.uk/)

Databases for Ongoing and Recently Completed Research

ClinicalTrials.gov (http://www.clinicaltrials.gov/)

MetaRegister of Controlled Trials (http://www.controlled-trials.com/)

National Research Register (NRR) (http://www.update-software.com/national/)

Clinical Guidelines and Systematic Reviews Resources

Clinical Evidence (BMJ Publishing Group)

Health Evidence Bulletin Wales (http://hebw.cf.ac.uk)

National Guideline Clearinghouse (http://www.guideline.gov/)

National Institute for Health and Clinical Excellence (NICE) (http://www.nice.org.uk/)

National Library for Health (NLH) Guidelines Finder (http://www.library.nhs.uk/guidelinesfinder/)

Scottish Intercollegiate Guidelines Network (SIGN) (http://www.sign.ac.uk/)

Turning Research Into Practice (TRIP+) (http://www.tripdatabase.com/index.html)

Topic Specific Websites

American Society of Colon and Rectal Surgeons (http://ascrs.affiniscape.com/index.cfm)

Association of Coloproctology of Great Britain and Ireland (http://www.acpgbi.org.uk)

Association of Surgeons of Great Britain and Ireland (http://www.asgbi.org.uk/)

Digestive Disorders Foundation (http://www.digestivedisorders.org.uk)

Hemorrhoids File (http://www.lifestages.com/health/hemorrho.html)

5.1.2 Inclusion and exclusion criteria

Two reviewers independently screened all titles and abstracts (JB, AB). Full paper manuscripts of any studies thought to be potentially relevant by either reviewer were obtained. The relevance of each study was assessed according to the criteria stated below. A table of retrieved studies that appeared relevant but were excluded during the screening process, is provided in Appendix 6. Any discrepancies were resolved by consensus, or where consensus could not be reached, a third reviewer was consulted (NW).

For any study retrieved only as an abstract, authors were contacted to request additional information. Where additional information was not obtained, abstracts were included only if sufficient outcome data were available. Studies of any language were included as long as a translator was available.

5.1.2.1 Study designs

Randomised controlled trials (RCTs) with 20 or more participants were used to evaluate efficacy. Studies with fewer than 20 participants were excluded, as these are likely to be underpowered and of poorer quality.

5.1.2.2 Interventions and comparators

The intervention of interest was SH and the comparator of interest was CH. Studies comparing circular SH (also called PPH: Procedure for Prolapse and Haemorrhoids; stapled mucosectomy; stapled prolapsectomy; stapled haemorrhoidectomy) with any conventional surgical haemorrhoidectomy where excision is conducted using scalpel, scissors or diathermy were included in the review. Studies comparing SH with non-excisional interventions were excluded.

Studies evaluating haemorrhoidopexy undertaken using a linear stapler were excluded, as linear staples were designed for use in gastrointestinal operations other than haemorrhoidectomy, and difficulty gaining access to the anal canal makes it a less suitable technique than circular SH.[60]

In the protocol, we stated that studies evaluating the use of circular staple guns for haemorrhoidopexy would be included in the review. Once studies evaluating SH were retrieved, it was apparent that a range of staple guns were used: PPH01; PPH33; ILS33; CDH33; and Autosuture. We investigated what type of gun each of these codes referred to, to ensure they were all circular staplers suitable for SH. ILS33 and CDH33 are circular staplers produced by EE-S (Johnson & Johnson), however, they are not designed to perform a SH. Autosuture® (Tyco Healthcare) is a stapler that can be converted for use during SH with an adaptor called the STRAM kit. On this information, studies evaluating ILS33, CDH33 and Autosuture without the STRAM kit adaptor were excluded from the review, as they are not designed for conducting SH. The use of the STRAM kit had to be confirmed either in the paper or by contact with the authors for the data to be included in the review.

Studies reporting the use of the HCS33 were classified as using PPH01, as the HCS33 was the first stapler to be produced by EE-S, and was part of the PPH01 package. Where studies stated the use of PPH33 or PPH, the decision to classify as PPH01 or PPH03 was made using the trial or publication date. PPH03 was introduced in 2004, and PPH01 discontinued. Therefore any trials undertaken or published in 2003 or before were classified as PPH01. Any trials conducted in 2005 and after were classified as PPH03. Studies stating that they used CAD33, the circular anal dilator that is contained in the PPH01 and PPH03 packages, were also categorised as PPH01 or PPH03 depending on the trial dates or date of publication, as above. Where the trial dates were not reported, and the publication date led to ambiguity, the trial authors were contacted. For those studies where information could not be obtained the gun used was classified as PPH-unspecified and the impact of the results of these studies on outcomes investigated using sensitivity analyses.

In summary, studies evaluating either PPH01 or PPH03 (EE-S) or Autosuture using the STRAM kit (Tyco Healthcare) were eligible for inclusion. No other staplers designed for SH were identified.

5.1.2.3 Population

Trials of people of any age with prolapsing haemorrhoids, including those with haemorrhoids that reduce spontaneously, for whom surgery is considered a relevant option were included in the review. Trials of patients undergoing emergency procedures for thrombosed haemorrhoids were excluded.

5.1.2.4 Outcomes

Outcomes were classified as peri-/post-operative (<6 weeks), short-term (>6weeks to <12 months), 12 months, and long-term (>12 months). Where studies reported continuous outcomes as medians and ranges, authors were contacted for mean and SD. Overall patient satisfaction, indicating a preference for one or other technique or no preference, was extracted at each time point if reported. A full list of outcomes extracted at each time point is provided in Appendix 10.2.

Peri-/post-operative outcomes (within 6 weeks)

Six weeks was chosen for the peri-/post-operative follow-up period as pain and discomfort can last for 3 to 4 weeks, particularly after CH. The primary outcomes were pain and bleeding. Secondary outcomes included residual prolapse, operating time, duration of hospital stay, wound healing, time to first bowel movement, complications (urinary retention; infection). Prolapse was not a primary outcome within this time-frame as patients are often too tender for rectal examination; although some studies may report residual prolapse, it could not be expected that this would be consistent across studies.

Pain: The time at which people often report the most severe pain is 2 to 4 days post-operatively, as any effects of local anaesthetics applied to the wounds cease. Ideally we wanted to extract the number of days that analgesia was required by patients in each arm of the trial, irrespective of the route of administration or dose. However, these data were lacking in most studies, with pain scores, the mean number of tablets/injections required (often with no indication over time period or effectiveness) or the number of patients requiring different types of analgesia being more commonly reported. Therefore the visual analogue scale (VAS) scores and number of patients

requiring different types of analgesia were extracted. All VAS scores were converted to a 10 mm scale and the value closest to 3 days and 14 days extracted. A mean score for the first 7 days was considered an acceptable value for the 3 day value. A mean score encompassing days between 10 and 20 days postoperatively was considered an acceptable value for the 14 day score. The types of analgesia administered were classified as opioid injections; other injections; opioid oral analgesia; and other oral analgesia.

Skin tags: Skin tags that remain after SH can cause pruritis and difficulty with personal hygiene. The only treatment is to excise them, but they are located on the sensitive anoderm, making the procedure painful. Although skin tags can cause serious irritation to some patients, they cause no problems for many; data on their incidence was not extracted. However, to gain an insight as to the incidence of troublesome skin tags, the number of reinterventions undertaken for their excision at subsequent time points was extracted. In addition, the excision of skin tags as a concomitant procedure during the initial surgery was noted, as this may impact on the pain experienced by patients post-operatively.

Bleeding: Where reported, the total number of patients with any bleeding episode, and the number requiring intervention were extracted separately.

Wound healing: Where reported, wound healing was recorded at both 6 and 12 weeks. The number of wounds healed at 6 weeks will give an indication as to the technique most likely to have delayed wound healing, and the number healed at 12 weeks will indicate the number of wounds not healing due to complications.

Duration of hospital stay: Day case was defined as being discharged from hospital within 24 hours of admission.

Infection: Wound and systemic infections were extracted separately. Patients reported as having a fever were presumed to have a systemic infection. Any studies just reporting ‘number of patients with infection’ were assumed to have wound infection.

Anal stenosis and anastomotic stricture: Anal stenosis (narrowing of the anal sphincter) is a complication that may be experienced after CH, and anastomotic stricture (narrowing at the staple line/anastomosis) after SH. These were considered equivalent outcomes for the two procedures and were directly compared.

Short-term outcomes (up to 12 months; nearest to 6 months)

The primary outcomes were prolapse, pain and bleeding. Secondary outcomes were the need for further intervention (for symptoms or complications) incontinence, urgency and assessment of quality of life. Although faecal urgency and faecal incontinence are both a result of sphincter dysfunction, we extracted these separately due to their different impact on the patient and potential for treatment. Squeeze and resting pressures are also measures of sphincter function (resting pressure indicates the ability to maintain passive continence, and squeeze pressure to delay defecation), but these were not extracted as they are recorded using a range of techniques and measures, and the outcomes of faecal urgency and incontinence are more relevant to the current review.

Outcomes at 12 months

The primary outcomes were prolapse, pain and bleeding and the need for further intervention. Secondary outcomes included incontinence, and assessment of quality of life.

Long-term outcomes (over 12 months)

The primary outcome was recurrent prolapse. Secondary outcomes included bleeding, incontinence, anal stenosis and the need for further intervention. Long-term outcomes at all time points beyond 12 months were extracted due to the paucity of such data.

5.1.3 Data extraction strategy

All data relating to both study design and quality were extracted by one reviewer and independently checked for accuracy by a second (JB, AB). Disagreements were

resolved through consensus, or where consensus could not be reached, a third reviewer was consulted (NW). Foreign language studies were extracted by one reviewer (JB) along with a native speaker of that language. Where multiple publications of the same study were identified, data were extracted and reported as a single study. A list of the type of data extracted at each time point is provided in Appendix 10.2.

5.1.4 Quality assessment strategy

The quality of the individual studies was assessed by one reviewer and independently checked by a second (JB, AB). Disagreements were resolved through consensus, or where consensus could not be reached, a third reviewer was consulted (NW). The quality of RCTs was assessed using standard checklists adapted to incorporate topic-specific quality issues[67] The checklist is provided in Appendix 10.3, together with the guidelines used to score each criterion.

5.1.5 Data analysis

Odd ratios (OR) and 95% confidence intervals (CI) were calculated for dichotomous outcomes. Mean differences and 95% CI were calculated for continuous outcomes. Data are reported separately for each outcome measure. All meta-analyses were conducted in RevMan 4.2.9 (Cochrane Collaboration). Pooled OR and 95% confidence intervals (CI) were calculated for dichotomous outcomes, and weighted mean differences (WMD) and 95% CI for continuous outcomes.

Studies were pooled in primary analyses if there was no statistically significant heterogeneity between studies. A random effects model was used, unless there were three or less studies included in the analysis, in which case a fixed effect model was used. Sources of heterogeneity, such as patient population and quality criteria were investigated by visual inspection of the forest plots and explored further using sensitivity analyses. Possible effects of study quality on the effectiveness data and review findings are discussed. For the primary outcomes (pain, prolapse, bleeding) sensitivity analyses were conducted to explore the impact of the high losses to follow-

up. For both primary and secondary outcomes, sensitivity analyses were conducted to explore the impact of outlying results.

The relationship between VAS pain score, days from primary surgery and treatment was explored further using Bayesian meta-regression (Appendix 10.4).

Predefined subgroups of interest included: degree of haemorrhoid prior to surgery; patients undergoing a first or repeated surgery; local, regional or general anaesthetic; and the presence of co-morbid conditions. We also attempted to determine any differences in outcome when the procedures were conducted as day case or in-patient surgery, to determine whether either technology is more suited to be undertaken as day case surgery. It was anticipated that insufficient data would be obtained to investigate the presence of co-morbid conditions, as they were likely to be excluded from studies.

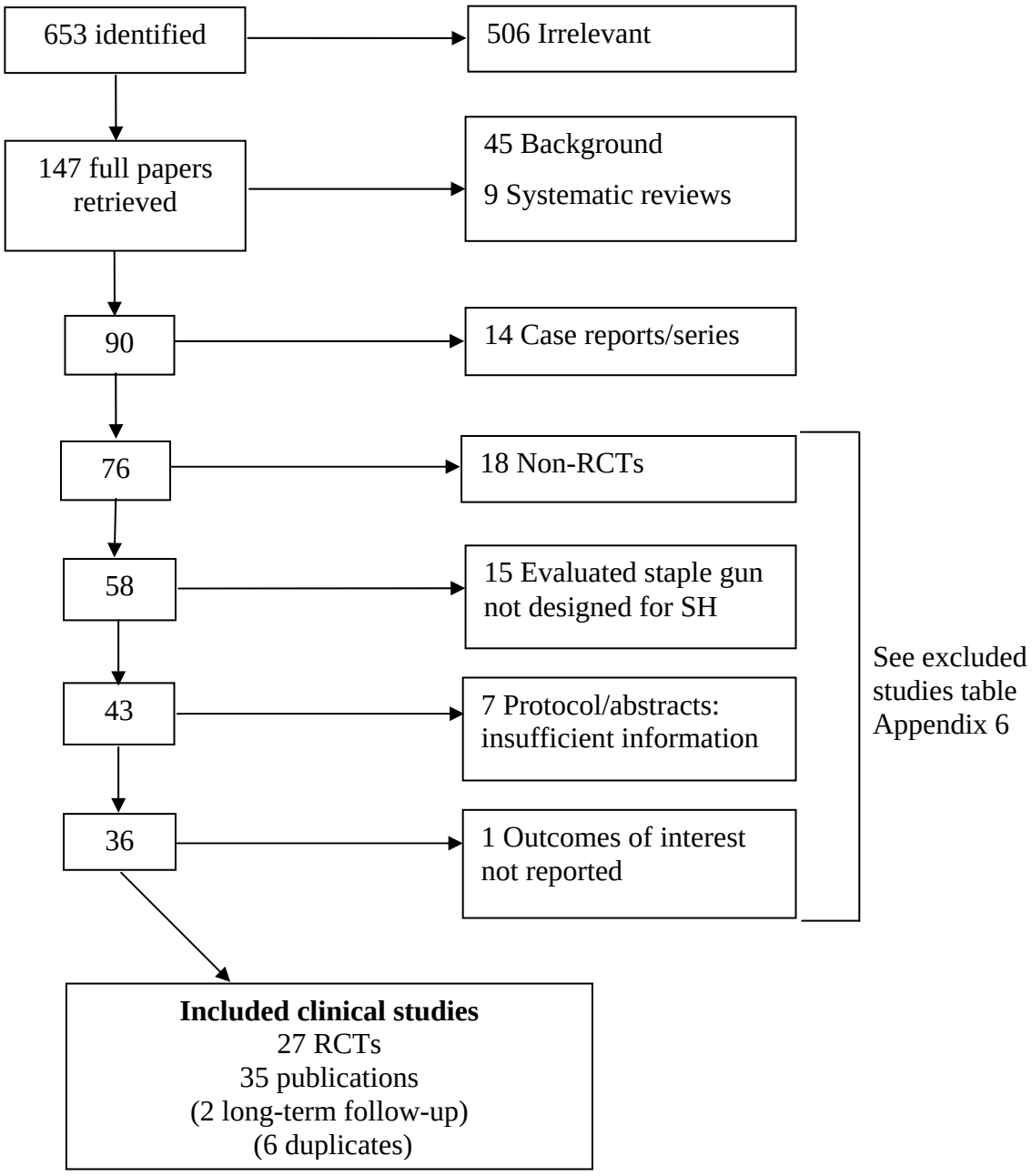
The company submission consisted of a review of clinical data already in the public domain, therefore confidentiality was not an issue for this review.

5.2 Results of Review of Clinical Effectiveness

5.2.1 Quantity and quality of research available

The electronic and hand searches retrieved 653 references. Of these, 147 full papers considered potentially relevant to the review of clinical effectiveness were retrieved and screened for relevance. Twenty seven RCTs, reported in 35 publications, met the inclusion criteria. Two publications were the long-term follow-up of RCTs reported as full manuscripts,[68, 69] and two abstracts reported different outcomes from the same RCT.[70, 71] The flow of studies through the review is shown in Figure 5.1.

Figure 5.1: Flow of studies through the review



Four RCTs were included in languages other than English; two German,[72, 73] one Italian[74] and one Chinese.[75] Two RCTs were only available as abstracts.[70, 71, 76] Four RCTs related to trials conducted in the UK,[43, 70, 71, 76, 77] fifteen in other European countries,[28, 68, 72-74, 78-88] one in the US,[89] four in Asia,[61, 69, 75, 90, 91] one in India,[92] one in Saudi Arabia[93] and one in Mexico.[94]

The main characteristics of the included trials are summarised in Table 5.1, with data extraction tables provided in Appendix 10.5.

The total number of participants was 2279; 1137 received SH and 1142 received CH.

Table 5.1: Main characteristics of the included studies

Study	Participants			Interventions
	Number	Population	Degree of haemorrhoids	
Ascanelli (2005)[74] Trial dates: Start: 2001 Finish: 2003	Total: 100 SH: 50 CH: 50	Age: Range: 30-73 Number male 21	Grades included II+III Grade II: Not reported Grade III: Not reported	Stapling gun: Mechanical suture Comparator: M&M + diathermy Anaesthesia: SH: Combination CH: Combination
Basdanis (2005)[82] Trial dates: Start: 2000 Finish: 2002	Total: 95 SH: 50 CH: 45	Age: Range: 22-72 Number male 54	Grades included III+IV Grade III: 73 Grade IV: 22	Stapling gun: PPH 01 Comparator: M&M + diathermy and ligasure Anaesthesia: SH: Combination CH: Combination
Bikhchandani (2005)[92] Trial dates: Start: 2001 Finish: 2003	Total: 84 SH: 42 CH: 42	Age: Mean: 47 Variance Not reported Number male 70	Grades included III+IV Grade III: 71 Grade IV: 13	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Regional CH: Regional
Boccasanta (2001)[85] Trial dates: Start: 1996 Finish: 1999	Total: 80 SH: 40 CH: 40	Age: Mean: 51 Range: 21-92 Number male 33	Grades included IV Grade IV: 80	Stapling gun: PPH 01 Comparator: M&M + HLB Anaesthesia: SH: Combination CH: Combination
Cheetham (2003)[77] Trial dates: Not reported	Total: 31 SH: 15 CH: 16	Age: Range: 26-72 Number male 22	Grades included Not reported All participants had symptomatic prolapsing haemorrhoids	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General

Study	Participants			Interventions
	Number	Population	Degree of haemorrhoids	
Chung (2005)[90] Trial dates: Start: 2001 Finish: 2003	Total: 88 SH: 43 CH: 45	Age: Mean: 45.7 Variance Not reported Number male 59	Grades included III Grade III: 88	Stapling gun: PPH 01 Comparator: M&M + Harmonic Scalpel Anaesthesia: SH: Combination CH: Combination
Correa-Rovelo (2002)[94] Trial dates: Not reported	Total: 84 SH: 42 CH: 42	Age: Mean: 45.15 Range: 27-77 Number male 41	Grades included III+IV Grade III: 60 Grade IV 24	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Combination CH: Regional
Docherty (2001)[76] Trial dates: Not reported	Total: 46 SH: 26 CH: 20	Age: Not reported Number male Not reported	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported
Gravie (2005)[81] Trial dates: Start: 1999 Finish: 2000	Total: 126 SH: 63 CH: 63	Age: Mean: 47.5 Variance Not reported Number male Not reported	Grades included Not reported 85% had reducable prolapse, 5% had non-reducible and 5 patients had no prolapse	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Not reported CH: Not reported
Hasse (2004)[73] Trial dates: Start: 1998 Finish: 2001	Total: 80 SH: 40 CH: 40	Age: Mean: 47.1 Variance: Not reported Number male 39	Grades included III Grade III: 80	Stapling gun: PPH 01 Comparator: Fransler and Anderson Anaesthesia: SH: General CH: General
Hetzer (2002)[88] Trial dates: Start: 1999 Finish: 2000	Total: 40 SH: 20 CH: 20	Age: Mean: 47.6 Range: 28-74 Number male 29	Grades included II+III Grade II: 12 Grade III: 28	Stapling gun: PPH 01 Comparator: Ferguson Anaesthesia: SH: Combination CH: Combination
Ho (2000)[61, 69] Trial dates: Start: 1999 Finish: 2000	Total: 119 SH: 57 CH: 62	Age: Mean: 48.6 Variance Not reported Number male 59	Grades included II+III Grade II: Not reported Grade III: Not reported Grade IV: Not reported	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General

Study	Participants			Interventions
	Number	**Population**	**Degree of haemorrhoids**	
Kairaluoma (2003)[80] Trial dates: Start: 1999 Finish: 2000	Total: 60 SH: 30 CH: 30	Age: Range: 17-65 Number male 32	Grades included III Grade III: 60	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General
Kraemer (2005)[28] Trial dates: Not reported	Total: 50 SH: 25 CH: 25	Age: Range: 28-82 Number male 27	Grades included III+IV Grade III: 46 Grade IV: 4	Stapling gun: PPH 01 Comparator: M&M + ligasure. Fransler-Arnold segmental plastic reconstruction in 6 patients Anaesthesia: SH: Combination CH: Combination
Krska (2003)[79] Trial dates: Not reported	Total: 50 SH: 25 CH: 25	Age: Mean: 50.8 Variance Not reported Number male 37	Grades included III Grade III: 50	Stapling gun: Not reported Comparator: M&M Anaesthesia: SH: Regional CH: Regional
Lau (2004)[91] Trial dates: Start: 2001 Finish: 2002	Total: 24 SH: 13 CH: 11	Age: Mean: 49.1 Variance: Not reported Number male 11	Grades included II-IV Grade II: 13 Grade III: 6 Grade IV: 4 1 patient not classified	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General
Ortiz (2002)[87] Trial dates: Start: 1999 Finish: 2000	Total: 55 SH: 27 CH: 28	Age: Mean: 47.6 Variance Not reported Number male 32	Grades included III+IV Grade III: 29 Grade IV: 26	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional
Ortiz (2005)[86] Trial dates: Start: 2001 Finish: 2002	Total: 31 SH: 15 CH: 16	Age: Mean: 48 Range: 28-69 Number male 19	Grades included IV Grade IV: 31	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional
Palimento (2003)[68, 84] Trial dates: Start: 1999 Finish: 2000	Total: 74 SH: 37 CH: 37	Age: Range: 25-84 Number male 47	Grades included III+IV Grade III: 34 Grade IV: 40	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional

Study	Participants			Interventions
	Number	Population	Degree of haemorrhoids	
Pavlidis (2002)[83] Trial dates: Start: 1999 Finish: 2000	Total: 80 SH: 40 CH: 40	Age: Mean: 47.5 Range: 29-75 Number male 47	Grades included II-IV Grade II: 16 Grade III: 55 Grade IV: 9	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional
Ren (2002)[75] Trial dates: Not reported	Total: 90 SH: 45 CH: 45	Age: Range: 29-82 Number male 60	Grades included III+IV Grade III: 68 Grade IV: 22	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: General CH: General
Schmidt (2002)[72] Trial dates: Start: 1998 Finish: 2000	Total: 152 SH: 72 CH: 80	Age: Range: 24-91 Number male 94	Grades included III+IV Grade III: 123 Grade IV: 29	Stapling gun: Not reported Comparator: Parks and Fransler-Arnold Anaesthesia: 105 had regional 47 had general
Senagore (2004)[89] Trial dates: Start: 2001 Finish: 2002	Total: 156 SH: 77 CH: 79	Age: Mean: 49.5 Range: 23-78 Number male 107	Grades included III Grade III: 156	Stapling gun: PPH 01 Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported
Shalaby (2001)[93] Trial dates: Start: 1997 Finish: 1998	Total: 200 SH: 100 CH: 100	Age: Mean: 46.6 SD: 13.1 Number male 124	Grades included II-IV Grade II: 23 Grade III: 62 Grade IV: 77 A further 37 patients were described as having prolapse 1 patient not classified	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: General CH: General
Thaha (2003)[71] Trial dates: Not reported	Total: 90 SH: 48 CH: 42	Age: Median: 50 Range: 24-81 Number male 52	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported
Thaha (2004)[70] Trial dates: Not reported	Total: 182 SH: 91 CH: 91	Age: Median: 50 Range: 24-81 Number male 103	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported

Study	Participants			Interventions
	Number	Population	Degree of haemorrhoids	
Van de Stadt (2005)[78] Trial dates: Start: 2000 Finish: 2001 Language: English	Total: 40 SH: 20 CH: 20	Age: Mean: 48 Range: 19-78 Number male 29	Grades included II+III Grade II: Not reported Grade III: Not reported Grade IV: Not reported	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Combination CH: Combination 1 patient in each did not have general anaesthesia
Wilson (2002)[43] Trial dates: Not reported	Total: 62 SH: 32 CH: 30	Age: Range: 40-67 Number male Not reported	Grades included III Grade III: 62	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Not reported CH: Not reported

Six RCTs did not report the stapling gun used.[70-72, 74, 76, 79, 94] The remaining twenty one RCTs used PPH01. Twenty studies used Milligan Morgan as the CH technique, with diathermy[61, 68, 69, 74, 77, 80, 82-84, 86, 87, 91] or without diathermy.[28, 43, 75, 78, 79, 81, 85, 90, 92, 93] One study using Milligan Morgan reported using Fansler-Arnold segmental plastic reconstruction in 6 patients.[28] Six studies used the Ferguson technique.[70, 71, 76, 88, 89, 94] One study used the Parks and Fansler-Arnold techniques,[72] and one study used the Fansler-Anderson technique.[73]

Twenty three studies reported the degree of haemorrhoids experienced by patients prior to surgery. Only three studies recruited the full spectrum of patients eligible for surgery; II, III and IV degree haemorrhoids.[83, 91, 93] Of the other studies, eight studies included patients with III and IV degree haemorrhoids,[28, 68, 72, 75, 82, 84, 87, 92, 94] four studies included patients with II and III degree,[69, 74, 78, 88] six were restricted to patients with III degree,[43, 73, 79, 80, 89, 90] and two restricted to patients with IV degree haemorrhoids (Table 5.1).[85, 86]

Twenty one studies reported the type of anaesthetic used in each arm of the trial. Seven studies used general anaesthetic (GA) in both arms,[69, 73, 75, 77, 80, 91, 93] six used regional anaesthetic (RA) in both arms,[68, 79, 83, 84, 86, 87, 92] seven used a GA in some patients and RA in others in both arm (combination),[28, 74, 78, 82, 85, 88, 90] one study used RA for those undergoing CH and a combination for those undergoing SH.[94]

Eight RCTs did not state whether they included or excluded people with co-morbid conditions.[70-72, 74-76, 82, 83, 88] One study specifically stated including people with fissures, anal prolapse, skin tags, and eczema.[28] The remaining eighteen studies excluded people with a range of co-morbid conditions, such as: bleeding disorders[61, 73, 77] and anticoagulation therapy;[77, 80, 86, 87, 89, 90] anal stenosis,[43] fissures,[78, 80, 81, 84, 86, 87, 90-93] fistulas,[78, 80, 81, 84, 86, 87, 90-93] prolapse,[91] or other associated anal pathology;[78, 80, 81, 90, 92, 94] previous anal surgery;[61, 86, 87, 90, 94] colorectal cancer,[78, 79, 84, 85, 89] rectal polyps[43] or radiotherapy;[78] inflammatory bowel disease;[78, 84-87, 90] incontinence;[87] irreducible,[61, 78, 91] external,[90] or thrombosed haemorrhoids;[73, 78, 81, 91, 93] HIV[73] or immunosuppresion;[94] abscesses;[84, 90] dermatitis[78, 87] or eczema.[86] Some studies excluded patients with diabetes or coronary artery disease;[79] women who were pregnant[73] or had had an episiotomy;[73] people under the age of 18 years[77, 78] or over the age of 70 years;[80] or people with mental deficits.[84]

Twenty one studies did not report whether the participants had undergone prior treatment for haemorrhoidal disease.[28, 43, 61, 68-72, 74-79, 82-87, 89, 90, 93, 94] One study reported that none of the participants had had any previous intervention,[73] and two that there had been no prior surgery.[81, 91] Three studies included patients that had undergone prior non-excisional interventions,[80, 91, 92] one of which also included patients that had previously undergone CH.[80]

The quality of the included studies varied; all included studies had some methodological flaws. Figure 5.2 gives the proportion of studies that scored 'Yes', 'No', 'Unclear' or 'Not applicable' (N/A) for each of the quality criteria. Full results of the quality assessment are available in Appendix 10.3.

Overall, 4% of studies were described as double blind; 4% reported that patients were blind to the surgical procedure, and 19% that outcomes assessors were blind. 37% of studies reported using an appropriate method of randomisation and/or allocation concealment. 37% of studies stated that the same surgeons conducted both SH and CH, and 33% that these surgeons were experienced in both techniques. Only 33% of studies reported the use of a power calculation, with one of these trials not recruiting the number of participants stated as being required to be adequately powered for the primary outcome.[77] 7% of RCTs had a loss to follow-up of greater than 80% at the

final time point, with a further 19% not reporting whether there were losses to follow-up or not.

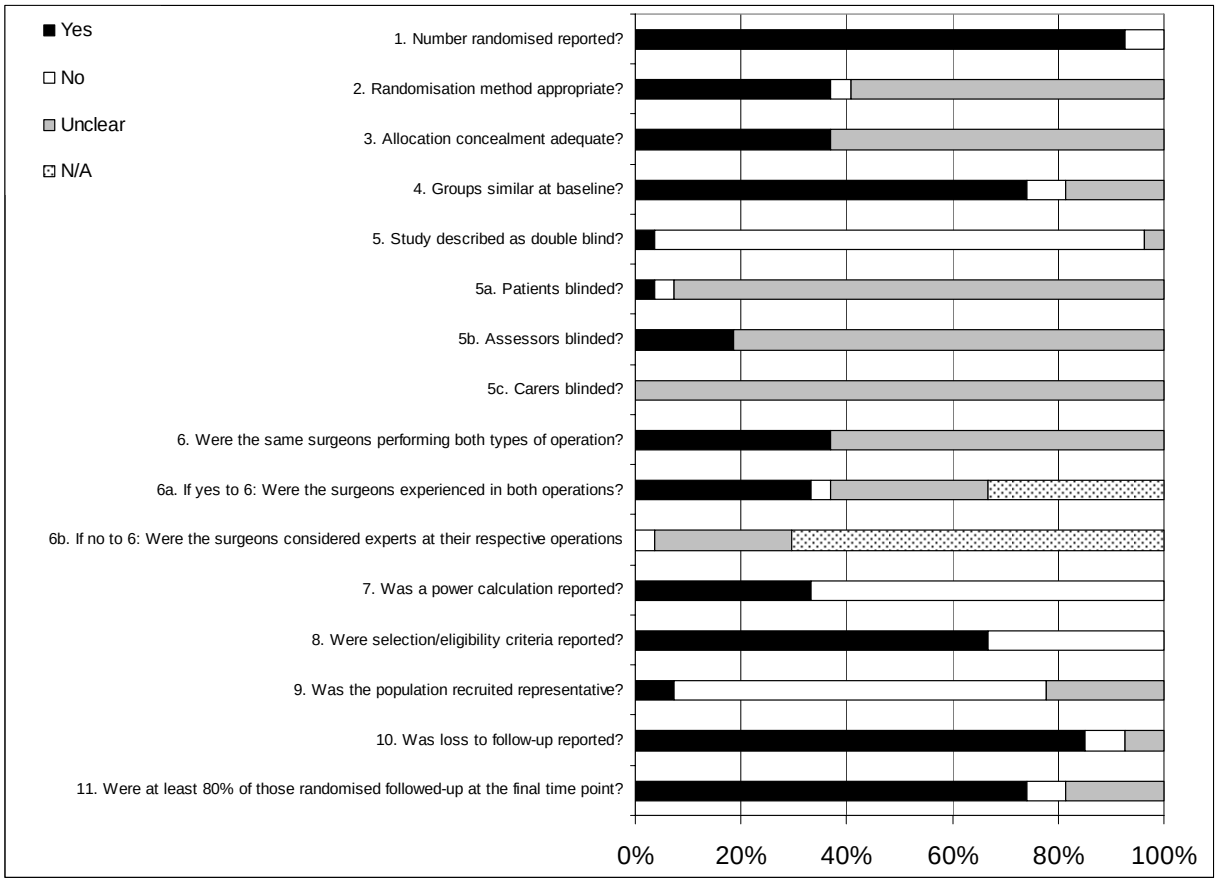
All three studies reporting recruiting what was considered an appropriate patient spectrum for this review (people with II, II and IV degree haemorrhoids) had other methodological flaws.[83, 91, 93] One did not report the method of randomisation or allocation concealment,[83] the second did not report the method of allocation concealment, nor whether outcomes assessors were blind to treatment,[93] and the third did nt report the method of randomisation or whether outcomes assessors were blind to treatment.[91] Some of the included studies recruited a restricted patient population, for example both Boccasanta (2001)[85] and Ortiz (2005)[86] recruited only patients with IV degree haemorrhoids. However, across the studies included in the current review a range of different populations across the entire patient spectrum; results from people with II, II and IV degree haemorrhoids were studied.

The study by Schmidt (2002) reported the use alternate randomisation, an inappropriate method of randomisation that may result in selection bias.[72] The lack of reporting of the method of randomisation in a further sixteen studies means that the potential for selection bias between the arms of the trial could not be assessed. Selection bias can lead to significant differences in the patient population in each arm of a trial, and therefore one arm may have more or less favourable outcomes as a result of the population recruited rather than the intervention being investigated. Of the sixteen trials where the method of randomisation was unclear, eleven reported that the groups were similar at baseline. The method of allocation concealment was also poorly reported, with ten trials reporting the use of an appropriate method. Both the method of randomisation and allocation concealment was either inappropriate or unclear for eleven trials. This means that the potential for selection and confounding biases could not be assessed in the remaining seventeen trials.

An issue to be considered when evaluating a recently introduced technology is the learning curve during the post-introduction period. It is therefore possible that the outcome after SH may be less favourable in trials conducted soon after the introduction of the technique. The trial by Kairuloama (2003) was conducted between 1999 and 2000, immediately after the introduction of staple guns.[80]

Although this is not the only trial that was conducted around this time, the authors did state that they had had technical problems during the SH procedure, and this does seem to impact on a range of post-operative outcomes. In addition, the study by Cheetham that did not report the dates between which the trial was conducted, but was published in 2003, suspended recruitment due to a high incidence of pain and urgency approximately 8 months post-operatively. The authors stated that these complications may have been due to incorporation of muscle into the resected tissue, differences in surgical practice, and the presence of concomitant anal pathology.[56, 77]

Figure 5.2: The proportion of included studies that scored 'Yes', 'No', 'Unclear' or 'Not applicable' (N/A) for each of the quality criteria.



5.2.2 Assessment of effectiveness

5.2.2.1 Pain

Early post-operative pain (up to 14 days)

Twenty one studies reported pain using a VAS scale in the early post-operative period (Table 5.2). Of these, twenty (95%) reported that patients experienced less pain following SH than CH; only eight provided a measure of variance, and six of which were statistically significant in favour of SH. Althought these eight studies provided sufficient data to include in a meta-analysis, there was statistically significant heterogeneity between them ($p<0.001$; $I^2=98.5\%$), and pooling was not undertaken.[61, 71, 75, 83, 91-94]

Table 5.2: VAS pain scores during the early post-operative period

Study	Number randomised SH	Number randomised CH	Time point	SH Mean (SD)	CH Mean (SD)	Mean difference (95% CI)
Ascanelli (2005)[74]	50	50	12h	2 (NR)	7 (NR)	-5
Correa-Rovelo (2002)[94]	42	42	24h	2.8 (1.4)	5.5 (1.4)	-2.70 (-3.30, -2.10)
Pavlidis (2002)[83]	40	40	24h	0.7 (0.2)	2.4 (0.5)	-1.70 (-1.87, -1.53)
Shalaby (2001)[93]	100	100	24h	2.5 (1.3)	7.6 (0.7)	-5.10 (-5.39, -4.81)
Lau (2004)[91]	13	11	Mean 2d	3.5 (2.5)	2.6 (1.5)	0.90 (-0.72, 2.52)
Ho (2000)[61]	57	62	In hospital	4.5 (3.0)	5 (3.1)	-0.50 (-1.61, 0.61)
Bikhchandani (2005)[92]	42	42	3d	1.52 (1.43)	4.5 (2.11)	-2.98 (-3.75, -2.21)
Hetzer (2002)[88]	20	20	3d	0.8 (NR)	5.4 (NR)	-4.6
Kraemer (2005)[28]	25	25	3d	4.2 (NR)	3.7 (NR)	0.5
Krska (2003)[79]	25	25	3d	4 (NR)	7.4 (NR)	-3.4
Van de Stadt (2005)[78]	20	20	3d	2.6 (NR)	4.7 (NR)	-2.1
Boccasanta (2001)[85]	40	40	3d	4 (NR)	6.5 (NR)	-2.5
Senagore (2004)[89]	77	79	3d	5 (NR)	6.25 (NR)	-1.25
Thaha (2003)[71]	48	42	Mean 7d	1.9 (1.58)	3.1 (1.97)	-1.20 (-1.94, -0.46)
Schmidt (2002)[72]	72	80	Mean 7d	1.83 (NR)	3.74 (NR)	-1.91
Ren (2002)[75]	45	45	Unclear	2.2 (0.4)	6.4 (2.1)	-4.20 (-4.82, -3.58)

Study	Number randomised SH	Number randomised CH	Time point	SH Median (Range)	CH Median (Range)
Basdanis (2005)[82]	50	45	24h	3 (1-6)	6 (3-7)
Palimento (2003)[84]	37	37	24h	3 (1-6)	5 (3-7)
Kairaluoma (2003)[80]	30	30	3d	3.36 (NR)	5.88 (NR)
Cheetham (2003)[77]	15	16	3d	2.7 (NR)	7 (NR)
Chung (2005)[90]	43	45	Mean 7d	1.5 (0.7-6)	3.5 (1.9-6)

By using visual examination of forest plots and consideration of the characteristics of the trials we identified possible causes of the heterogeneity observed between studies reporting pain scores in the early post-operative period. These were the pre-operative degree of haemorrhoids of the recruited patients, country in which the trial was conducted, and sample size. There was no indication that the following factors contributed to the heterogeneity: the time point at which pain was recorded, study quality, the inclusion or exclusion of people with co-morbid conditions, and the stapling gun used. There was insufficient information to examine whether the excision of skin tags as a concomitant procedure impacted on the degree of post-operative pain experienced.

The study by Lau (2004)[91] that reported SH to be more painful than CH was a small, underpowered study conducted in Hong Kong, which recruited a high proportion of patients (57%) with II degree haemorrhoids and had the longest operating time of all studies for SH (SH: mean 35.4 minutes, SD 9.89; CH: mean 29.8 minutes, SD 13.01). Exclusion of this trial from the analysis did not eliminate, or even diminish, the highly significant heterogeneity between studies ($p<0.001$; $I^2=98.7\%$; Appendix 10.7, Figure 10.2).[91]

In addition to these factors, the VAS is a subjective outcome measure, and its application may vary across studies causing heterogeneity. The VAS scores could be influenced by such basic factors as: how the use of a VAS is described to patients; when the scores are recorded; the post-operative analgesic regimen employed; and whether the VAS score was recorded before or after analgesia was administered. This is reflected in the different effect sizes reported in the trials, but with each effect size having tight confidence intervals.

The number of patients requiring different types of analgesia in the immediate post-operative period was reported in eleven studies (Table 5.3). Given that the standard post-operative analgesic regimens may vary between hospitals, with different regimens being administered for similar pain levels, it was deemed inappropriate to pool these results, regardless of the presence or absence of statistical heterogeneity. There were no clear trends in favour of SH or CH.

Table 5.3: Number of people requiring intramuscular or oral analgesia (opioids or other) during the immediate post-operative period

	SH n/N (%)	CH n/N (%)	OR (95% CI)
Injections: opioid			
Kraemer (2005)[28]	1/25 (4.0)	0/25 (0)	3.12 (0.12, 80.39)
Ortiz (2005)[86]	1/15 (6.7)	2/16 (12.5)	0.50 (0.04, 6.17)
Gravie (2005)[81]	11/63 (17.5)	24/63 (38.1)	0.34 (0.15, 0.78)
Injections: Other			
Correa-Rovelo (2002)[94]	1/42 (2.4)	2/42 (4.8)	0.49 (0.04, 5.59)
Injections: not specified/combination			
Wilson (2002)[43]	0/32 (0)	0/30 (0)	-
Shalaby (2001)[93]	49/100 (49.0)	100/100 (100)	0 (0, 0.08)
Cheetham (2003)[77]	2/15 (13.3)	0/16 (0)	6.11 (0.27, 138.45)
Ortiz (2002)[87]	3/27 (11.1)	5/28 (17.9)	0.58 (0.12, 2.69)
Ren (2002)[75]	6/45 (13.3)	17/45 (37.8)	0.25 (0.09, 0.72)
Oral: opioid			
Kraemer (2005)[28]	8/25 (32.0)	6/25 (24.0)	1.49 (0.43, 5.17)
Ascanelli (2005)[74]	2/50 (4.0)	4/50 (8.0)	0.48 (0.08, 2.74)
Oral: not specified/combination			
Kraemer (2005)[28]	25/25 (100)	25/25 (100)	-
Gravie (2005)[81]	62/63 (98.4)	62/63 (98.4)	1.00 (0.06, 16.35)
Senagore (2004)[89]	54/77 (70.1)	67/79 (84.8)	0.48 (0.22, 1.01)
Ortiz (2002)[87]	27/27 (100)	28/28 (100)	-

5.2.2.2 Pain in the later post-operative period

The degree of pain experienced by patients after both SH and CH lessened over the three weeks post-operatively (Table 5.4). However, all eight studies evaluating pain using a VAS scale between 10 and 15 days post-operatively reported that patients experienced less pain following SH than CH; only three provided a measure of variance, two of which showed a statistically significant difference in favour of SH.[61, 92, 94] These three studies reported sufficient data to be included in a meta-analysis, however, there was statistically significant heterogeneity between studies ($p<0.001$, $I^2=91\%$).[61, 92, 94] Given the potential sources of heterogeneity related to VAS scores already discussed, pooling was not undertaken.

Table 5.4: VAS pain scores 10 to 15 days post-operatively

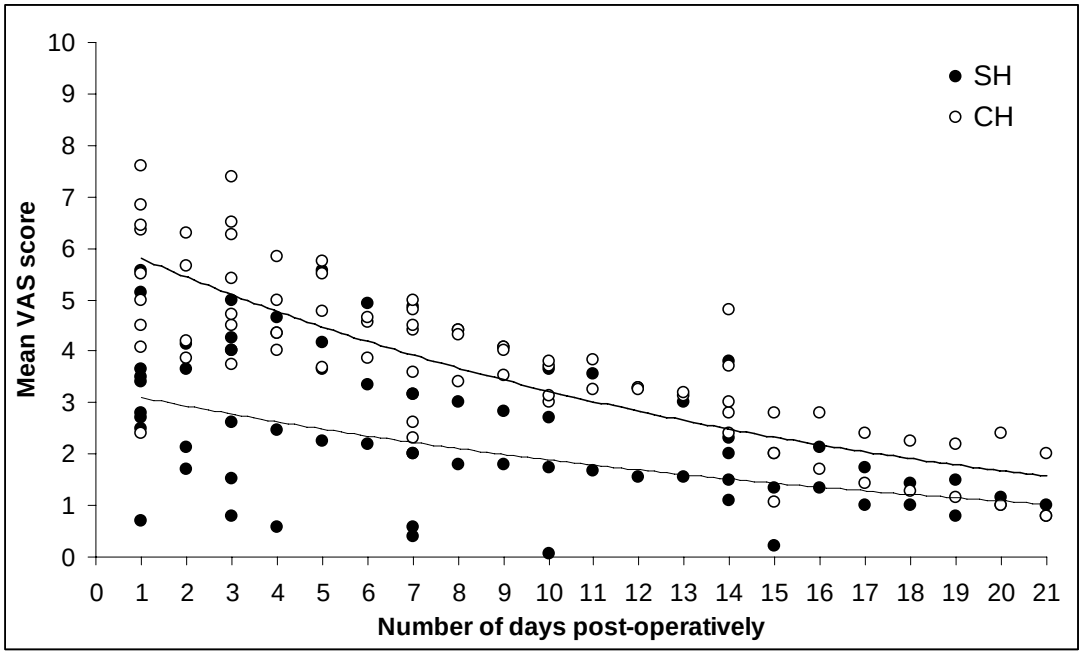
Study	Number randomised		Time point	SH	CH	Mean difference (95% CI)
	SH	CH		Mean (SD)	Mean (SD)	
Boccasanta (2001)[85]	40	40	10d	2.7 (NR)	3.8 (NR)	-1.1
Ascanelli (2005)[74]	50	50	10d	0 (NR)	3 (NR)	-3
Correa-Rovelo (2002)[94]	42	42	14d	1.1 (SD 1.4)	3.7 (SD 1.5)	-2.60 (-3.22, -1.98)
Ho (2000)[61]	57	62	14d	3.8 (SD 3.78)	4.8 (SD 3.15)	-1.00 (-2.25, 0.25)
Kraemer (2005)[28]	25	25	14d	2.3 (NR)	2.4 (NR)	-0.1
Van de Stadt (2005)[78]	20	20	14d	1.5 (NR)	2.8 (NR)	-1.3
Senagore (2004)[89]	77	79	14d	2 (NR)	3 (NR)	-1.0
Bikhchandani (2005)[92]	42	42	15d	0.21 (SD 0.52)	1.05 (SD 1.21)	-0.84 (-1.24, -0.44)
Study	**Number randomised**		**Time point**	**SH**	**CH**	
	SH	**CH**		**Median (Range)**	**Median (Range)**	
Cheetham (2003)[77]	15	16	10d	0.7 (NR)	2.3 (NR)	
Kairaluoma (2003)[80]	30	30	14d	0 (NR)	1.47 (NR)	

Although few trials could be included in the meta-analysis, given that 97% of all studies reporting mean VAS scores over the first 15 days reported less pain after SH, we considered it prudent to investigate this further. All mean VAS scores were extracted for each time point measured in any study that reported this outcome (Figure 5.3). VAS scores were measured each day up to 21 days post-operatively in at least one study. Each data point was plotted and a trend line fitted to give a visual

representation of the trend in post-operative pain over time. A value of 0.05 was added to one VAS score of zero to allow the curve to be fitted.

Bayesian meta-regression of these data (Appendix 10.4) predicts that VAS pain (on a scale of 0 to 10) is on average 3.0 in the SH group and 5.3 in the CH group at day 1, decreasing to less than 0.5 in both groups at 21 days. It is therefore not meaningful to extrapolate to time points beyond 21 days using this model.

Figure 5.3: Mean VAS pain scores reported in the included RCTs over the 21 day post-operative period



5.2.2.3 Pain at follow-up

For short term follow-up (>6 weeks and <12 months) the results and the time points varied considerably. The trial conducted by Cheetham (2003)[77] reported a significantly greater number of patients complaining of discomfort after SH. Recruitment to this study was suspended due to the high incidence of pain and urgency experienced by patients after SH, resulting in the study being small and underpowered. The authors stated that the incorporation of muscle into the resected tissue (in 4 out of 5 patient experiencing these complications) could have resulted in an increased incidence of pain and urgency, but other factors such as differences in surgical practice and the presence of concomitant anal pathology, may also have

contributed.[56, 77] this study seemed to be responsible for the heterogeneity observed. When this study was removed from the analysis the pooled OR was reduced to 0.30 (95% CI: 0.09, 1.01, p=0.05; Appendix 10.7, Figure 10.5), further favouring SH. Although this did not reach statistical significance, there was no longer any significant heterogeneity between studies (Chi^2 p=0.48; I^2=0%).

At 12 months and later the number of patients complaining of pain was low. When results were pooled, there was no significant difference between SH and CH at any subsequent time point (Table 5.5).

Table 5.5: Number of people complaining of pain at follow-up

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Ho (2000)[61]	3 months	1/57 (1.8)	3/62 (4.8)	0.35 (0.04, 3.48)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6 months	2/41 (4.9)	3/41 (7.3)	0.65 (0.10, 4.11)
Cheetham (2003)[77]	8 months	7/14 (50.0)	2/16 (12.5)	7.00 (1.14, 42.97)
Bikhchandani (2005)[92]	11 months	0/39 (0)	5/40 (12.5)	0.08 (0, 1.53)
			Pooled result	0.73 (0.12, 4.46) p=0.74
			Test for heterogeneity	Chi^2 p=0.04; I^2=64%
Hetzer (2002)[88]	12 months	0/20 (0)	0/20 (0)	-
Kairaluoma (2003)[80]	12 months	0/30 (0)	0/30 (0)	-
Ortiz (2005)[86]	12 months	0/15 (0)	0/16 (0)	-
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Ortiz (2002)[87]	16 months	1/27(3.7)	0/28 (0)	3.23 (0.13, 82.71)
Ho (2000)[61, 69]	18 months	1/27 (3.7)	1/33 (3.0)	1.23 (0.07, 20.64)
Palimento (2003)[84]	18 months	6/37 (16.2)	7/37 (18.9)	0.83 (0.25, 2.76)
			Pooled result	1.03 (0.37, 2.88) p=0.95
			Test for heterogeneity	Chi^2 p=0.73; I^2=0%
Van de Stadt (2005)[78]	46 months	6/20 (30.0)	3/20 (15.0)	1.37 (0.29, 6.61)
Palimento (2003)[68, 84]	5 years	4/37 (10.8)	3/37 (8.1)	2.43 (0.51, 11.51)
			Pooled result	1.84 (0.61, 5.52) p=0.28
			Test for heterogeneity	Chi^2 p=0.61; I^2=0%

Pain: Summary

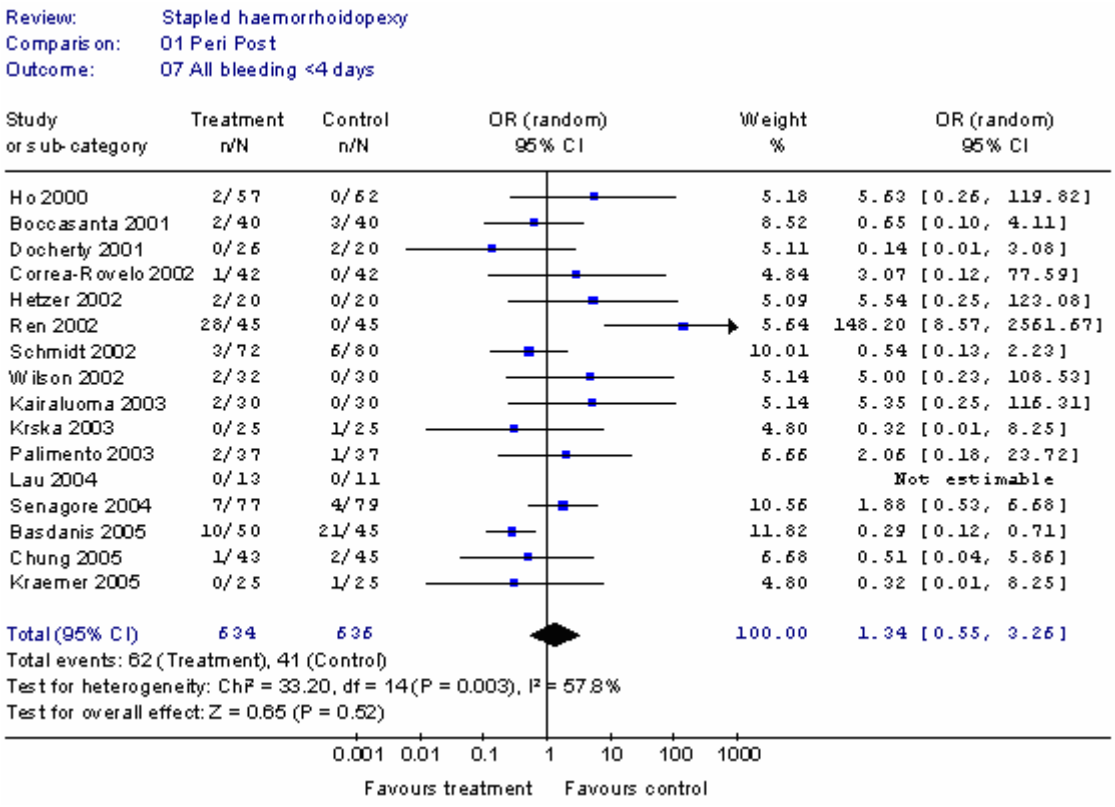
During the early post-operative period, SH was less painful than CH. The pain experienced lessened over time after both SH and CH, however, patients still experienced less pain following SH than CH at 10 to 15 days post-operatively, but there was little difference by day 21. Up to and at one year and beyond, there was no difference in the number of patients experiencing pain between the two types of surgery.

5.2.2.4 Bleeding

Bleeding in the immediate post-operative period

Sixteen studies reported bleeding in the early post-operative period;[28, 43, 61, 72, 75, 76, 79, 80, 82, 84, 85, 88-91, 94] fourteen of which reported no statistically significant difference in the incidence of bleeding between the SH and CH. The pooled OR demonstrated no statistically significant difference in rate of bleeding between SH and CH (Figure 5.4), however, the confidence intervals of the pooled result only just reached the line of no effect (p=0.05).

Figure 5.4: Number of people with bleeding in the immediate post-operative period

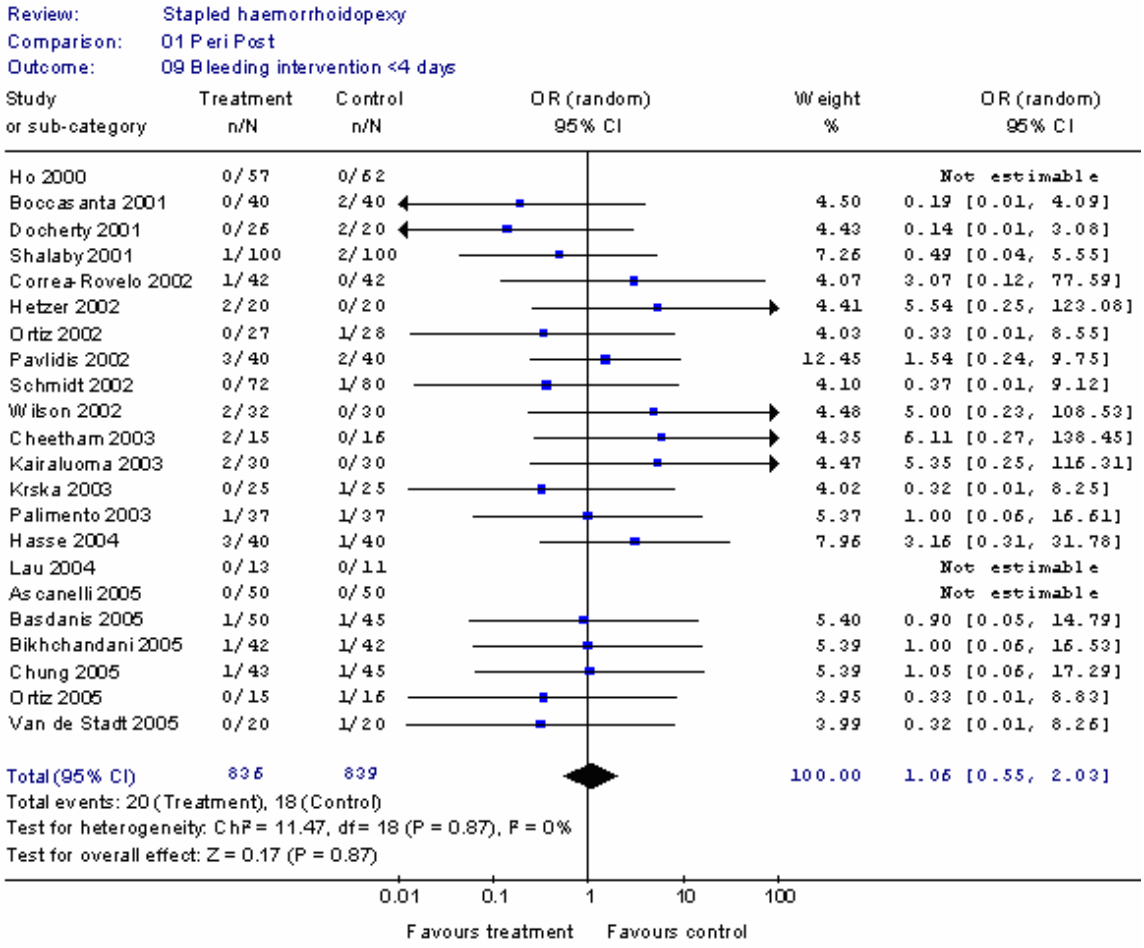


There was evidence of moderate heterogeneity between the studies (I^2=57.8, P=0.003). The study by Ren (2002)[75] reported a particularly high incidence of bleeding after SH which seemed to be responsible for this heterogeneity. This study, published in Chinese, may have included the number of patients that required haemostatic sutures during the peri-operative period of SH, which were not included in the data extracted from the other studies. When this study was excluded from the

analysis (Appendix 10.7, Figure 10.7), there was no longer any significant heterogeneity between studies (Chi^2 p=0.24; I^2=19.2%). In addition, there was a shift in the direction of effect, with the OR now 0.86 (95% CI: 0.46, 1.61; p=0.63), and clearly no statistically significant difference between SH and CH. The results of this sensitivity analysis seem to be far more representative of the incidence of bleeding than the analysis including Ren (2002).[75]

Twenty two studies reported the rate of patients who required intervention for bleeding during the early post-operative period (Figure 5.5).[43, 61, 72-74, 76-80, 82-88, 90-94] In general, the number of patients requiring intervention was small (0-3 patients wiht SH; 0-2 patients with CH) and none of these studies found any statistically significant differences in the rate of interventions required for bleeding, hence the pooled result was not statistically significant.

Figure 5.5: Number of people with bleeding that required intervention in the immediate post-operative period



Bleeding in the later post-operative period (14 days and 8 weeks)

Six studies reported bleeding between 14 days and 8 weeks after the operation (Table 5.6). The pooled OR of two studies demonstrated a significantly higher incidence of bleeding after CH at 14 days. At 4 to 6 weeks post-surgery, there was generally a higher incidence of bleeding in patients after SH, however, the pooled OR demonstrated no significant difference between SH and CH. Only one study (Ho 2000[61]) reported the incidence of bleeding requiring intervention; 0% after SH and 4.8% after CH (OR 0.94; 95% CI: 0.36, 2.49).

Table 5.6: Number of people with bleeding between 14 days and 8 weeks post-operatively

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Correa-Rovelo (2002)[94]	14 days	14/42 (33.3)	23/42 (54.8)	0.41 (0.17, 1.00)
Ho (2000)[61]	14 days	19/57 (33.3)	33/62 (53.2)	0.44 (0.21, 0.92)
			Pooled result	0.43 (0.0.24, 0.76) p=0.003
			Test for heterogeneity	Chi^2 p=0.92; I^2=0%
Basdanis (2005)[82]	4 weeks	0/50 (0)	1/45 (2.2)	0.29 (0.01, 7.39)
Cheetham (2003)[77]	6 weeks	4/15 (26.7)	1/16 (6.3)	5.45 (0.53, 55.80)
Ho (2000)[61]	6 weeks	9/57 (15.8)	7/62 (11.3)	1.47 (0.51, 4.26)
Kairaluoma (2003)[80]	6 weeks	10/30 (33.3)	2/30 (6.7)	7.00 (1.38, 35.48)
Kraemer (2005)[28]	6 weeks	3/25 (12.0)	4/25 (16.0)	0.72 (0.14, 3.59)
Correa-Rovelo (2002)[94]	8 weeks	6/42 (14.3)	5/42 (11.9)	1.23 (0.35, 4.40)
			Pooled result	1.75 (0.97, 3.14) p=0.06
			Test for heterogeneity	Chi^2 p=0.26; I^2=22.7%

Bleeding during short term follow-up (6 weeks to one year)

Six studies reported the incidence of bleeding between 6 weeks and one year post-operatively (Table 5.7). The incidence of bleeding varied greatly, ranging from 0% to 28.6% after SH and 0% to 21.5% after CH; none of the studies reported a significant difference between SH and CH; consequently, nor did the pooled estimates.

Table 5.7: Number of patients complaining of bleeding at follow-up

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Ho (2000)[61]	3 months	1/57 (1.8)	2/62 (3.2)	0.54 (0.05, 6.07)
Correa-Rovelo (2002)[94]	6 months	8/41 (19.5)	2/41 (4.9)	4.73 (0.94, 23.82)
Senagore (2004)[89]	6 months	10/77 (13.0)	17/79 (21.5)	0.54 (0.23, 1.28)
Cheetham (2003)[77]	8 months	4/14 (28.6)	3/16 (18.8)	1.73 (0.31, 9.57)
Boccasanta (2001)[85]	<1 year	0/40 (0)	2/40 (5.0)	0.19 (0.01, 4.09)
			Pooled result	1.00 (0.36, 2.77) p=1.00
			Test for heterogeneity	Chi^2 p= 0.13; I^2=43.7%
Ascanelli (2005)[74]	12 months	2/50 (4.0)	0/50 (0)	5.21 (0.24, 111.2445)
Hasse (2004)[73]	12 months	3/38 (7.9)	1/38 (2.6)	3.17 (0.31, 31.95)
Kairaluoma (2003)[80]	12 months	4/30 (13.3)	1/30 (3.3)	4.46 (0.47, 42.51)
Ortiz (2005)[86]	12 months	1/15 (6.7)	1/16 (6.3)	1.07 (0.06, 18.82)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Senagore (2004)[89]	12 months	9/59 (15.3)	6/58 (10.3)	1.56 (0.52, 4.70)
			Pooled result	2.09 (0.91, 4.83) p=0.08
			Test for heterogeneity	Chi^2 p=0.85; I^2=0%
Ortiz (2002)[87]	16 months	2/27 (7.4)	1/28 (3.6)	2.16 (0.18, 25.32)
Palimento (2003)[84]	18 months	8/37 (21.6)	5/37 (13.5)	1.77 (0.52, 6.01.45)
			Pooled result	1.84 (0.62, 5.50) p=0.28
			Test for heterogeneity	Chi^2 p=0.89; I^2=0%
Van de Stadt (2005)[78]	46 months	5/20 (25.0)	6/20 (30.0)	0.78 (0.19, 3.13)
Palimento (2003)[68, 84]	5 years	3/37 (8.1)	2/37 (5.4)	1.54 (0.24, 9.82)
			Pooled result	(0.33, 3.01) p=1.00
			Test for heterogeneity	Chi^2 p=0.56; I^2=0%

Six studies reported the incidence of bleeding at 12 months (Table 5.7), none of which reported a significant difference between SH and CH; consequently, nor did the pooled estimates.

One study (Ortiz 2002[87]) reported bleeding at 16 months post-operatively, one at 18 months and 5 years (Palimento 2003[84]), and another at 46 months (Van de Stadt 2005[78]). None of these reported a statistically significant difference in bleeding between SH and CH, consequently, nor did the pooled estimates (Table 5.7).

Bleeding: Summary

The only time point were there was a significant difference in the incidence of bleeding was at 14 days post-operatively, However, this was based on the meta-analysis of only two studies. Generally there was no significant difference in incidence of bleeding between SH and CH during the late post-operative period, or at subsequent follow up.

5.2.2.5 Prolapse

Prolapse in the post-operative period

Only nine studies reported residual prolapse post-operatively, and the number of events in most trials was low (Table 5.8).

Table 5.8: Number of patients with prolapse

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Shalaby (2001)[93]	1 week	1/100 (1.0)	2/100 (2.0)	0.49 (0.04, 5.55)
Bikhchandani (2005)[92]	15 days	2/42 (4.8)	0/42 (0)	5.25 (0.24, 112.66)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Cheetham (2003)[77]	6 weeks	2/15 (13.3)	0/16 (0)	6.11 (0.27, 138.45)
Kairaluoma (2003)[80]	6 weeks	12/30 (40.0)	1/30 (3.3)	19.33 (2.31, 161.57)
Kraemer (2005)[28]	6 weeks	2/25 (8.0)	0/25 (0)	5.43 (0.25, 118.96)
Ortiz (2005)[86]	6 weeks	0/15 (0)	0/16 (0)	-
Ortiz (2002)[87]	6 weeks	0/27 (0)	0/28 (0)	-
Lau (2004)[91]	8 weeks	6/13 (46.2)	1/11 (9.1)	8.57 (0.84, 87.83)
			Pooled result	5.18 (1.73, 15.50) p=0.003
			Test for heterogeneity	Chi^2 p= 0.38; I^2=5.8%
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Basdanis (2005)[82]	6 months	3/50 (6.0)	0/40 (0)	5.97 (0.30, 119.01)
Correa-Rovelo (2002)[94]	6 months	1/41 (2.4)	0/41 (0)	3.07 (0.12, 77.69)
Senagore (2004)[89]	6 months	5/77 (6.5)	0/79 (0)	12.06 (0.66, 221.98)
Cheetham (2003)[77]	8 months	2/14 (14.3)	1/16 (6.3)	2.50 (0.20, 31.00)
Boccasanta (2001)[85]	<1 year	0/40 (0)	0/40 (0)	-
			Pooled result	4.68 (1.11, 19.71) p=0.04
			Test for heterogeneity	Chi^2 p= 0.86; I^2=0%
Hasse (2004)[73]	12 months	6/38 (15.8)	0/38 (0)	15.40 (0.84, 283.85)
Hetzer (2002)[88]	12 months	1/20 (5.0)	1/20 (5.0)	1.00 (0.06, 17.18)
Kairaluoma (2003)[80]	12 months	5/30 (16.7)	0/30 (0)	13.16 (0.69, 249.48)
Ortiz (2005)[86]	12 months	8/15 (53.3)	0/16 (0)	37.40 (1.90, 736.26)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Senagore (2004)[89]	12 months	2/59 (3.4)	2/58 (3.4)	0.98 (0.13, 7.22)
Shalaby (2001)[93]	12 months	1/95 (1.1)	2/80 (2.5)	0.41 (0.04, 4.66)
			Pooled result	3.20 (0.71, 14.45) p=0.13
			Test for heterogeneity	Chi^2 p= 0.08; I^2=48.8%
Ortiz (2002)[87]	16 months	7/27 (25.9)	0/28 (0)	20.85 (1.13, 368.05)
Ho (2000)[61, 69]	18 months	3/27 (11.1)	1/33 (3.0)	4.00 (0.39, 40.88)
Gravie (2005)[81]	2 year	4/52 (7.7)	1/57 (1.8)	4.67 (0.50, 43.18)
			Pooled result	6.25 (1.53, 25.54) p=0.01
			Test for heterogeneity	Chi^2 p= 0.64; I^2=0%
Van de Stadt (2005)[78]	46 months	5/20 (25.0)	0/20 (0)	14.55 (0.75, 283.37)
Palimento (2003)[68, 84]	5 years	0/31 (0)	0/29 (0)	-
			Pooled result for 12 to 46 months	4.34 (1.67, 11.28) p=0.003
			Test for heterogeneity	Chi^2 p= 0.20; I^2=26%

The scarcity of data for this time point is likely to be due to patients being too tender for rectal examination. Where residual prolapse was reported, it tended to be observed more often after SH than CH. The pooled result showed a statistically significantly higher incidence of residual prolapse after SH. However, only one trial (Kairaluoma 2003[80]) reported a significantly higher incidence of residual prolapse after SH than CH. This trial reported experiencing technical difficulties during SH and seemed to account for the significance of the pooled result. When it was removed from the analysis, the OR decreased to 3.38 (95% CI: 1.00, 11.47; p=0.05; Test for heterogeneity: Chi^2 p0.50, I^2=0%; Appendix 10.7, Figure 10.9).

Prolapse between 6 weeks and one year

Six studies reported prolapse between 6 weeks and one year post-operatively (Table 5.8). When the trials reporting the rate of prolapse at 6 and 8 months were pooled, there was a significantly higher incidence of prolapse after SH than CH.

Prolapse at 12 months and after

Seven studies reported prolapse at 12 months (Table 5.8).[73, 80, 83, 86, 88, 89, 93] The pooled estimate did not show any statistically significant difference in rate of prolapse between SH and CH at 12 months. There was some evidence of heterogeneity between the studies (I^2=48.8, P=0.08). Pre-operative degree of haemorrhoids is a possible reason for heterogeneity between these studies; the study by Ortiz (2005) only recruited patients with grade IV haemorrhoids.[86] When this study was removed from the analysis, there remained no significant differences between SH and CH, but there was no longer any significant heterogeneity between studies (Chi^2 p=0.18, I^2=35.5%; Appendix 10.7, Figure 10.11).

Five studies reported prolapse at longer-term follow-up (Table 5.8). The pooled estimate showed that prolapse were observed significantly more often at 16 to 24 months post-operatively after SH than CH. The pooled OR for 12 to 46 months demonstrated that prolapse was, again, significantly more common after SH (Table 5.8). This analysis contained the study by Ortiz (2005)[86] that only recruited patients with grade IV haemorrhoids and the study by Kairaluoma (2003)[80] that experienced

technical difficulties. When these were removed from the analysis (Appendix 10.7, Figure 10.14), the OR decreased to 3.11, but was still significant (95% CI: 1.14, 8.49; p=0.03), with no; there was still no significant heterogeneity between studies (Chi^2 p=0.26, I^2=21.2%).

Prolapse: Summary

Prolapse was significantly more common after SH than CH during the immediate post-operative period (residual prolapse) and the short term (up to 1 year). Although the incidence of prolapse was not significantly different between SH and CH when data from only 12 months was analysed, the significantly higher rate of prolapse after SH became evident when data from later time points were included in the analysis.

5.2.2.6 Symptoms controlled

Fifteen studies reported the number of patients with symptoms controlled, or recurrent symptoms (Table 5.9). There was no evidence that the number of patients with haemorrhoidal symptoms was consistently greater after either SH or CH, either post-operatively or in the longer-term. Significant heterogeneity was observed between studies for each meta-analysis, therefore pooling was not undertaken. When the trials by Kairaluoma (2003)[80] (technical difficulties), and Ortiz (2005)[86] (only IV degree haemorrhoids) were excluded from the analysis, there was no longer any statistical heterogeneity between studies at <3 months (Chi^2 p=0.66, I^2=0%; Appendix 10.7, Figure 10.16). There was still moderate heterogeneity at 12 months (Chi^2 p=0.11, I^2=59.9%; Appendix 10.7, Figure 10.18). Neither analysis showed a significant difference between SH and CH in the control of symptoms (<3 months: OR 0.85, 95% CI: 0.48, 1.53, p=0.59; 12 months: OR 1.05, 95% CI: 0.52, 2.11, p=0.89).

Table 5.9: The number of patients with symptoms controlled/uncontrolled, or complaining of recurrent symptoms.

Symptoms controlled		**SH**	**CH**	**Symptoms uncontrolled**		
Study	**Time point**	**n/N (%)**	**n/N (%)**	**SH**	**CH**	**OR (95% CI)**
Cheetham (2003)[77]	6 weeks	8/15 (53.3)	11/16 (68.8)	7/15 (46.7)	5/16 (31.2)	1.93 (0.44, 8.33)
Hasse (2004)[73]	6 weeks	31/40 (77.5)	28/40 (70.0)	9/40 (22.5)	12/40 (30.0)	0.68 (0.25, 1.85)
Kairaluoma (2003)[80]	6 weeks	15/30 (50.0)	27/30 (90.0)	15/30 (50.0)	3/30 (10.0)	9.00 (2.24, 36.17)
Kraemer (2005)[28]	6 weeks	21/25 (84.0)	21/25 (84.0)	4/25 (16.0)	4/25 (16.0)	1.00 (0.22, 4.54)
Correa-Rovelo (2002)[94]	2 months	31/41 (75.6)	28/41 (68.3)	10/41 (24.4)	13/41 (31.7)	0.69 (0.26, 1.83)
Pavlidis (2002)[83]	3 months	40/40 (100)	40/40 (100)	0/40 (0)	0/40 (0)	-
					Test for heterogeneity	Chi^2 p=0.03; I^2=63.9%
Ren (2002)[75]	4 months	40/45 (88.9)	37/45 (82.2)	5/45 (11.1)	8/45 (17.8)	0.58 (0.17, 1.93)
Chung (2005)[90]	6 months	41/43 (95.3)	43/45 (95.6)	2/43 (4.7)	2/45 (4.4)	1.05 (0.14, 7.80)
Correa-Rovelo (2002)[94]	6 months	32/41 (78.1)	35/41 (85.4)	9/41 (21.9)	6/41 (14.6)	1.64 (0.53, 5.12)
Hasse (2004)[73]	6 months	32/38 (84.2)	21/38 (55.3)	6/38 (15.8)	17/38 (44.7)	0.23 (0.08, 0.68)
Senagore (2004)[89]	6 months	63/77 (81.8)	51/79 (64.6)	14/77 (18.2)	28/79 (35.4)	0.40 (0.19, 0.85)
Cheetham (2003)[77]	8 months	5/14 (35.7)	11/16 (68.8)	9/14 (64.3)	5/16 (31.2)	3.96 (0.87, 18.12)
					Test for heterogeneity	Chi^2 p=0.02; I^2=62.3%
Hasse (2004)[73]	12 months	33/38 (86.8)	29/38 (76.3)	5/38 (13.2)	9/38 (23.7)	0.49 (0.15, 1.62)
Kairaluoma (2003)[80]	12 months	22/30 (73.0)	28/30 (93.3)	8/30 (26.7)	2/30 (6.7)	5.09 (0.98, 26.43)
Pavlidis (2002)[83]	12 months	40/40 (100)	40/40 (100)	0/40 (0)	0/40 (0)	-
Senagore (2004)[89]	12 months	44/59 (74.6)	48/58 (82.8)	15/59 (25.4)	10/58 (17.2)	1.64 (0.67, 4.02)
					Test for heterogeneity	Chi^2 p=0.07; I^2=63.2%

Symptom recurrence		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Correa-Rovelo (2002)[94]	2 months	0/42 (0)	0/42 (0)	-
Basdanis (2005)[82]	6 months	3/50 (6.0)	0/40 (0)	5.97 (0.30, 119.01)
Hetzer (2002)[88]	12 months	1/20 (5.0)	1/20 (5.0)	1.00 (0.06, 17.18)
Ascanelli (2005)[74]	12 months	2/50 (4.0)	0/50 (0)	5.21 (0.24, 111.24)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
			Pooled result	3.35 (0.67, 16.67) p=0.14
			Test for heterogeneity	Chi^2 p=0.63; I^2=0%

5.2.2.7 Persistent minor symptoms

Ten RCTs reported the incidence of itching or pruritis post-operatively (Table 5.10). Overall, the pooled OR demonstrated no significant difference in the incidence of itching or pruritis after SH or CH at any time point.

Only two studies reported the incidence of mucus or slime discharge (one at 6 weeks and one at 6 months), and both studies reported a higher incidence after CH than SH (Table 5.10).

Table 5.10: The number of patients complaining of itching/pruritis or mucus/slime discharge

Itching/pruritis		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Correa-Rovelo (2002)[94]	2 weeks	1/42 (2.4)	2/42 (4.8)	0.02 (0, 0.40)
Basdanis (2005)[82]	4 weeks	2/50 (4.0)	1/45 (2.2)	1.83 (0.16, 20.93)
Senagore (2004)[89]	4 weeks	3/77 (3.9)	3/79 (3.8)	1.03 (0.20, 5.25)
Ho (2000)[61]	6 weeks	5/57 (8.8)	11/62 (17.7)	0.45 (0.14, 1.37)
Kraemer (2005)[28]	6 weeks	2/25 (8.0)	1/25 (4.0)	2.09 (0.18, 24.61)
Lau (2004)[91]	8 weeks	1/13 (7.7)	4/11 (36.4)	0.15 (0.01, 1.58)
			Pooled result	0.49 (0.17, 1.43) p=0.19
			Test for heterogeneity	Chi^2 p=0.12; I^2=42.6%
Ho (2000)[61]	3 months	2/57 (3.5)	2/62 (3.2)	1.09 (0.15, 8.04)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6 months	2/41 (4.9)	4/41 (9.8)	9.25 (1.01, 84.73)
			Pooled result	2.41 (0.56, 10.43) p=0.24
			Test for heterogeneity	Chi^2 p=0.15; I^2=50.6%
Ortiz (2005)[86]	12 months	6/15 (40.0)	1/16 (6.3)	10.00 (1.03, 97.04)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Ortiz (2002)[87]	16 months	3/27 (11.1)	2/28 (7.1)	1.63 (0.25, 10.58)
Ho (2000)[61, 69]	18 months	1/27 (3.7)	2/33 (6.1)	0.60 (0.05, 6.95)
Van de Stadt (2005)[78]	46 months	4/20 (20.0)	1/20 (5.0)	4.75 (0.48, 46.91)
			Pooled result	2.60 (0.83, 8.14) p=0.10
			Test for heterogeneity	Chi^2 p=0.35; I^2=7.8%
Mucus/slime discharge		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Ho (2000)[61]	6 weeks	0/57 (0)	3/62 (4.8)	0.15 (0.01, 2.93)
Shalaby (2001)[93]	6 months	2/100 (2.0)	14/100 (14.0)	0.13 (0.03, 0.57)

5.2.2.8 Complications

Anal stenosis/anastomotic stricture

Eighteen studies reported the incidence of anal stenosis after CH or anastomotic stricture after SH (Table 5.11). The pooled OR demonstrated no significant difference in the incidence of anal stenosis between SH and CH at any time point.

Table 5.11: The number of patients with anal stenosis/anastomotic stricture at follow-up

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Van de Stadt (2005)[78]	Post-operative	0/20 (0)	2/20 (10.0)	0.18 (0.01, 4.01)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Ren (2002)[75]	4 weeks	0/45 (0)	0/45 (0)	-
Senagore (2004)[89]	4 weeks	2/77 (2.6)	0/79 (0)	5.26 (0.25, 111.47)
Hasse (2004)[73]	6 weeks	3/40 (7.5)	0/40 (0)	7.56 (0.38, 151.28)
Ho (2000)[61]	6 weeks	5/57 (8.8)	5/62 (8.1)	1.10 (0.30, 4.00)
Kairaluoma (2003)[80]	6 weeks	1/30 (3.3)	1/30 (3.3)	1.00 (0.06, 16.76)
Kraemer (2005)[28]	6 weeks	0/25 (0)	1/25 (4.0)	0.32 (0.01, 8.25)
Correa-Rovelo (2002)[94]	8 weeks	1/42 (2.4)	1/42 (2.4)	1.00 (0.06, 16.53)
			Pooled result	1.15 (0.47, 2.79) p=0.76
			Test for heterogeneity	Chi^2 p=0.61; I^2=0%
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6-14 months	1/41 (2.4)	1/41 (2.4)	1.00 (0.06, 16.55)
Bikhchandani (2005)[92]	11 months	0/39 (0)	0/40 (0)	-
Boccasanta (2001)[85]	<1 year	2/40 (5.0)	3/40 (7.5)	0.65 (0.10, 4.11)
			Pooled result	0.74 (0.16, 3.46) p=0.70
			Test for heterogeneity	Chi^2 p=0.80; I^2=0%
Ascanelli (2005)[74]	12 months	0/50 (0)	1/50 (2.0)	0.33 (0.01, 8.21)
Hetzer (2002)[88]	12 months	0/20 (0)	0/20 (0)	-
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Shalaby (2001)[93]	12 months	2/95 (2.1)	5/80 (6.3)	0.32 (0.06, 1.71)
			Pooled result	0.32 (0.07, 1.42) p=0.14
			Test for heterogeneity	Chi^2 p=0.99; I^2=0%
Ortiz (2002)[87]	16 months	0/27 (0)	0/28 (0)	-
Van de Stadt (2005)[78]	46 months	0/20 (0)	2/20 (10.0)	0.18 (0.01, 4.01)
Palimento (2003)[68, 84]	5 years	0/31 (0)	0/29 (0)	-

Faecal incontinence/urgency

Twenty one studies reported the incidence of faecal incontinence (Table 5.12). The reported OR demonstrated no significant differences in the incidence of incontinence at any of the time points. There were no incidents of incontinence reported in the longer-term.

Table 5.12: The number of patients with faecal incontinence

Study	Time point	SH n/N (%)	CH n/N (%)	OR
Pavlidis (2002)[83]	1 week	0/40 (0)	1/40 (2.5)	0.33 (0.01, 8.22)
Correa-Rovelo (2002)[94]	2 weeks	0/42 (0)	1/42 (2.4)	0.33 (0.01, 8.22)
Hetzer (2002)[88]	3 weeks	0/20 (0)	0/20 (0)	-
Chung (2005)[90]	4 weeks	0/43 (0)	0/45 (0)	-
Ren (2002)[75]	4 weeks	6/45 (13.3)	7/45 (15.6)	0.84 (0.26, 2.71)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Senagore (2004)[89]	4 weeks	3/77 (3.9)	4/79 (5.1)	0.76 (0.16, 3.5124)
Ho (2000)[61]	6 weeks	0/57 (0)	2/62 (3.2)	0.21 (0.01, 4.48)
Kairaluoma (2003)[80]	6 weeks	4/30 (13.3)	2/30 (6.7)	2.15 (0.36, 12.76)
Kraemer (2005)[28]	6 weeks	0/25 (0)	0/25 (0)	-
Lau (2004)[91]	8 weeks	0/25 (0)	0/25 (0)	-
Schmidt (2002)[72]	12 weeks	0/13 (0)	0/11 (0)	0.15 (0.01, 3.01)
			Pooled result	0.73 (0.35, 1.51) p=0.39
			Test for heterogeneity	Chi^2 p=0.72; I^2=0%
Ho (2000)[61]	3 months	0/57 (0)	1/62 (1.6)	0.36 (0.01, 8.93)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Chung (2005)[90]	6 months	0/43 (0)	0/45 (0)	-
Correa-Rovelo (2002)[94]	6 months	0/41 (0)	2/41 (4.9)	0.19 (0.01, 4.09)
Senagore (2004)[89]	6 months	3/77 (3.9)	10/79 (12.7)	0.28 (0.07, 1.06)
Van de Stadt (2005)[78]	6 months	2/20 (10.0)	0/20 (0)	5.54 (0.25, 123.08)
Bikhchandani (2005)[92]	11 months	3/39 (7.7)	4/40 (10.0)	0.75 (0.16, 3.59)
Boccasanta (2001)[85]	<1 year	1/40 (2.5)	1/40 (2.5)	1.00 (0.06, 16.56)
			Pooled result	0.51 (0.22, 1.20) p=0.12
			Test for heterogeneity	Chi^2 p=0.56; I^2=0%
Ascanelli (2005)[74]	12 months	0/50 (0)	1/50 (2.0)	0.33 (0.01, 8.21)
Hetzer (2002)[88]	12 months	0/20 (0)	0/20 (0)	-
Kairaluoma (2003)[80]	12 months	3/30 (10.0)	1/30 (3.3)	3.22 (0.32, 32.89)
Ortiz (2005)[86]	12 months	0/15 (0)	0/160 (0)	-
Pavlidis (2002)[83]	12 months	1/40 (2.5)	1/40 (2.5)	1.00 (0.06, 16.56)
Senagore (2004)[89]	12 months	3/59 (5.1)	6/58 (10.3)	0.46 (0.11, 1.95)
Shalaby (2001)[93]	12 months	0/95 (0)	0/80 (0)	-
			Pooled result	0.75 (0.26, 2.15) p=0.59
			Test for heterogeneity	Chi^2 p=0.52; I^2=0%
Ortiz (2002)[87]	16 months	0/27 (0)	0/28 (0)	-
Palimento (2003)[84]	18 months	0/27 (0)	0/37 (0)	-
Van de Stadt (2005)[78]	46 months	0/20 (0)	0/20 (0)	-
Palimento (2003)[68, 84]	5 years	0/37 (0)	0/37 (0)	-

Ten studies reported the incidence of faecal urgency (Table 5.13). This outcome was infrequently reported, and there was no evidence that urgency was any more common after SH or CH at any time point.

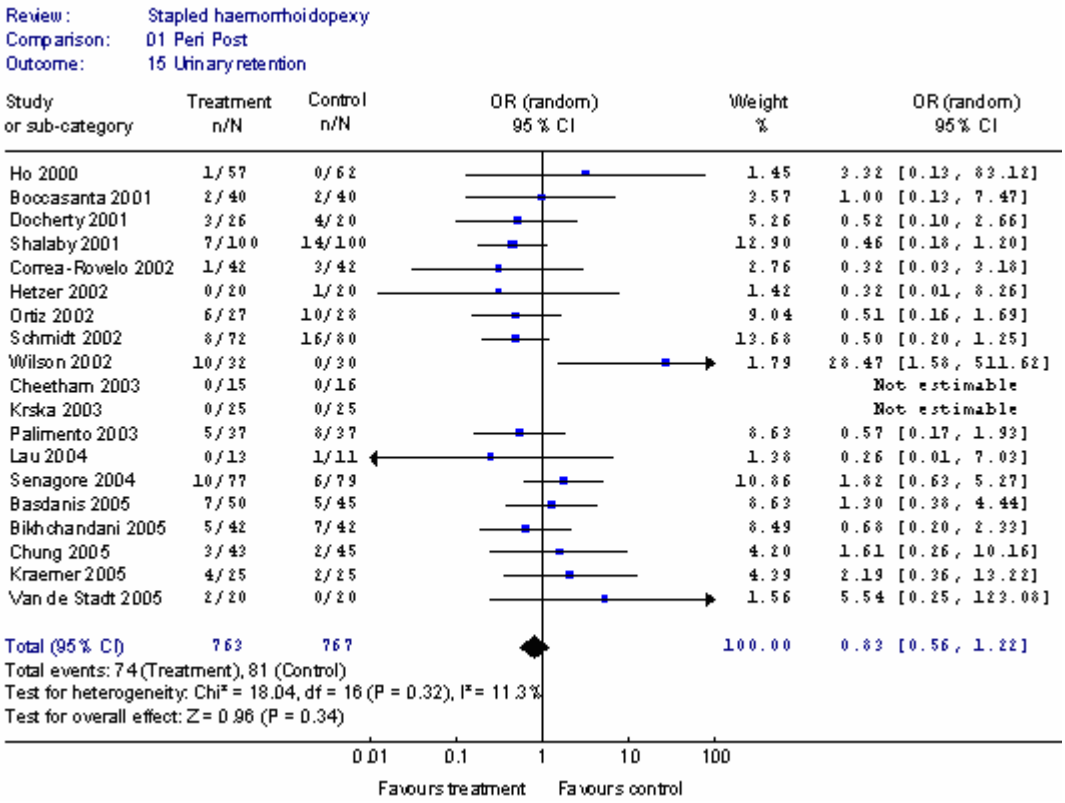
Table 5.13: The number of patients with faecal urgency

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Chung (2005)[90]	4 weeks	0/43 (0)	0/45 (0)	-
Senagore 2004 (2004)[89]	4 weeks	0/77 (0)	1/79 ()	0.34 (0.01, 8.24)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Correa-Rovelo (2002)[94]	2 months	0/42 (0)	1/42 ()	0.33 (0.01, 8.22)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Chung (2005)[90]	6 months	0/43 (0)	0/45 (0)	-
Van de Stadt (2005)[78]	6 months	2/20 (10.0)	2/20 (10.0)	1.00 (0.13, 7.89)
Cheetham (2003)[77]	8 months	3/15 (21.4)	0/16 (0)	9.24 (0.44, 195.69)
		Pooled result for 2 to 8 months		1.58 (0.43, 5.79) p=0.49
		Test for heterogeneity		Chi^2 p=0.30; I^2=16.4%
Ortiz (2005)[86]	12 months	2/15 (13.3)	3/16 (18.8)	0.67 (0.10, 4.67)
Ascanelli (2005)[74]	12 months	3/50 (6.0)	0/50 (0)	7.44 (0.37, 147.92)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Ortiz (2002)[87]	16 months	2/27 (7.4)	4/28 (14.3)	0.48 (0.08, 2.87)
Van de Stadt (2005)[78]	46 months	0/20 (0)	0/20 (0)	-
		Pooled result for 12 months and over		1.04 (0.36, 3.03) p=0.94
		Test for heterogeneity		Chi^2 p=0.27; I^2=22.6%

Urinary retention

Nineteen studies reported urinary retention post-operatively; three reported the same incidence after both SH and CH [77, 79, 85], nine a lower incidence after SH [72, 76, 84, 87, 88, 91-94] and seven a lower incidence after CH.[28, 43, 61, 78, 82, 89, 90] The pooled estimate revealed no significant difference between SH and CH (Figure 5.6). One study (Wilson 2002[43]) reported a much higher incidence of urinary retention after SH (31%) compared to CH and other studies. When this study was removed from the analysis (Appendix 10.7, Figure 10.20), the OR decreased and favoured SH, but not statistically significantly so (OR: 0.76; 95% CI: 0.53, 1.09; p=0.14; Test for heterogeneity: Chi^2 p=0.70; I^2=0%).

Figure 5.6: Number of people with urinary retention in the immediate post-operative period



Other complications

Complications reported included: anal fissure; anal fistula; haemorrhoidal thrombosis; pelvic/perianal sepsis; rectovaginal fistula; infection; and mortality (Table 5.14). The results of the individual trials were variable. The pooled OR, where calculable, failed to demonstrate significant differences between SH and CH.

Table 5.14: The number of patients with anal fissure, anal fistula, haemorrhoidal thrombosis or died

Anal fissure		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Van de Stadt (2005)[78]	Post-operative	1/20 (5.0)	2/20 (10.0)	0.47 (0.04, 5.69)
Shalaby (2001)[93]	1 week	1/100 (1.0)	0/100 (0)	3.03 (0.12, 75.28)
Senagore (2004)[89]	4 weeks	0/77 (0)	2/79 (2.5)	0.20 (0.01, 4.23)
Krska 2003 (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Cheetham (2003)[77]	6 weeks	1/15 (6.7)	0/16 (0)	3.41 (0.13, 90.49)
Kraemer (2005)[28]	6 weeks	0/25 (0)	1/25 (4.0)	0.32 (0.01, 8.25)
			Pooled result	0.72 (0.19, 2.77) p=0.64
			Test for heterogeneity	Chi^2 p=0.62; I^2=0%
Shalaby (2001)[93]	6 months	0/100 (0)	3/100 (3.0)	0.14 (0.01, 2.72)
Anal fistula		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Senagore (2004)[89]	4 weeks	0/77 (0)	2/79 (2.5)	0.20 (0.01, 4.23)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Ortiz (2002)[87]	6 weeks	0/27 (0)	1/28 (3.6)	0.33 (0.01, 8.55)
Hetzer (2002)[88]	12 months	0/20 (0)	0/20 (0)	-
Haemorrhoidal thrombosis		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Van de Stadt (2005)[78]	Post-op	2/20 (10.0)	0/20 (0)	5.54 (0.25, 123.08)
Shalaby (2001)[93]	1 week	3/100 (3.0)	3/100 (3.0)	1.00 (0.20, 5.08)
Boccasanta (2001)[85]	10 days	2/40 (5.0)	6/40 (15.0)	0.47 (0.08, 2.75)
Hetzer (2002)[88]	3 weeks	1/20 (5.0)	0/20 (0)	3.15 (0.12, 82.16)
Chung (2005)[90]	4 weeks	2/43 (4.7)	0/45 (0)	5.48 (0.26, 117.55)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Ortiz (2005)[86]	6 weeks	1/15 (6.7)	0/16 (0)	3.41 (0.13, 90.49)
Ortiz (2002)[87]	6 weeks	1/27 (3.7)	0/28 (0)	3.23 (0.13, 82.71)
Ho (2000)[61]	6 weeks	1/57 (1.8)	0/62 (0)	3.32 (0.13, 83.12)
Correa-Rovelo (2002)[94]	2 months	0/42 (0)	0/42 (0)	-
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
			Pooled result	1.55 (0.64, 3.74) p=0.33
			Test for heterogeneity	Chi^2 p=0.76; I^2=0%
Correa-Rovelo (2002)[94]	6 months	0/41 (0)	0/41 (0)	-
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Van de Stadt (2005)[78]	46 months	1/20 (5.0)	0/20 (0)	3.15 (0.12, 82.16)
Mortality		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Hetzer (2002)[88]	3 weeks	0/20 (0)	0/20 (0)	-
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-

Of the six studies reporting the occurrence of anal fissure, three reported this complication after SH,[77, 78, 93] and three after CH.[78, 89, 95] Of the four studies reporting the occurrence of anal fistula, none reported this complication after SH,[79, 87-89] but two reported anal fistula after CH.[87, 89] Of the eleven studies reporting the occurrence of haemorrhoidal thrombosis, eight reported this complication after SH,[61, 78, 79, 83, 85-88, 90, 93, 94] and two after CH.[85, 93] Three studies reported no incidences of haemorrhoidal thrombosis after either procedure.[79, 83, 94] Where reported, there were no incidents of pelvic/perianal sepsis (five studies),[61, 79, 82, 83, 92] or rectovaginal fistula (3 studies)[82, 83, 92] at any time point.

Of 349 patients across 4 trials, there were only 3 reports of wound infection, one after SH and two after CH (Table 5.15). The incidence of systemic infection/fever was also low, ranging from 0% to 3.3% after SH and 0% to 5.1% after CH in the six studies that reported this outcome (Table 5.15).

Table 5.15: The number of patients with wound or systemic infections

Wound		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Chung (2005)[90]	4 weeks	0/43 (0)	0/45 (0)	-
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Senagore (2004)[89]	4 weeks	0/77 (0)	1/79 (1.3)	0.34 (0.01, 8.42)
Ortiz (2002)[87]	6 weeks	1/27 (3.7)	1/28 (3.6)	1.04 (0.06, 17.49)
Systemic		**SH**	**CH**	
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Bikhchandani (2005)[92]	15 days	1/42 (2.4)	0/42 (0)	3.07 (0.12, 77.59)
Chung (2005)[90]	4 weeks	0/43 (0)	0/45 (0)	-
Senagore (2004)[89]	4 weeks	0/77 (0)	4/79 (5.1)	0.11 (0.01, 2.05)
Krska (2003)[79]	4 weeks	0/25 (0)	0/25 (0)	-
Kairaluoma (2003)[80]	6 weeks	1/30 (3.3)	1/30 (3.3)	1.00 (0.06, 16.76)
Ho (2000)[61]	6 weeks	0/57 (0)	1/62 (1.6)	0.36 (0.01, 8.93)
			Pooled result	0.56 (0.12, 2.57) p=0.46
			Test for heterogeneity	Chi^2 p=0.46; I^2=0%

Complications: Summary

There does not appear to be any significant difference between SH and CH in relation to the incidence of post-operative complications.

5.2.2.9 Wound healing

Of the nine trials that reported the number of wounds healed/not healed at 6 weeks (Table 5.16), two reported that 5% of patients still had unhealed wounds after SH, and eight reported between 6.7% and 52.5% of patients with unhealed wounds after CH at 6 weeks. The pooled estimate demonstrated a highly significant difference, with fewer patients with unhealed wounds at 6 weeks after SH.

Three trials that reported the number of wounds healed/not healed at 12 weeks; all SH wounds had healed, however, two trials reported 6.3% and 20% of patients still had unhealed wounds after CH.

Table 5.16: The number of patients with unhealed wounds between three and twelve weeks post-operatively

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Hetzer (2002)[88]	3 weeks	0/20 (0)	4/20 (20.0)	0.09 (0, 1.78)
Basdanis (2005)[82]	4 weeks	0/50 (0)	0/45 (0)	-
Ren (2002)[75]	4 weeks	0/45 (0)	3/45 (6.7)	0.13 (0.01, 2.66)
Senagore (2004)[89]	4 weeks	0/77 (0)	6/79 (7.6)	0.07 (0, 1.32)
Cheetham (2003)[77]	6 weeks	0/15 (0)	2/16 (12.5)	0.19 (0.01, 4.24)
Hasse (2004)[73]	6 weeks	2/40 (5.0)	21/40 (52.5)	0.05 (0.01, 0.22)
Ho (2000)[61]	6 weeks	0/57 (0)	9/62 (14.5)	0.05 (0, 0.86)
Van de Stadt (2005)[78]	6 weeks	1/20 (30.0)	6/20 (5.0)	0.12 (0.01, 1.14)
Correa-Rovelo (2002)[94]	2 months	0/42 (0)	4/42 (9.5)	0.10 (0.01, 1.93)
			Pooled result	0.08 (0.03, 0.19) p<0.001
			Test for heterogeneity	Chi^2 p=0.99; I^2=0%

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Van de Stadt (2005)[78]	> 6 weeks	0/20 (0)	0/20 (0)	-
Hetzer (2002)[88]	12 weeks	0/20 (0)	4/20 (20.0)	0.09 (0, 1.78)
Cheetham (2003)[77]	12 weeks	0/15 (0)	1/16 (6.3)	0.33 (0.01, 8.83)
Ho (2000)[61]	12 weeks	0/57 (0)	0/62 (0)	-
			Pooled result	0.15 (0.02, 1.28) p=0.08
			Test for heterogeneity	Chi^2 p=0.56; I^2=0%

5.2.2.10 Reinterventions

Total number of reinterventions

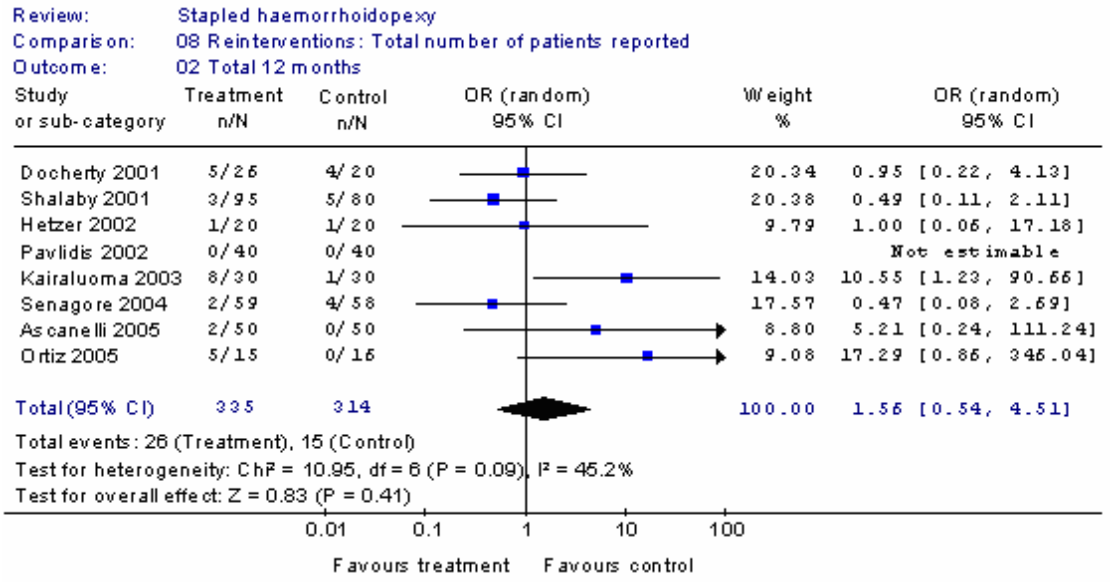
Fourteen studies reported the total number of people requiring a reintervention; the pooled ORs demonstrated no significant difference between SH and CH at any time point (Table 5.17). Two studies reported much higher rates of reintervention after SH than CH; one by Kairaluoma (2003)[80] that reported an uncharacteristically high incidence of prolapse after SH possibly due to technical difficulties during SH; and the other by Ortiz (2005)[86] that included only patients with IV degree haemorrhoids. When these were removed from the analysis, there remained no significant difference between SH and CH (OR: 0.75; 95% CI: 0.33, 1.70), however, significant heterogeneity between the studies was no longer observed (Chi^2 p=0.68, I^2=0%; Appendix 10.7, Figure 10.22).

Table 5.17: The total number of patients reported as having undergone a secondary intervention up to 46 months post-surgery

Study	Time point	SH n/N (%)	CH n/N (%)	OR (95% CI)
Gravie (2005)[81]	within 2 months	3/63 (4.8)	3/63 (4.8)	1.00 (0.19, 5.15)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6 months	1/41 (2.4)	0/41 (0)	3.07 (0.12, 77.69)
Boccasanta (2001)[85]	<1 year	2/40 (5.0)	3/40 (7.5)	0.65 (0.10, 4.11)
			Pooled result	(0.33, 3.05) p=1.00
			Test for heterogeneity	Chi^2 p=0.71; I^2=0%
Hetzer (2002)[88]	12 months	1/20 (5.0)	1/20 (5.0)	1.00 (0.06, 17.18)
Shalaby (2001)[93]	12 months	3/95 (3.2)	5/80 (6.3)	0.49 (0.11, 2.11)
Senagore (2004)[89]	12 months	2/59 (3.4)	4/58 (6.9)	0.47 (0.08, 2.69)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Docherty (2001)[76]	12 months	5/26 (19.2)	4/20 (20.0)	0.95 (0.22, 4.13)
Kairaluoma (2003)[80]	12 months	8/30 (26.7)	1/30 (3.3)	10.55 (1.23, 90.66)
Ortiz (2005)[86]	12 months	5/15 (33.3)	0/16 (0)	17.29 (0.86, 346.04)
Ascanelli (2005)[74]	12 months	2/50 (4.0)	0/50 (0)	5.21 (0.24, 11.24)
			Pooled result	1.56 (0.54, 4.51) p=0.41
			Test for heterogeneity	Chi^2 p=0.09; I^2=45.2%
Ortiz (2002)[87]	16 months	3/27 (11.1)	0/28 (0)	8.14 (0.40, 165.53)
Ho (2000)[61, 69]	18 months	2/27 (7.4)	4/33 (12.1)	0.58 (0.10, 3.44)
Gravie (2005)[81]	2 year	0/52 (0)	0/57 (0)	-
Van de Stadt (2005)[78]	46 months	4/20 (20.0)	0/20 (0)	11.18 (0.56, 222.98)
			Pooled result	2.36 (0.77, 7.28) p=0.13
			Test for heterogeneity	Chi^2 p=0.13; I^2=51.0%
			Pooled estimate for 12 months and over	1.74 (0.71, 4.24) p=0.23
			Test for heterogeneity	Chi^2 p=0.08; I^2=41.0%

When the data for 12 months or over were pooled, there was no significant difference between SH and CH; there was a modest degree of heterogeneity between studies (Figure 5.7).

Figure 5.7: Number of people requiring some type of reintervention at 12 months or longer post-operatively



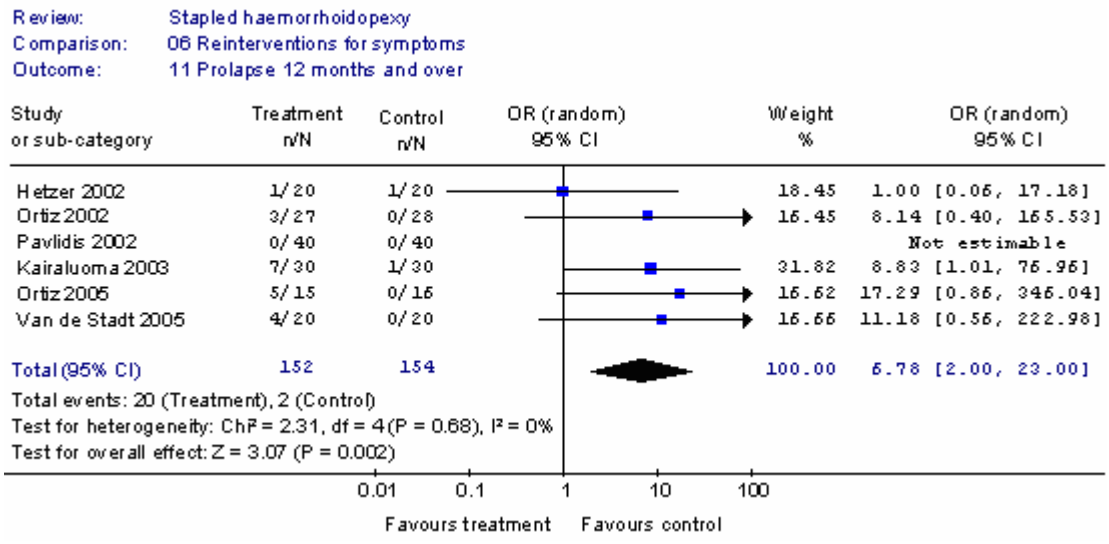
Reinterventions for prolapse

The most commonly reported reason for a reintervention was the presence of prolapse (Table 5.18). Of the six studies that reported a reintervention for prolapse, five reported a higher incidence after SH than CH, and the pooled OR demonstrated a significantly higher incidence of reintervention for prolapse at 12 months or longer post-operatively after SH than CH (Figure 5.8). When the studies by Ortiz (2005)[86] and Kairaluoma (2003)[80] were removed from the analysis (Appendix 10.7, Figure 10.24), there was still a statistically significantly higher rate of reintervention for prolapse after SH than CH (OR 4.99; 95% CI: 1.05, 23.60, p=0.04).

Table 5.18: The number of patients with the symptom that required reintervention

		SH	CH	
Prolapse				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6 months	1/41 (2.4)	0/41 (0)	3.07 (0.12, 77.69)
Ortiz (2005)[86]	12 months	5/15 (33.3)	0/16 (0)	17.29 (0.86, 346.04)
Hetzer (2002)[88]	12 months	1/20 (5.0)	1/20 (5.0)	1.00 (0.06, 17.18)
Kairaluoma (2003)[80]	12 months	7/30 (23.3)	1/30 (3.3)	8.83 (1.01, 76.96)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Ortiz (2002)[87]	16 months	3/27 (11.1)	0/28 (0)	8.14 (0.40, 165.53)
Van de Stadt (2005)[78]	46 months	4/20 (20.0)	0/20 (0)	11.18 (0.56, 222.98)
	Pooled estimate for 12 months and over			6.78 (2.00, 23.00) p=0.002
	Test for heterogeneity			Chi^2 p=0.68; I^2=0%
Bleeding				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Gravie (2005)[81]	< 2 months	2/63 (3.2)	0/63 (0)	5.16 (0.24, 109.73)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Ascanelli (2005)[74]	12 months	2/50 (4.0)	0/50 (0)	5.21 (0.24, 111.24)
Kairaluoma (2003)[80]	12 months	7/30 (23.3)	1/30 (3.3)	8.83 (1.01, 76.96)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Van de Stadt (2005)[78]	46 months	0/20 (0)	0/20 (0)	-
	Pooled estimate for 12 months and over			7.44 (1.27, 43.43) p=0.03
	Test for heterogeneity			Chi^2 p=0.78; I^2=0%
Pain				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Van de Stadt (2005)[78]	46 months	0/20 (0)	0/20 (0)	-

Figure 5.8: Number of people requiring reintervention for prolapse at 12 months or longer post-operatively



Reinterventions for bleeding

Reinterventions for bleeding were reported in five trials (Table 5.18), however the data was sparse and the event rates low, making it difficult to draw conclusions.[74, 78, 80, 81, 83] The pooled OR based on only two trials [74, 80] demonstrated a statistically significant higher rate of reinterventions after SH than CH for bleeding at 12 months or later post-operatively (Table 5.18). However, one of these trials experienced technical difficulties during the SH procedure.[80] Two further trials reported no patients requiring reintervention for bleeding at 12[83] and 46 months.[78]

Reinterventions for pain

Across three trials, no patient was reported as having undergone a reintervention due to pain (Table 5.18).

Reinterventions for complications

The data regarding reinterventions for complications was sparse and the event rates were generally low, again making it difficult to draw conclusions. Pooled results demonstrated no statistically significant difference in the rate of reinterventions for skin tag removal or anal stenosis (Table 5.19).

Table 5.19: The number of patients with a complication that required reintervention

		SH	CH	
Anal stenosis				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Gravie (2005)[81]	< 2 months	0/63 (0)	1/63 (1.6)	0.33 (0.01, 8.21)
Boccasanta (2001)[85]	<1 year	2/40 (5.0)	3/40 (7.5)	0.65 (0.10, 4.11)
Shalaby (2001)[93]	12 months	2/95 (2.1)	5/80 (6.3)	0.32 (0.06, 1.71)
		Pooled estimate for within 12 months		0.42 (0.13, 1.32) p=0.14
		Test for heterogeneity		Chi^2 p=0.85; I^2=0%
Skin tag removal				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Kairaluoma (2003)[80]	12 months	1/30 (3.3)	0/30 (0)	3.10 (0.12, 79.23)
Senagore (2004)[89]	12 months	0/59 (0)	1/58 (1.7)	0.32 (0.01, 8.07)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
		Pooled estimate for 12 months		0.99 (0.14, 7.15) p=0.99
		Test for heterogeneity		Chi^2 p=0.33; I^2=0%
Faecaloma				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Gravie (2005)[81]	< 2 months	0/63 (0)	2/63 (3.2)	0.19 (0.01, 4.12)

Reinterventions for symptoms and complications: summary

Overall, there was no difference in the total number of reinterventions required, or reintervention for pain, bleeding or complications, between SH and CH. However, there was a significantly greater number of reintervention for prolapse after SH.

Type of reintervention undertaken

The reinterventions undertaken in the trials were CH, SH, unspecified surgery, RBL, sclerotherapy, skin tag removal and an unspecified medical intervention (Table 5.20).

Table 5.20: The number of patients requiring surgical reintervention

		SH	CH	
Conventional haemorrhoidectomy				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Gravie (2005)[81]	2 days	1/63 (1.6)	0/63 (0)	3.05 (0.12, 76.26)
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Ortiz (2005)[86]	12 months	5/15 (33.3)	0/16 (0)	17.29 (0.86, 346.04)
Kairaluoma (2003)[80]	12 months	4/30 (13.3)	0/30 (0)	10.63 (0.53, 201.45)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Docherty (2001)[76]	12 months	4/26 (15.4)	0/20 (0)	8.20 (0.42, 161.83)
Ho (2000)[61, 69]	18 months	1/27 (3.7)	1/33 (3.0)	1.23 (0.07, 20.64)
Ortiz (2002)[87]	16 months	3/31 (11.1)	0/28 (0)	8.14 (0.04, 165.53)
		Pooled estimate for 12 months and over		6.54 (1.75, 24.50) p=0.005
		Test for heterogeneity		Chi^2 p=0.75; I^2=0%
Stapled haemorrhoidopexy				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Shalaby (2001)[93]	12 months	1/95 (1.1)	0/80 (0)	2.56 (0.10, 63.60)
Surgery: unspecified				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Shalaby (2001)[93]	12 months	1/95 (1.1)	2/80 (2.5)	0.41 (0.04, 4.66)
Senagore (2004)[89]	12 months	0/59 (0)	3/58 (5.2)	0.13 (0.01, 2.64)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Van de Stadt (2005)[78]	46 months	4/20 (20.0)	0/20 (0)	11.18 (0.56, 222.98)

The need to undertake a CH was reported in seven trials (Table 5.20). The pooled OR demonstrated a significantly higher rate of CH 1 year or later after SH than CH. However, this analysis includes the trial that experienced technical difficulties (Kairaluoma 2003)[80] and the trial that included only people with IV degree haemorrhoids (Ortiz 2005).[86] When these trials were removed from the analysis, the OR decreased to 4.76 (95% CI: 0.99, 23.04; p=0.05) (Appendix 10.7, Figure 10.26). Two trials reported the incidence of SH as a reintervention technique (Table 5.20);

one reported a single patient requiring SH at12 months after SH;[93] the other reported no incidence of SH as a reintervention.[83] Three trials reported the need of repeat surgery without specifying the type of surgery undertaken (Table 5.20);[78, 89, 93] none reported a significant difference between SH and CH.

Six trials reported the use of RBL within 18 months of the original procedure (Table 5.21) the pooled OR demonstrated no significant difference between SH or CH. One trial (Ascanelle (2005)[74] reported the use of sclerotherapy in two patients following SH (Table 5.21). One study (Ho 2000[61]/Ooi 2002[69]) reported the need for an unspecified medical intervention, carried out in 1 patient after SH and two after CH (Table 5.21).

Table 5.21: The number of patients requiring non-excisional surgery as the reintervention procedure

		SH	CH	
Rubber band ligation				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Correa-Rovelo (2002)[94]	6 months	1/41 (2.4)	0/41 (0)	3.07 (0.12, 77.69)
Kairaluoma (2003)[80]	12 months	3/30 (10.0)	1/30 (3.3)	3.22 (0.32, 32.89)
Hetzer (2002)[88]	12 months	1/20 (5.0)	1/20 (5.0)	1.00 (0.06, 17.18)
Senagore (2004)[89]	12 months	2/59 (3.4)	0/58 (0)	5.09 (0.24, 108.29)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Docherty (2001)[76]	12 months	1/26 (3.8)	1/20 (5.0)	0.76 (0.04, 12.95)
Ho (2000)[61, 69]	18 months	0/27 (0)	1/33 (3.0)	0.39 (0.02, 10.07)
	Pooled estimate for 12 months and over			1.52 (0.43, 5.34) p=0.51
	Test for heterogeneity			Chi^2 p=0.74; I^2=0%
Sclerotherapy				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Ascanelli (2005)[74]	12 months	2/50 (4.0)	0/50 (0)	5.21 (0.24, 111.24)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Skin tag removal				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Pavlidis (2002)[83]	3 months	0/40 (0)	0/40 (0)	-
Kairaluoma (2003)[80]	12 months	1/30 (3.3)	0/30 (0)	3.10 (0.12, 79.23)
Pavlidis (2002)[83]	12 months	0/40 (0)	0/40 (0)	-
Senagore (2004)[89]	12 months	0/59 (0)	1/58 (1.7)	0.32 (0.01, 8.0724)
Medical				
Study	**Time point**	**n/N (%)**	**n/N (%)**	**OR (95% CI)**
Ho (2000)[61, 69]	18 months	1/27 (3.7)	2/33 (6.1)	0.60 (0.05, 6.95)

Type of reintervention undertaken: summary

It seems that those requiring reintervention for haemorrhoidal disease rather than complications underwent CH, and therefore the requirement for CH as a reintervention was significantly higher after SH, relfecting the increased rate of prolapse. There was no significant difference in the requirement of any other type of reintervention between SH and CH.

5.2.2.11 Operating time

Mean operating time was reported in 19 studies ranging from 9 to 35.4 minutes for SH and 11.5 to 53 minutes for CH (Table 5.22).

Table 5.22: The mean or median number of minutes operating time

Study	Number randomised SH	Number randomised CH	SH Mean (Measure of variance)	CH Mean (Measure of variance)	Mean difference (95% CI)
Bikhchandani (2005) [92]	42	42	24.28 (SD 4.25)	45.21 (SD 5.36)	-20.93 (-23.00, -18.86)
Boccasanta (2001) [85]	40	40	25 (SD 3.1)	50 (SD 5.3)	-25.00 (-26.90, -23.10)
Chung (2005)[90]	43	45	17 (SD 7.3)	18.5 (SD 6.4)	-1.50 (-4.37, 1.37)
Correa-Rovelo (2002)[94]	42	42	11.9 (SD 3.1)	46.4 (SD 10.4)	-34.50 (-37.78, -31.22)
Hasse (2004)[73]	40	40	16.3 (SD 0.8)	49 (SD 11.8)	-32.70 (-36.37, -29.03)
Ho (2000) [61]	57	62	17.6 (SD 9.8)	11.4 (SD 7.1)	6.20 (3.10, 9.30)
Kairaluoma (2003)[80]	30	30	21.86 (SD 9.1)	22.46 (SD 6.4)	-0.06 (-4.58, 3.38)
Lau (2004) [91]	13	11	35.4 (SD 9.89)	29.8 (SD 13.01)	5.60 (-3.78, 14.98)
Pavlidis (2002) [83]	40	40	23 (SD 5)	35 (SD 10)	-12.00 (-15.46, -8.54)
Ren (2002) [75]	45	45	12.3 (SD 6.7)	17.6 (SD 9.3)	-5.30 (-8.65, -1.95)
Shalaby (2001) [93]	100	100	9 (SD 2.7)	19.7 (SD 4.7)	-10.70 (-11.76, -9.64)
Ascanelli (2005)[74]	50	50	22 (Range 18-38)	35 (Range 30-45)	-13.0
Kraemer (2005) [28]	25	25	21 (Range 6-54)	26 (Range 10-80)	-5.0
Ortiz (2002)[87]	27	28	19 (Range 14.35)	33.5 (Range 15-90)	-14.5
Ortiz (2005)[86]	15	16	24 (Range 15-37)	39 (Range 10-90)	-15.0
Senagore (2004) [89]	77	79	31 (Range 5-79)	35 (Range 12-89)	-4.0
Gravie (2005)[81]	63	63	21 (NR)	31 (NR)	-10.0
Krska (2003) [79]	25	25	28 (NR)	46 (NR)	-18.0
Schmidt (2002) [72]	72	80	21.65 (NR)	52.98 (NR)	-31.33
Van de Stadt (2005) [78]	20	20	22.2 (NR)	25.7 (NR)	-3.5
Study	**Number randomised SH**	**Number randomised CH**	**SH Median (Range)**	**CH Median (Range)**	
Basdanis (2005) [82]	50	45	15 (8-17)	13 (9.2-16.1)	
Hetzer (2002) [88]	20	20	30 (15-45)	43 (25-60)	
Kairaluoma (2003) [80]	30	30	21 (11-59)	22 (14-40)	
Palimento (2003) [84]	37	37	25 (15-49)	30 (20-44)	
Wilson (2002)[43]	32	30	12 (NR)	18 (NR)	

Two studies reported a longer mean operating time for SH than CH;[61, 91] the remainder reported a shorter operating time for SH. Five further studies reported median operating times, ranging from 12 to 30 minutes for SH and 13 to 43 minutes for CH (Table 5.22); only one (Basdanis 2005[82]) reported a longer operating time for SH than CH; the remainder reported a shorter operating time for SH. Eleven studies provided sufficient data to include in a meta-analysis, however, significant heterogeneity between studies ($p<0.001$; $I^2=98.7\%$) meant pooling was not undertaken.[61, 73, 75, 80, 83, 85, 90-94]

The heterogeneity between studies may be due the method by which the operating time was measured; some studies measured operating time from the onset of anaesthesia, whereas others measured time in the operating theatre, or actual operating time from incision to application of a dressing. With this a potential confounder, we were unable to determine whether the anaesthetic used or the degree of haemorrhoids had an impact on the results of this outcome (Appendix 10.7, Table 10.5).

Overall, operating time seems to be shorter for SH compared to CH.

5.2.2.12 Duration of hospital stay

Nineteen trials reported data on duration of hospital stay (Table 5.23). Sixteen studies reported the mean length of hospital stay; this ranged from 0.75 to 5.8 days after SH and 0.92 to 11.2 days after CH. Fourteen of these studies reported a shorter hospital stay after SH than CH. Due to significant heterogeneity between the studies that provided sufficient data to be included in a meta-analysis ($p<0.001$; $I^2=97.5\%$), pooling was not undertaken.

Table 5.23: The mean or median duration of hospital stay (days)

Study	Number randomised SH	Number randomised CH	SH Mean (Measure of variance)	CH Mean (Measure of variance)	Mean difference (95% CI)
Bikhchandani (2005) [92]	42	42	1.24 (SD 0.62)	2.76 (SD 1.01)	-1.52 (-1.88, -1.16)
Boccasanta (2001) [85]	40	40	2 (SD 0.5)	3 (SD 0.4)	-1.00 (-1.20, -0.80)
Gravie (2005)[81]	63	63	2.2 (SD 1.2)	3.1 (SD 1.7)	-0.90 (-1.41, -0.39)
Hasse (2004)[73]	40	40	1 (SD 0.5)	4 (SD 0.7)	-3.00 (-3.27, -2.73)
Ho (2000) [61]	57	62	2.1 (SD 0.76)	2 (SD 0.79)	0.10 (-0.18, 0.38)
Lau (2004) [91]	13	11	1.44 (SD 0.53)	2.13 (SD 0.84)	-0.69 (-1.26, -0.12)
Pavlidis (2002) [83]	40	40	1.7 (SD 0.5)	3.2 (SD 0.3)	-1.50 (-1.68, -1.32)
Ren (2002) [75]	45	45	5.8 (SD 2.3)	11.2 (SD 3.7)	-5.40 (-6.67, -4.13)
Shalaby (2001) [93]	100	100	1.1 (SD 0.2)	2.2 (SD 0.5)	-1.10 (-1.21, -0.99)
Ascanelli (2005)[74]	50	50	0.75 (Range 0.25-1.67)	0.92 (Range 0.25-2)	-0.17
Basdanis (2005) [82]	50	45	1.6 (Range 1-2)	2.1 (Range 2-3)	-0.5
Hetzer (2002) [88]	20	20	2.4 (Range 1-4)	2.1 (Range 1-4)	0.3
Kraemer (2005) [28]	25	25	4 (Range 2-10)	5 (Range 2-10)	-1.0
Schmidt (2002) [72]	72	80	3.04 (Range 1-8)	6.14 (Range 3-9)	-3.1
Krska (2003) [79]	25	25	3.5 (NR)	6.2 (NR)	-2.5
Van de Stadt (2005) [78]	20	20	1.5 (NR)	2.25 (NR)	-0.75

Study	Number randomised SH	Number randomised CH	SH SH Median (Range)	CH CH Median (Range)
Chung (2005)[90]	43	45	1 (1-5)	3 (2-5)
Wilson (2002)[43]	32	30	1 (0.9-2)	1.9 (1-2)
Senagore (2004) [89]	77	79	NR (0-2)	NR (1-2)

Pre-operative degree of haemorrhoids, differences in hospital discharge protocols and the methods by which length of stay was measured may be the possible reasons for heterogeneity between these studies. Studies recruiting people with grade II haemorrhoids seem to have shorter durations of hospital stay than studies recruiting people with more severe haemorrhoidal disease, although this is more apparent after CH than SH (Appendix 10.7, Table 10.6).[28, 72, 73, 75, 79]

Two studies favoured SH far more than the other studies (Table 5.23).[73, 75] The trial by Hasse (2004) was restricted to patients with III degree haemorrhoids, and the trail by Ren (2002) recruited 76% of patients with III degree haemorrhoids, with the remainder with IV degree haemorrhoids. Another study (Pavlidis 2002[83]) had a similar high proportion of patients with III degree haemorrhoids (69%), but this study had a more representative population with patients with both II and IV degree haemorrhoids recruited. When the studies by Hasse (2004) and Ren (2002) were removed from the analysis, there was little effect on the result and there was still significant heterogeneity between studies (Appendix 10.7, Figure 10.28).

Two additional studies reported the median length of hospital stay; both reported a shorter hospital stay after SH.[43, 90] One further study (Senagore 2004[89]) reported only the range. Two studies did not report data for hospital stay: one (Kairaluoma 2003[80]) reported that all procedures were day cases for both SH and CH, and the other (Cheetham 2003[77]) that 80% of SH and 88% of CH were undertaken as day cases.

When placed in chronological order, there was no indication that the length of hospital stay decreased with more recent trials.

Overall, SH resulted in a shorter hospital stay than CH. Trials recruiting patients with II degree haemorrhoids generally reported shorter hospital stays than those recruiting patients with III and/or IV degree haemorrhoids.

5.2.2.13 Time to first bowel movement

All seven studies measuring the mean number of days to first bowel movement reported a shorter time following SH than CH (Table 5.24). Two studies reporting the median days to first bowel movement showed no difference between SH and CH.[43, 90] When the results of studies that provided sufficient data to be included in a meta-analysis, there was a significantly shorter time to first bowel movement after SH.

Table 5.24: The mean or median number of days to first bowel movement

Author	Number randomised SH	Number randomised CH	SH Mean (Measure of variance)	CH Mean (Measure of variance)	Mean difference (95% CI)
Bikhchandani (2005) [92]	42	42	2.16 (SD 0.79)	2.33 (SD 0.79)	-0.17 (-0.51, 0.17)
Correa-Rovelo (2002)[94]	42	42	1.1 (SD 0.3)	1.43 (SD 0.59)	-0.33 (-0.53, -0.13)
Gravie (2005)[81]	63	63	1.6 (SD 1)	2.1 (SD 1.1)	-0.50 (-0.87, -0.13)
				Pooled estimate	-0.33 (-0.48, -0.17) p<0.001
				Test for heterogeneity	Chi^2 p=0.43; I^2=0%
Kraemer (2005) [28]	25	25	2 (Range 1-4)	3 (Range 1-5)	-1.0
Ortiz (2005)[86]	15	16	3.14 (Range 1-5)	3.5 (Range 1-6)	-0.36
Ortiz (2002)[87]	27	28	2.9 (Range 0-5)	3.2 (Range 1-6)	-0.3
Senagore (2004) [89]	77	79	1.4 (95% CI 1, 1.8)	2 (95% CI 1.6, 2.5)	-0.6
Author	**Number randomised SH**	**Number randomised CH**	**SH Median (Range)**	**CH Median (Range)**	
Chung (2005)[90]	43	45	2 (1-3)	2 (1-4)	
Wilson (2002)[43]	32	30	1 (1-3)	1 (1-2)	

Overall, SH resulted in a shorter time to first bowel movement than CH.

5.2.2.14 Time to return to work/normal activity

Twenty trails reported the time to resume normal activity/return to work (Table 5.25); nineteen reported a shorter time after SH, and Thaha (2004)[70] reported the same time after SH and CH. Fifteen trails reported the mean number of days to normal activity; this ranged from 6.1 to 23.1 days after SH and 9.8 to 53.9 after CH. For all ten trials for which it could be tested, the number of days to normal activity was significantly shorter after SH than CH (Table 5.25). However, there was statistically significant heterogeneity between these studies ($P<0.001$; $I^2=99.8\%$), therefore a pooled effect size was not calculated.

Table 5.25: The mean or median number of days to normal activity

Study	Number randomised SH	Number randomised CH	SH Mean (Measure of variance)	CH Mean (Measure of variance)	Mean difference (95% CI)
Basdanis (2005) [82]	50	45	6.3 (SD 1.5)	9.8 (SD 1.9)	-3.50 (-4.19, -2.81)
Bikhchandani (2005) [92]	42	42	8.12 (SD 2.48)	17.62 (SD 5.59)	-9.50 (-11.35, -7.65)
Boccasanta (2001) [85]	40	40	8 (SD 0.9)	15 (SD 1.4)	-7.00 (-7.52, -6.48)
Chung (2005)[90]	43	45	6.7 (SD 4.3)	15.6 (SD 6.0)	-8.90 (-11.07, -6.73)
Correa-Rovelo (2002)[94]	42	42	6.1 (SD 3.5)	15.2 (SD 4.8)	-9.10 (-10.90, -7.30)
Gravie (2005)[81]	63	63	14 (SD 10)	24 (SD 13)	-10.00 (-14.05, -5.95)
Hasse (2004)[73]	40	40	11.2 (SD 7.1)	21.2 (SD 9.2)	-10.00 (-13.60, -6.40)
Ho (2000) [61]	57	62	17.1 (SD 14.35)	22.9 (SD 14.17)	-5.80 (-10.93, -0.67)
Ren (2002) [75]	45	45	7.9 (SD 3.2)	14.2 (SD 6.5)	-6.30 (-8.42, -4.18)
Shalaby (2001) [93]	100	100	8.2 (SD 1.9)	53.9 (SD 5.8)	-45.70 (-46.90, -44.50)
Hetzer (2002) [88]	20	20	6.7 (Range)2-14	20.7 (Range 7-45)	-14.0
Ortiz (2002)[87]	27	28	23.1 (Range 0-98)	26.6 (Range 0-112)	-2.7
Schmidt (2002) [72]	72	80	6.2 (Range 3-14)	14.5 (Range 7-34)	-8.3
Krska (2003) [79]	25	25	12 (NR)	25.5 (NR)	-13.5
Thaha (2004)[70]	91	91	14 (NR)	14 (NR)	-
Study	**Number randomised SH**	**Number randomised CH**	**SH Median (Range)**	**CH Median (Range)**	
Cheetham (2003)[77]	15	16	10 (3-38)	14 (3-21)	
Kairaluoma (2003)[80]	30	30	8 (1-21)	14 (1-33)	
Palimento (2003) [84]	37	37	28 (12-40)	34 (16-50)	
Wilson (2002)[43]	32	30	14 (NR)	18 (NR)	
Ascanelli (2005)[74]	50	50	NR (10-25)	NR (20-45)	

The definition of return to normal activity may vary between trails (return to work, period of disability etc.) and the interpretation and assessment of normal activity may differ between patients. These factors may explain some of the heterogeneity observed between the studies. In addition, one study (Shalaby 2001[93]) reported an

unusually long convalescence time after CH. When this trail was removed from the analysis, there was still statistically significant heterogeneity between studies precluding pooling ($P<0.001$; $I^2=93.2\%$; Appendix 10.7, Figure 10.30).

Four trails reported the median number of days to normal activity; this ranged from 8 to 28 days after SH and 14 to 34 after CH. The study by Ascanelli (2005)[74] reported only the range.

Overall, SH resulted in a shorter period of time before patients could resume normal activity or return to work compared to CH.

5.2.2.15 Patient satisfaction

Fourteen studies reported the preference of patients for SH or CH, or their level of satisfaction (Table 5.26). Generally, there was no preference for one or other procedure. Where a preference was reported, it was for SH within the first year post-operatively,[74, 83, 90, 92, 93] and CH approximately 4 years post-operatively.[78]

Table 5.26: Overall patient satisfaction

Study	Time point	Patient preference/satisfaction
Bikhchandani (2005)[92]	15 days	SH
Kraemer (2005)[28]	6 weeks	No preference
Ho (2000)[61]	6 weeks	No preference
Correa-Rovelo (2002)[94]	2 months	No preference
Ascanelli (2005)[74]	Not reported	SH
Ho (2000)[61]	3 months	No preference
Pavlidis (2002)[83]	3 months	SH
Correa-Rovelo (2002)[94]	6 months	No preference
Chung (2005)[90]	6 months	SH
Cheetham (2003)[77]	8 months	No preference
Shalaby (2001)[93]	6 months	SH
Bikhchandani (2005)[92]	11 months	More patients were satisfied with SH Mean satisfaction scores the same for SH and CH
Pavlidis (2002)[83]	12 months	No preference
Kairaluoma (2003)[80]	12 months	No preference
Hasse (2004)[73]	12 months	No preference
Ortiz (2002)[87]	16 months	No preference
Palimento (2003)[84]	18 months	No preference
Ho (2000)[61, 69]	18 months	No preference
Van de Stadt (2005)[78]	46 months	CH
Palimento (2003)[68, 84]	5 years	No preference

5.2.3 Discussion of the clinical evaluation

5.2.3.1 Effectiveness

The findings of the review of clinical effectiveness are summarised in Table 5.26.

Table 5.27: Summary of clinical effectiveness: Whether results show a statistically significant difference in favour SH or CH for each outcome evaluated

Outcome	Time point			
	<6 weeks	**>6weeks <12 months**	**12 months**	**> 12months**
Pain	SH	Neither	Neither	Neither
Bleeding	Neither[a]	Neither	Neither[b]	Neither
Haemorrhage	Neither	N/A	N/A	N/A
Prolapse	CH	CH	Neither	CH
Urinary retention	Neither	N/A	N/A	N/A
Operating time	SH[c]	N/A	N/A	N/A
Hospital stay	SH[c]	N/A	N/A	N/A
Time to first bowel movement	SH[c]	N/A	N/A	N/A
Return to work/normal activity	SH[c]	N/A	N/A	N/A
Faecal incontinence	Neither	Neither	Neither	Neither
Faecal urgency	Neither	Neither	Neither	Neither
Anal stenosis/anastomotic stricture	Neither	Neither	Neither	Neither
Anal fistula	Neither	-	Neither	-
Anal fissure	Neither	Neither	-	-
Haemorrhoidal thrombosis	Neither	Neither	-	-
Pelvic sepsis	Neither	Neither	Neither	Neither
Wound infection	Neither	N/A	N/A	N/A
Systemic infection	Neither	N/A	N/A	N/A
Wound healing	SH	N/A	N/A	N/A
Symptom control	N/A	Neither	Neither	Neither
Reintervention - overall	N/A	Neither	Neither	Neither
Reintervention – for prolapse	N/A	-	CH	CH
Reintervention – for complications	N/A	-	Neither	Neither
Reintervention – requiring CH	N/A	-	CH	CH
Reintervention – requiring non-excisional	N/A	-	Neither	Neither

[a] Results are from a sensitivity analysis thought to be more representative than the analysis of including all trials

[b] Non-significant trend towards CH observed (p<0.1)

[c] Pooling was no undertaken due to heterogeneity between studies, however, the overall trend was apparent.

In the immediate post-operative period SH was less painful than CH. There was no increase in bleeding associated with SH compared with CH, however, there was a higher rate of residual prolapse. SH was associated with shorter operating times, hospital stay, time to first bowel movement, and time to normal daily activities. By day 21, the pain reported following SH and CH was minimal, with little difference between the two techniques.

In the short-term (>6 weeks to <1 year) prolapse was more common after SH. There was no difference in the number of patients complaining of pain between SH and CH. However, wound healing was significantly better at 6 weeks after SH.

In the longer-term (12 months and beyond) there was a significantly higher rate of prolapse after SH compared with CH. Although there was no difference between SH and CH in the total number of reinterventions undertaken, there was a significantly higher rate of reintervention for prolapse, and the use of CH as a secondary procedure after SH.

Overall, there was no significant difference in the rate of complications between SH and CH. The most serious complications associated with haemorrhoidal surgery are faecal urgency and incontinence, as these can lead to a life-long reduction in quality of life due to the inability to treat these conditions. Our review found no differences in the incidence of incontinence or urgency between SH and CH at any time point during the follow-up period, and there were no incidents of incontinence reported beyond 1 year post-operatively after either procedure. One of the most frequently reported complications of haemorrhoidal surgery is anastomotic stricture (after SH) or anal stenosis (after CH). Our review found that the frequency of these complications was low (0% to 8.8% for anastomotic stricture; 0% to 10% anal stenosis after CH); there was no difference in their incidence after SH and CH at any time point. There was also no evidence to suggest that the incidence of urinary retention, anal fissure, anal fistula, rectovaginal fistula, pelvic/perianal sepsis, haemorrhoidal thrombosis, and infection were more common after either surgical procedure.

5.2.3.2 Variability between studies

The quality of studies did not appear to impact on the results of any meta-analysis. However, all the included studies had some methodological flaws, and there were no large, high quality RCTs conducted in a representative population for comparison.

There was no evidence that the type of CH undertaken impacted on the relative difference to SH for any post-operative outcome. There was also no indication that those studies that did not report the type of staple gun used, and may therefore have used either PPH03 or a staple gun not designed for SH, adversely affected any post-operative outcome measure.

Two factors seemed to be foremost as causing variability between studies for particular outcomes; the degree of haemorrhoids and the apparent experience of the surgeons.

The degree of haemorrhoids is thought to impact on the clinical outcome following haemorrhoidal surgery. It is thought that SH may be unsuitable for people with IV degree haemorrhoids due to difficulty gaining access to the anal canal;[25] difficult placement of the pursestring suture;[66] excess tissue to be excised being to bulky to fit into the housing of the staple gun;[25] incomplete mucosal resection,[66] and residual symptomatic prolapse.[66] Two studies included in this review, Ortiz (2005)[86] and Boccasanta (2001),[85] restricted recruitment to those with IV degree haemorrhoids. The studies recruiting a high proportion of patients with IV degree haemorrhoids seemed to contribute to the heterogeneity for some outcomes. Unlike Ortiz (2005),[86] Boccasanta (2001)[85] reported data for only a few outcomes for which meta-analyses could not be conducted, or for post-operative complications for which incidents were low and heterogeneity between studies was not observed. Thus the effect of this trial was not explored in sensitivity analyses. Most notably, the study by Ortiz (2005)[86] reported a greater proportion of patients requiring reintervention after SH compared to CH at one year than any other study. These studies also tended to report higher levels of post-operative pain, however, this was after both procedures. The degree of haemorrhoids did not seem to cause heterogeneity in the analyses of bleeding,[85, 86],

prolapse,[85, 86] anal stenosis/anastomotic stricture,[85] urinary retention,[85] faecal incontinence,[85, 86] or haemorrhoidal thrombosis.[85, 86]

The learning curve when introducing a new procedure may result in the new procedure appearing less effective and less safe. One of the included studies reported experiencing technical difficulties during the SH procedure (Kairaluoma 2003[80]). This was one of the earliest trials undertaken after the introduction of SH, conducted between 1999 and 2000. The technical difficulties experienced during SH seemed to have led to an uncharacteristically high incidence of residual prolapse, and the requirement for reintervention. When this study was excluded from these analyses, heterogeneity was eliminated.

Most studies did not report whether patients with co-morbid conditions were included in the study, those that did, generally reported that they were excluded. Only one study (Kraemer 2005[28]) reported that they included patients with co-morbid conditions. The only outcome for which this study provided results and seemed to differ from other studies, was the tendency for a longer duration of hospital stay.

The use of general anaesthesia did not appear to result in longer operating times or length of hospital stay. There was no evidence that older studies used general anaesthetic more frequently, or had longer durations of hospital stay than more recent trials. There was also no apparent impact of the type of anaesthesia used and the outcomes following surgery.

5.2.3.3 Comparison with other systematic reviews

The findings of our review are generally similar to results reported by previous reviews.[30, 64, 96, 97] The review by EE-S reported that the incidence of prolapse was not significantly higher after SH in people with III degree haemorrhoids,[64] but their findings were based on a meta-analysis of four RCTs, one of which was excluded from the current study due to it's use of a staple gun not designed for SH.[98] Of sixteen studies reporting the incidence of prolapse in the current review, four were restricted to patients with III degree haemorrhoids. Of these one reported a significant increase in the incidence of prolapse in the early post-operative period,[80] and the others either

no difference between SH, or a tendency towards increased prolapse after SH compared to CH at other time points.[73, 79, 89] Considering the general trend in favour of CH in both patients with III degree haemorrhoids and a wider spectrum of patients, it is possible that these trials were underpowered. There is currently no evidence to recommend SH as particularly suitable for patients with III degree haemorrhoids.

When considering the difference between SH and CH in relation to complications, we found no differences in the incidence major complications: incontinence, urgency, or anastomotic stricture/ anal stenosis, at any time during the follow-up period. In relation to incontinence, the EE-S review and recent Cochrane review reported a non-significant trend favouring SH,[64, 97] and other reviews reported inconclusive results[30, 96] due to the lack of available studies and an insufficient period of follow-up in those studies available. The finding that there was no significant difference in the incidence of anastomotic stricture/anal stenosis between SH and CG in the current review is reflected by previous reviews,[30, 64, 96, 97, 99] although the EE-S review[64] and recent Cochrane review[97] did report a non-significant trend towards a reduced incidence after SH.

5.2.4 Conclusions of the evaluation of clinical effectiveness

SH was associated with less pain in the immediate post-operative period, however it was also associated with a higher rate of residual prolapse, prolapse in the longer term and reintervention for prolapse.

There was no clear difference in the rate or type of complications associated with the two techniques.

The absolute and relative rates of recurrence and reintervention, for SH and CH, are still uncertain.

6 Assessment of cost-effectiveness evidence

To assess the cost-effectiveness of circular SH for the treatment of haemorrhoids, this chapter: (i) reviews the existing cost-effectiveness evidence, including the Endo Ethicon-Surgery (EE-S) submission to the National Institute for Health and Clinical Excellence (NICE) (Section 6.1); and (ii) reports York's independent economic assessment of the cost-effectiveness of circular SH for the treatment of haemorrhoids (Section 6.2).

6.1 Systematic review of existing cost-effectiveness evidence

6.1.1 Methods

To review the existing cost-effectiveness evidence base, papers obtained during the clinical effectiveness review (Section 5.1.1) were searched to check whether they included cost-effectiveness data. In addition, four economics databases were searched to identify additional economic evaluations (Appendix 10.1.2).

To obtain data to populate parameters of the York economic model (Section 6.2), a series of specific searches were undertaken. These included searches for relevant data on health related quality of life (HRQoL), the incidence and prevalence of haemorrhoids, RCTs evaluating open versus closed haemorrhoidectomy, cohort studies of complications and symptoms associated with haemorrhoidal surgery and the length of hospital stay following haemorrhoidal surgery as reported in Appendix 10.1.3.

In terms of the inclusion criteria, a broad range of studies was considered in the assessment of cost-effectiveness, including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Any duplicate references that were obtained were taken out and the remaining references were checked for relevance by a health economist. Studies were included in the cost-effectiveness review if they considered the costs and outcomes associated with two or more surgical procedures in the treatment of haemorrhoids. Therefore, studies based

on cost-consequence analysis, cost-utility analysis, cost-effectiveness analysis, cost-minimisation and cost-benefit analysis, were eligible for inclusion.

A data extraction form for use in previous Technology Assessment Reviews was used to abstract data on all economic evaluations reviewed. The quality of the cost-effectiveness studies was assessed based on a checklist updated from that developed by Drummond *et al* [100] and which reflects the criteria for economic evaluation detailed in the methodological guidance developed by NICE.[101] (Appendices 10.3 and 10.5.2) In addition, Endo Ethicon-Surgery (EE-S) (Johnson and Johnson) submitted an economic model which is discussed below.

6.1.2 Results

Based on the above review, no formal full economic evaluations assessing the cost-effectiveness of SH for the treatment of haemorrhoids were found in the published literature. One study [65] examined the costs associated with surgical procedures for haemorrhoids in some detail and is summarised in Appendix 10.8.

6.1.2.1 Economic evaluation received from Endo Ethicon-Surgery

Overview

The EE-S submission compared the use of SH with CH (using Milligan Morgan open haemorrhoidectomy), in the treatment of III and IV degree haemorrhoids. A cost-utility analysis was undertaken using a probabilistic, cohort-based decision tree. Data on clinical effectiveness for use in the model were obtained from a systematic review of the literature. The model followed a one year time horizon and was undertaken from the perspective of the UK NHS.

Model Structure

Patients entered the model having had initial surgery; SH or CH. Subsequently patients could follow one of four pathways through the model (Figure 6.1). These were;

(i) Full recovery and no recurrent prolapse

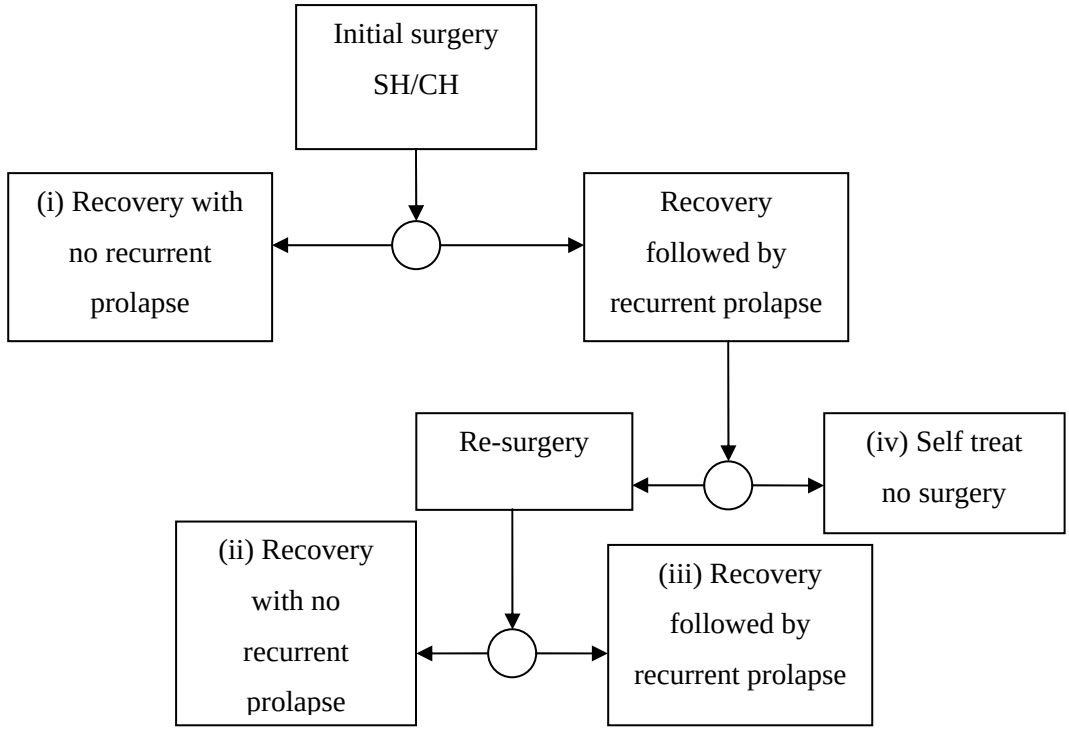
(ii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery, followed by no further prolapse

(iii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery followed by a second recurrent prolapse

(iv) A recovery period in which the patient experiences a less severe recurrent prolapse which can be self-treated.

Therefore no account was taken of symptoms other than prolapse, or complications. For those patients with recurrent prolapse, reintervention was determined by the level of prolapse severity. Patients with more severe recurrent prolapse had re-surgery whilst patients with less severe recurrent prolapse self-treated. Following re-surgery, patients were at risk of a second recurrent prolapse.

Figure 6.1: Structure of the EE-S economic model



In the model it was assumed that the type of re-surgery undergone was the same as that on entry into the model. Therefore the benefits and costs associated with surgery, including those incurred in the recovery period, were repeated in pathways (ii) and (iii) above. It was assumed that the average time from initial surgery to recurrence of prolapse was 120 days. The waiting time from recurrence with severe symptoms to reintervention was assumed to be 10 days.

A one year time horizon was modelled since EE-S suggested that there is no difference in treatment effect after one year and that any prolapse beyond that time is a new prolapsing haemorrhoid, rather than a recurrence due to treatment failure. Therefore it was not necessary to discount costs or benefits associated with the treatment, given the short time horizon of the model.

Data used in EE-S model

Effectiveness and utility data used in the EE-S model

Based on the NICE reference case, EE-S aimed to estimate the relative treatment effect of SH compared to CH in terms of quality adjusted life years (QALYs) using a generic measure of HRQoL. QALYs are calculated by multiplying the length of time in a particular health state by its corresponding utility value. Utility values for the NICE reference case should be elicited using a choice-based preference measure. Since data were not estimated directly in any trial, they were estimated indirectly by synthesising evidence from a number of sources.

To convert generic HRQoL data into utility values for each day during the recovery period, EE-S took a series of steps

- First, the HRQoL of SH and CH at about 7 weeks post surgery were estimated from an RCT (Wilson *et al*.) which reported mean scores for the four physical health dimensions of the SF-36.[43]
- Second, these mean SF-36 dimensions were mapped to utilities.
- Third, to incorporate post-operative pain (a key outcome associated with surgery), the mean SF-36 Bodily Pain (BP) dimension score was adjusted

using data on pain in the early post operative period, reported by a separate RCT (Van de Stadt, 2005)[78].

- Lastly, the data were extrapolated to predict pain, SF-36 dimensions and ultimately utilities for the entire first year and used to generate a QALY associated with SH and CH over one year. Each step is explained in more detail next.

The first step was to estimate the HRQoL of CH and SH at 7 weeks. Wilson *et al*, 2002 [43] used the SF-36 to measure HRQoL pre-operatively and at around seven weeks post-operatively and these data are shown in Table 6.1. Mean summary scores of the four physical health dimensions of the SF-36 scores were reported; that is for bodily pain (BP), general health (GH), physical functioning (PF) and role-physical (RP). The study did not report the four mental health dimensions of the SF-36.

Table 6.1: Pre-operative and post-operative SF-36 scores for patients undergoing SH and CH

SF-36 Dimension	SF-36 score (a)			
	SH (b)		CH (c)	
	Pre Operation	6-8 weeks post operation	Pre operation	6-8 weeks post operation
PF	90	95	90	90
RP	100	100	100	100
BP	81	50	49	41
GH	61	61	61	61

(a)Results read from graph in Wilson *et al* [43]

(b) SH includes patients with Endo Ethicon PPH and Autosuture devices

(c) CH was open haemorrhoidectomy

The second step was to predict utilities from the mean SF-36 dimensions. It is possible to generate utilities from the SF-36 using the SF-6D (Brazier *et al*, 2002).[102] However, individual patient data were not available from the trial so using the Brazier SF-6D scoring algorithm was not an option. Instead, EE-S estimated a relationship between the SF-36 dimension scores and utility, using a cross-sectional dataset of patients aged 39 to 67 who were registered with a general practitioner in Sheffield.[103] The SF-6D algorithm was used to calculate the utility for each individual in the dataset. SF-36 dimension scores were calculated for each individual for the four physical health dimensions. Multivariate linear regression was carried out to estimate

how utility would change, on average, for a one point change in the SF-36 summary dimensions, assuming all other dimensions remained constant. The mean coefficients estimated by this regression were:

Equation 1:

SF-6D utility score = 0.4339 + (0.0008 * PF score) + (0.0008 * RP score) + (0.0016 * BP score) + (0.0012 * GH score)

Standard errors and regression diagnostics were not reported so it was not possible to reflect fully the uncertainty in the utility estimates.

Predicted utility scores were calculated by summing the product of the SF-36 dimension scores from Table 6.1 with the corresponding regression coefficient for the pre-operative period and at seven weeks post-operatively for CH and for SH. The results of this calculation are shown in Table 6.2.

Table 6.2: Predicted utility scores for SH and CH pre-operatively and at 6 to 8 weeks post-operatively,

SF-36 dataset	Predicted utility score	
	SH	CH
Pre operation	0.789	0.738
6 to 8 weeks post operation	0.743	0.726

Note: This was obtained by summing the product of the SF-36 dimension scores from the Wilson RCT[43] with the corresponding regression coefficient (Equation 1)

The third step taken by EE-S to estimate utility each day was to adjust the utilities predicted in Table 6.2 to reflect daily changes in pain. Pain is a key short-term outcome associated with surgery for haemorrhoids. It is most severe in the days immediately after surgery and diminishes over time. The assumption made by EE-S is that the utilities estimated in Table 6.2 from the SF-36 after 6 to 8 weeks represent the utilities at that particular point in time rather than average utility over the preceding recovery period. The methods and data used to make these calculations are described next.

A single study (Van de Stadt, 2005) [78] was used to estimate the pain each day associated with SH and CH, over a 21 day recovery period, based on a VAS scale. For each arm of the study, an exponential curve was fitted to the observed VAS scores over the first 21 days to predict VAS scores every day up to seven weeks. The mean coefficients estimated by this function were:

Equation 2:

Mean VAS after CH at day t = exp(1.59-0.039*t)

Mean VAS after SH at day t = exp(1.00-0.073*t)

A mapping exercise was carried out to predict what the mean SF-36 BP dimension score would have been if this instrument had been used by patients each day instead of the VAS. No studies were found that reported both SF-36 and VAS scores at a corresponding time point. Instead, it was assumed that the SF-36 BP score observed in each arm of the Wilson study (2002) at seven weeks, corresponded to an extrapolated VAS pain score (Table 6.3).[43] Two more data points were imputed. It was assumed that the maximum VAS pain score of 10 maps to an SF-36 bodily pain score of 1 and a zero VAS pain score maps to a bodily pain score of 100. It was then assumed there was an exponential relationship between VAS pain and SF-36 bodily pain and this was fitted using these four data points. The EE-S submission did not state whether other ways were tried to predict the SF-36 BP score from the VAS score, for example, assuming a linear relationship. The mean coefficients estimated by this function were:

Equation 3:

Mean SF-36 BP score= exp(4.2025 – 0.4216* mean VAS)

Table 6.3: Sources of data used by the EE-S to map mean SF-36 BP to mean VAS pain

VAS pain score (0 to 10 scale)	Mean VAS	SF-36 bodily pain score (0 to 100 scale)	Mean SF-36BP
Van de Stadt[78] SH arm (extrapolated from weeks 3 to 7)	0.093	7 weeks SH arm .[43]	50
Van de Stadt[78] CH arm (extrapolated from weeks 3 to 7)	0.786	7 weeks CH arm [43]	42
Assumption	0	Assumption	100
Assumption	10	Assumption	0

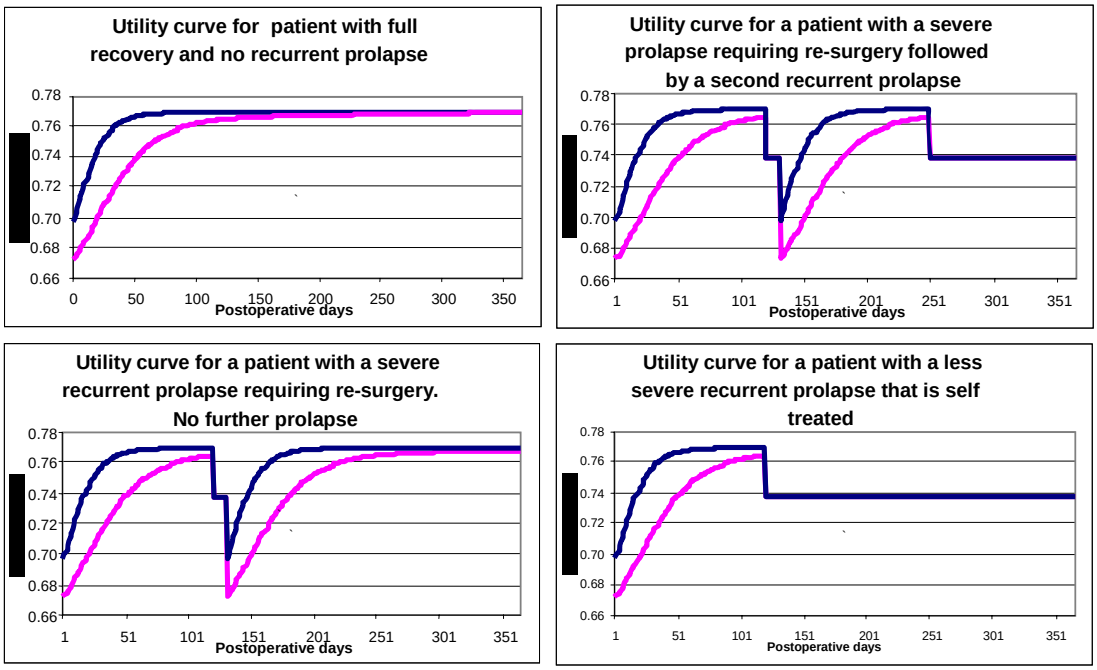
The final step taken to estimate utilities over the first year was to extrapolate the data. Mean VAS pain scores were available from a single RCT (Van de Stadt, 2005)[78]each day for the first 21 days. These scores were extrapolated using the functions estimated by Equation 2 to predict pain scores each day after SH and CH for the first year. The predicted pain scores were used to predict the mean SF-36 BP dimension scores each day over the same period using Equation 3. A further adjustment was made to other SF-36 dimensions from the Wilson *et al* (2005) RCT[43] to reflect possible changes in HRQoL over the first year. As shown in Table 6.1, based on the SF-36 the average PF score was 95 following SH, and 90 following CH. For the other dimensions (i.e. RP and GH) the scores were the same for both interventions and were assumed to remain so for the duration of the model. The model assumed that the score in the SH arm remained constant whereas the score in the CH arm increased linearly from 90 at seven/eight weeks to 95 at 12 months, though data was not available to support this assumption, other than the findings in Wilson *et al* (2002).[43] The predicted SF-36 dimension scores were multiplied by the coefficients estimated in Equation 1 to generate utility values for each day of the year following SH and CH. Finally, the predicted utility scores for each day over the first year were used to generate a QALY for a patient undergoing a prolapse free recovery (pathway (i)) (Table 6.4).

Table 6.4: QALYs gained in the EE-S cost-utility model

Health state	Mean
Treatment with SH	
(i) Full recovery and no recurrent prolapse	0.769
(ii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery, followed by no further prolapse	0.764
(iii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery followed by a second recurrent prolapse	0.753
(iv) A recovery period in which the patient experiences a less severe recurrent prolapse which can be self-treated	0.747
Treatment with CH	
(i) Full recovery and no recurrent prolapse	0.760
(ii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery, followed by no further prolapse	0.748
(iii) A recovery period in which the patient experiences a severe recurrent prolapse requiring re-surgery followed by a second recurrent prolapse	0.738
(iv) A recovery period in which the patient experiences a less severe recurrent prolapse which can be self-treated	0.739

There is evidence that some patients will experience a recurrent prolapse following the initial operation (pathways (ii), (iii) and (iv)). EE-S undertook a meta-analysis of recurrent prolapse and re-surgery due to prolapse, based on the results of 13 studies. As stated above, it was assumed that for those patients experiencing a recurrent prolapse, this was observed 120 days post-operatively, based on Oritz *et al*, (2002).[87] The results of seven studies were meta-analysed to obtain the proportion of patients who were diagnosed with a recurrent prolapse who then self-treated (pathway (iv)). Since no corresponding data on HRQoL for these patients was available, the model assumed that patient utility was equivalent to the pre-operative utility in patients with a severe prolapse (Wilson *et al*. 2002).[43] For patients with severe recurrent prolapse it was assumed that re-surgery was required (pathways (ii) and (iii)) and the associated QALYs were the same as those associated with the initial recovery curves. The patients who experienced a second recurrent prolapse (pathway (iii)) were assumed to remain in that state for the remainder of the model. Figure 6.2 illustrates the utility curves associated with each of the four patient pathways.

Figure 6.2: Utility curves for the 4 patient pathways through the model (dark blue line for SH, lighter/purple line for CH)



Resource use and cost data summary

To calculate the costs associated with SH and CH, EE-S estimated the resource use and costs of either procedure comprising surgical and hospital costs, the use of staple gun for SH, day case and inpatient stays. Table 6.5 shows key resource use and cost inputs. EE-S used a micro-costing study, based on data from laparoscopic-colorectal surgery, to estimate the cost of haemorrhoidal surgery. The list price for the haemorrhoidal circular stapler was used. Based on a meta-analysis of five studies, time spent in surgery was estimated and these data were combined with the cost per minute of surgery and the cost of the staple gun as appropriate, to calculate the total surgery cost.

Table 6.5: Resource use and unit cost data used in the EE-S model

Variable	Procedure	
	SH	CH
Cost of surgery per minute (excluding haemorrhoidal circular stapler)	£7.95	£7.95
Cost of haemorrhoidal circular stapler	£420	-
Time in surgery (minutes)	18.49	28.20
Total surgery cost	£567	£224
Cost of hospital stay (day)	£224	£224
Percentage of patients incurring inpatient stay	42.9%	73.2%
Inpatient length of stay (nights) for patients not undergoing day-surgery	1.60	2.58
Total procedure cost	£849	£707
Percentage of patients suffering prolapse	10.10%	2.60%
Time to recurrent prolapse (days)	120	120
Time to surgery post recurrent prolapse (days)	10	10
Probability of re-surgery for recurrent prolapse	66.2%	27.2%

Inpatient and day case costs were calculated using Hospital Episode Statistics (HES) data and Office of Populations Census and Surveys (OPCS) data. In the UK for 2004/5 it was estimated that approximately 23,000 haemorrhoidal procedures were undertaken, of which 13,000 were RBL and sclerotherapy and 8,000 were CH (OPCS code H511). Based on patients aged 15 to 74 years old inclusive, it was estimated that 26.8% of cases were undertaken as day case procedures, whilst 73.2% required an inpatient stay. EE-S used these inpatient figures for CH. For SH, the proportion of inpatients was taken from a single study (Beattie *et al* 2006).[104] The inpatient length of stay for patients who were not day case was based on a meta-analysis of two studies (Roswell, 2002; [105] Racalbuto, 2004 [106]). The average hotel cost per day on an inpatient ward was estimated by the long stay outlier payment from the Admitted

Patient Care Tariff, which lists the prices of hospital care in England and Wales. No specific data on the cost of day case excluding surgery were found and therefore this was assumed to be the same as a day on an inpatient ward. Follow-up management costs and the cost of self-treatment were not included. The average cost of hospital stay (excluding surgery) was calculated for SH and CH by:

Equation 4:

$$AvCost_t = P_t * C + (1 - P_t) * N_t * C$$

Where t = SH or CH

P_t = proportion of patients undergoing day surgery for treatment t

N_t = average inpatient nights for patients not undergoing day surgery for treatment t

C = hotel cost per day on an inpatient ward

Results

Results from the base-case scenario are shown in Table 6.6. The incremental cost per QALY gained with SH relative to compared to CH was £22,416 in the model. Based on a cost-effectiveness acceptability curve (CEAC) it was shown that at a threshold incremental cost-effectiveness ratio (ICER) of £30,000 there was a greater than 70% probability that SH was a more cost-effective option than CH.

Table 6.6: Cost-effectiveness results from the EE-S model

Procedure	Mean Cost per Patient	Mean QALYs Gained per Patient	ICER (approx 95% CI)
SH	£904	0.77	£22,416 (dominating to £49,621)
CH	£713	0.76	-
Difference	£191	0.009	

Sensitivity analysis

One-way sensitivity analyses were performed to test the robustness of the results to variation in the following costs and effects; cost of surgery, the cost of hospital stay, the percentage of inpatient episodes, the mean inpatient length of stay, the percentage of patients suffering recurrent prolapse, the time to recurrent prolapse, the probability of re-surgery following recurrent prolapse and the physical functioning score (Table

6.7). The sensitivity analyses showed that the results for SH ranged from dominating CH, through to an ICER of £47,000.

Table 6.7: Several one-way sensitivity analysis results*

Variable adjusted in one-way sensitivity analysis	Cost per QALY of SH
Cost of surgery – extreme case in which there is no surgery saving time using SH	£30,000
Cost of haemorrhoidal stapler – discounted by 30%	£6,970
Cost of hospital stay – varied from £100 to £300 per day	
£100 per day	£35,000
£300 per day	£15,000
Percentage of inpatient episodes - % of patients incurring an inpatient stay	
0%	£47,000
100%	£21,000
Percentage of inpatient episodes - % of SH incurring an inpatient stay	
0%	£16,000
100%	£33,000
Mean inpatient length of stay – varying the weighted mean difference of inpatient length of stay between SH and CH	
0	£42,500
2.2	SH dominates
Adding an additional 0.5 day stay to the mean length of stay of both procedures (WMD remains the same)	SH dominates
Assuming all day case episodes to calculate the cost of a hospital stay	£13,439
Percentage of patients suffering recurrent prolapse	
Assuming rate of recurrence is 2.6% for either procedure	£16,558
Stapled procedure prolapse rate fixed at 10.1% - Open procedure re-proplase rate varied	
0% patients suffering recurrent prolapse	£25,000
20% patients suffering recurrent prolapse	£14,000
Open procedure prolapse rate fixed at 2.6% - Stapled procedure re-prolapse rate varied	
0% patients suffering recurrent prolapse	£15,000
20% patients suffering recurrent prolapse	£35,000
Time to recurrent prolapse	
At 25 days	£23,496
At 335 days	£21,000
Time to surgery post recurrent prolapse	
0 days	£22,801
100 days	£24,169
Probability of re-surgery following recurrent prolapse	
If 100% of patients undergo SH re-surgery and 0% undergo CH re-surgery	£22,614
If 0% of patients undergo SH re-surgery and 100% undergo CH re-surgery	£24,747
If 0% of patients undergo SH re-surgery and 0% undergo CH re-surgery	£24,589
If 100% of patients undergo SH re-surgery and 100% undergo CH re-surgery	£22,747
Physical functioning score	
If physical functioning scores at 56 days are assumed equal across procedures	£27,000
If physical functioning scores at 56 days become equal at day 300	£23,000

*Many of these figures were read off a graph

Conclusion

The EE-S submission to NICE suggested that SH is cost effective when compared to CH, based on the results of the use of the "Proximate* PPH Procedure for Prolapse and Haemorrhoids Set" for haemorrhoidopexy. The EE-S report argued that SH is associated with less pain, faster healing, shorter operative time, a lower length of stay in hospital and greater potential to deliver SH on a day case basis, as compared to CH.

6.1.2.2 Comments on Methodology

Time Horizon

EE-S assumed that the treatment effects of the two surgical procedures were equivalent at one year. They based this on the assumption that utility in patients with successful surgery is equal at one year and that any prolapse beyond this point was a new prolapse rather than a recurrent prolapse. As reported in the clinical review (Section 5.2.2.6) when data were pooled for 12 month data and beyond, recurrent prolapse was significantly more common after SH than CH.

As well as potential differences in treatment effect, exposure time may influence the number of recurrent prolapses that are recorded. However, this is not considered in the EE-S analysis. A possible implication of not designing a model with a longer time horizon might be that the disutility associated with further recurrent prolapse is not fully captured.

The EE-S model also assumes that the time to re-surgery (i.e. pathways (ii) and (iii)) takes place very shortly after recurrence of symptoms (i.e. 10 days). This is a highly optimistic clinical assumption. The expert clinical advice to the York group was that the average time from recurrence of symptoms to re-surgery in the NHS is typically around 12 months, with a typical minimum of six months. Minimising the time to re-surgery minimises the disutility associated with the pre-operative period(s). Since SH is associated with a higher recurrent prolapse rate, minimising the impact of pre-operative disutility, under-estimates the disutility associated with SH compared to CH.

Further to this, in the EE-S model, the recovery period post surgery and re-surgery extends for about 120 days. As reported by EE-S, and as reported in Section 5.2.2.1), SH was less painful than CH during the early post-operative period, pain lessening in the later post-operative period (post 14 days) in both arms of the trials. Nevertheless, patients still experienced less pain following SH than CH. Based on a meta-regression of the ten studies which reported a mean VAS and a measure of variance (standard deviation), at 21 days the average pain score for all patients decreased to less than 0.5 (on a scale of 0 to 10) (Figure 5.3). Given such a low level of pain, it seems inappropriate to extend the average difference in pain in the recovery period for as long as 120 days, simply by extrapolating the short term data.

Resource use data

EE-S stated that the probability of re-surgery for recurrent prolapse, given a prolapse had occurred, was 66% following SH and 27% following CH. There is no explanation as to why, if a prolapse does recur, it should be more serious in the SH group. Since the model assumes a short waiting time of 10 days for surgery, patients with severe prolapse only experience a brief disutility from the symptoms. On the other hand, the model assumes that mild symptoms persist for the rest of the year, with the same disutility as severe symptoms. Furthermore, patients with severe symptoms have a repeat of their original surgery. The combined effect of these assumptions is that, although the model recognises that patients have a greater risk of recurrence following SH, the symptoms are of a brief duration and the disutility following a revision of surgery is relatively low, and has less overall impact on health in the SH group than in the CH group.

EE-S calculated mean overall length of stay in each group as the proportion of day cases plus the proportion who were not day cases multiplied by the expected length of stay of patients who were not day cases. The number of day cases in each group was not based on RCT data. Instead different sources of data were used, thus the patients may differ in other characteristics apart from the intervention received. EE-S used two RCTs to estimate the 'nights spent in hospital' of patients who were not day cases.(Rowsell 2000 [105] and Racalbuto 2004 [106]). They estimated a weighted average length of stay of 1.60 nights for SH and 2.58 for CH (Difference = -0.95 [-2.46 , 0.5]).

Of these studies, Racalbuto 2004 [106] stated that they did not take advantage of the opportunity offered by SH to adopt day case surgery, and the other (Rowsell 2000)[105] data were not extracted correctly to estimate length of stay of patients who were not day cases. Also, both studies were excluded from the York group's meta-analysis since the staple gun CDH33 was used, and this is not designed for SH.

To estimate the time spent in theatre, EE-S synthesised data using a random effects meta-analysis of five studies.[83, 90, 92, 93, 106] EE-S estimated a weighted mean surgery time of 18.49 minutes for SH and 28.20 minutes for CH (WMD = 9.71 [3.60, 15.82]). Again Racalbuto, 2004 [106] was the study excluded from the York group's meta-analysis as the CDH33 staple gun was used.

VAS pain and utility data

A single study (Van de Stadt 2005[78]) was used to incorporate the effects of pain experienced post-operatively. The authors justified this on the basis that Van de Stadt provided the most comprehensive VAS pain scores, reporting daily mean scores for patients at rest from day 0 to day 21 post-operatively. As reported in Section 5.2.2.2, studies reported mean VAS pain scores; therefore, by selecting one study EE-S do not make use of all the available data.[28, 61, 71, 72, 74, 75, 77-80, 82-85, 88-91, 93, 94]

Wilson *et al* (2002) [43] was a key source of data, since it was the only RCT which recorded the SF-36 in the early post-operative period. However, there are problems with this study which limit both its external and internal validity. To obtain scores for the physical health dimensions of the SF-36, Wilson *et al* (2002) [43] combined the results of SH using the Autosuture device without using the STRAM kit adaptor (Tyco Healthcare) with those using a PPH-01 (EE-S). Therefore, the Autosuture arm of this trial was excluded from review of clinical effectiveness (Chapter 5).. In addition, the pre-operative SF-36 scores in the combined SH and the CH arm differ substantially. The summary of the SF-36 scores for the BP component were 50 in the pre-operative CH arm compared to 80 in the pre-operative combined SH arm which suggests that there may be a problem with the random assignment of patients to one of the three interventions. It is worth noting that these figures were taken from a graph. EE-S recognised this and their correction was to assume that both groups

started from the lower SF-36 baseline score. Lastly, the SF-36 was only reported for four out of the eight dimensions.

The approach taken by EE-S to estimate utility was (i) to start from the SF-36 dimensions reported in Wilson (2006) [43], (ii) to adjust the SF-36 BP score using RCT evidence on daily VAS pain during the early post-operative period, (iii) make assumptions about how the other seven dimensions of the SF-36 might also have changed over the same period, and (iv) to score the adjusted SF-36 eight dimensions in terms of utility.

There are a number of differences between the SF-36 instrument and the VAS pain score which create difficulty in mapping VAS to the SF-36 BP score. The two HRQoL instruments ask the responder to consider their health over different time periods. The VAS score asks about current pain, whereas the SF-36 asks about "average" health during the previous four weeks. The VAS score is a single numeric rating scale asking about current pain, whereas SF-36 BP consists of two questions; ***Q7.*** *How much physical pain have you had during the last 4 weeks? and* ***Q8.*** *During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?* The VAS score is a continuous scale of 0 (no pain) to10 (worst pain imaginable), whereas the SF-36 questions are categorised into five or six ordinal responses. Table 6.8 shows the SF-36 BP responses and the scoring system on a scale of 0 (worst) to 100 (best).

Table 6.8: SF-36 scoring system for bodily pain dimension [107]

	Q8: How much does pain restrict daily activities					
Q7: Pain	**Q8 not answered**	**Not at all**	**A little**	**Moderate**	**Quite a bit**	**Extreme**
None	100	100	80	70	60	50
Very mild	88	84	74	64	54	44
Mild	64	72	62	52	42	32
Moderate	42	61	51	41	31	21
Severe	24	52	42	32	22	12
Very severe	0	40	30	20	10	0

The SF36 is a measure of average health over a 4 week period, rather than a measure of current health. Furthermore, it includes information about function as well as severity of pain. For these reasons it is unlikely that there would be a close correlation between the VAS score each day and the SF-36BP, and therefore it seems unreasonable to use the VAS score to try and predict what the SF-36BP would have been if patients had been given the SF-36 every day instead of the VAS.

There was a lack of good quality RCTs which recorded either HRQoL or utility in the crucial early post-operative period; therefore modelling assumptions such as those used by the EE-S were essential. However, the EE-S submission did not carry out sensitivity analyses to explore alternative modelling approaches to reflect the uncertainty about such methods.

Recurrence of prolapse

EE-S estimated that 10.1% of patients would experience recurrence of prolapse following SH and 2.6% following CH. These estimates were the weighted mean of the results of a meta-analysis. However, a series of meta-analyses were reported to explore potential subgroup effects. It is not clear from the report which meta-analysis was used to inform the base-case, and therefore the assessment group cannot comment on whether it was appropriate.

Reinterventions

No account was taken of the use of non-excisional procedures (e.g. skin tags, RBL or sclerotherapy) in patients experiencing a recurrence of symptoms following surgery. The York group's expert clinical advice was that it is more likely that most surgeons would recommend non-excisional procedures in the first instance, and only if this failed would further surgery be considered.

The authors assumed that the same surgical procedure was applied to any patients requiring re-surgery. The York group's expert clinical advice was that it is more likely that in actual practice, about half of patients requiring re-surgery would undergo a SH, and about half would undergo CH.

Summary of review of literature and critical appraisal of EE-S model

In summary, this section did not find any published cost-effectiveness studies which compared circular SH with CH. EE-S submitted an economic evaluation, which identified several of the challenges required to assess the cost-effectiveness of these technologies. These included: dealing with a lack of RCTs comparing utility in the early post-operative period, estimating the rate of treatment failure in the first year and estimating the utility following treatment failure.

There were some limitations to the EE-S model:

- The time horizon required to include all relevant costs and consequences associated with treatment may be longer than one year.
- The model did not use all the available evidence from the RCTs to estimate pain and other outcomes.
- The model did not consider complications and symptoms, other than prolapse.
- The model did not conduct sensitivity analyses on alternative ways to estimate utility.

In an attempt to synthesise all of the available evidence and in order to overcome these limitations a new cost-effectiveness model was developed.

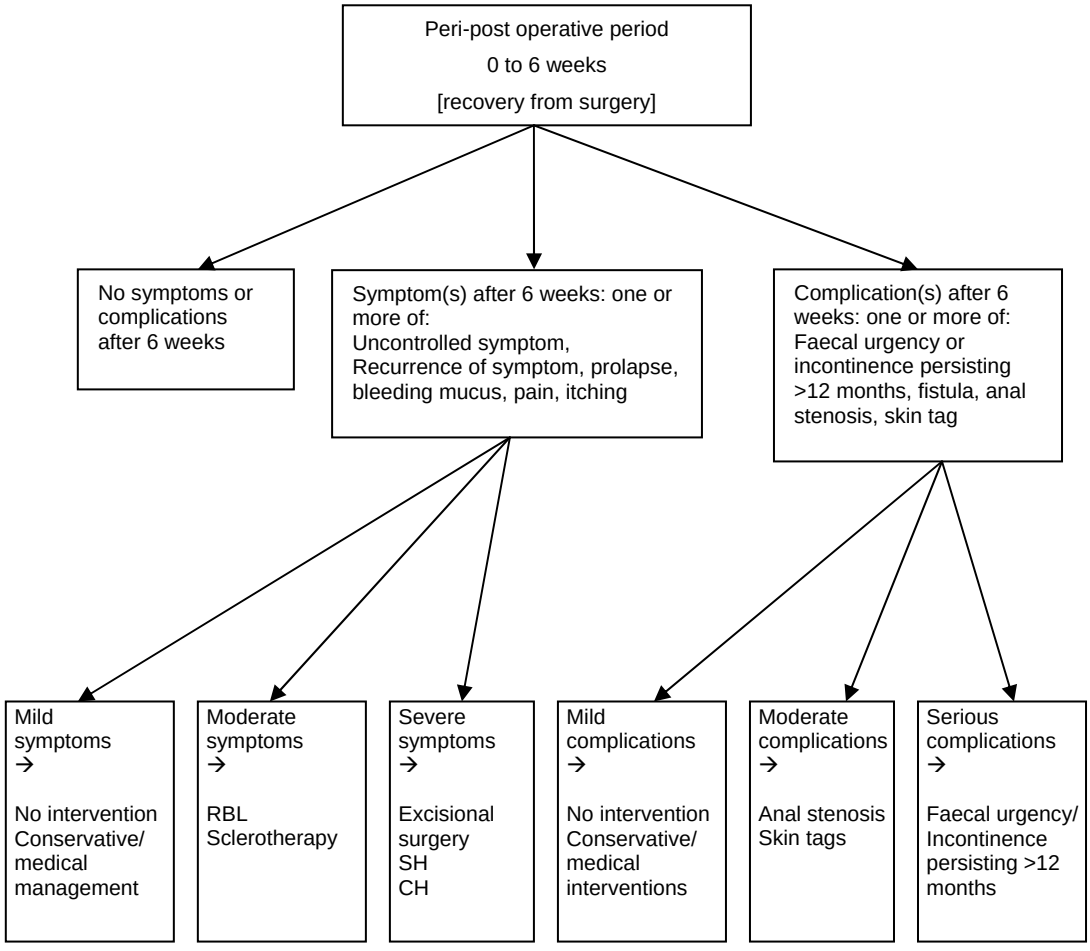
6.2 York Economic Assessment

This section is in five parts. The first part describes the objectives of the York economic assessment, the structure of the model and the assumptions underlying the base-case. In the second part the data used to populate parameters of the model are described comprising effectiveness, utility, resource use and cost estimates associated with SH and CH, from zero to six week post-operatively and over the medium and longer time up to three years. The third part shows the results of the base-case and sensitivity analyses. In the fourth part the York economic assessment is compared to the EE-S model. The section concludes with a discussion.

6.2.1 Model Structure

A model was developed to estimate the costs and QALYs of SH and CH over a three year period (Figure 6.3). The perspective of the model was the health and social care system of England and Wales. The price year was 2005/06 and the discount rate for cost and health benefits was 3.5%. The patient group was assumed to be aged between 46 and 65 and requiring surgery for haemorrhoidal symptoms. This is the most common age category in which people are affected by haemorrhoidal disease.[9]

Figure 6.3: Structure of the York model



The three year time horizon was chosen because, based on clinical advice, serious complications of surgery such as incontinence may have long term consequences. Futhermore, it is possible for symptoms to recur after one year. However, based on clinical advice, it is likely that further prolapses that occur after three years are new haemorrhoids rather than recurrence.

The structure of the model in Figure 6.3 is a decision tree. Patients undergo either SH or CH and have a six week recovery period, based on clinical opinion that most wounds would heal within this time. It was assumed that peri and post-operative pain, or complications, do not affect future prognosis or costs. A distinction is made in the model between complications and recurrent symptoms. They arise from distinct processes. Complications are a technical failure of surgery, which represents the safety of the technology, whereas control of symptoms represents the effectiveness of the technology. Section 5.2.2.9 identified the complications of surgery as incontinence, urgency, troublesome skin tags, anal stenosis, anastomatic stricture and fistula and fissure haemorrhoidal thrombosis, and the symptoms of treatment failure as prolapse, bleeding, itching and persistent pain. In practice, there may be some patients whose wounds have not healed by 6 weeks and in whom late bleeding or pain may be a complication of surgery; however, clinical advice was that the majority of wounds would have healed by this time. Seven mutually exclusive and exhaustive health states were identified:

(i) no symptoms or complications
(ii) mild symptoms
(iii) moderate symptoms
(iv) severe symptoms
(v) mild complications not requiring reinterventions
(vi) complications requiring reinterventions, and
(vii) serious complications for which no reintervention is feasible.

If symptoms of haemorrhoids recur, patients typically start with conservative management such as dietary advice or mild laxatives, and progressed through increasingly more intensive procedures in cases where symptoms were not satisfactorily controlled.[108] Symptoms of haemorrhoid were classified as: mild, requiring no further reintervention; moderate requiring RBL or sclerotherapy; or severe requiring SH or CH. This classification assumes that there is no censoring in the studies; that is, no further interventions occur after the end of the study that are not recorded by the trial authors.

The complications of surgery were also classified in order of severity as: requiring no further reintervention, requiring reintervention (i.e. dilation for stenosis, procedures

for fistula or excision of skin tag); or serious with no available intervention (i.e. urgency or incontinence persisting at one year).

It was assumed that if RBL or sclerotherapy did not resolve recurrence of symptoms then patients would have progressed to re-surgery by the end of the model (three years). Clinical opinion was that very few patients would fail re-surgery, so this outcome was not included in the model. After their reintervention patients returned to the utility of patients without symptoms or complications, and were not at risk of further adverse events. Patients with mild symptoms and no further reinterventions experienced a modest but sustained loss of utility for the remainder of the time period of the economic model. It was assumed that urgency or incontinence persisting at one year had a serious long term effect on quality of life, but that further reinterventions were not feasible.

Selection of base-case assumptions

Table 6.9 shows a summary of the assumptions used for the base-case for the York group's model, and the reasons why these were chosen. Table 6.10 shows the mean values and standard errors of the parameters used in the base-case. Detailed descriptions of the methods used to estimate each parameter are explained in subsequent sections of this report. Although in the judgement of the York group the base-case represents the most likely scenario, for some of these parameter values there is considerable uncertainty about the methods and data used. Alternative scenarios are therefore explored in a series of sensitivity analyses.

Table 6.9: Summary of base-case assumptions and rationales

Parameter	Assumption	Reason
Method of estimation and extrapolation of VAS pain score in the recovery period	Average reduction in pain from CH to SH estimated by meta-regression of 10 RCTs	Uses all the available RCT data
Source of SF-36 data in the recovery period	HODaR data represent average SF-36 during the recovery period after CH. Assume a given % reduction in the pain score of SH compared with CH corresponds with the same % improvement in SF-36BP dimension, with other dimensions unchanged	HODaR data are a validated source of SF-36 data post surgery. No data were found linking pain score with SF-36 dimensions
Method of valuation of utility in early post-operative period	SF-36 mapped to utility using a matching algorithm (Kind *et al*)	Avoid having to make parametric assumptions about the relationship between SF-36 dimensions and utility
Duration of the recovery period	6 weeks	Expert opinion that most patients wounds would heal within this time period
Time horizon of model	3 years	Serious complications may have long term consequences. Mild symptoms may persist. Recurrence may occur after the first year
Period over which patients are at risk of recurrence of symptoms	1 year	No data found on incidence of symptoms after the first year, though there is clinical opinion that recurrence is possible after the first year. Explored as sensitivity analysis.
Health states used in the model	No symptoms; Symptoms: Mild, moderate + severe; Complications: non-serious and serious.	Clinical opinion that these states represent the important outcomes for resource use and health during follow-up
Probability of symptoms, complications and reinterventions	Meta-analysis of 16 RCTs	Uses all the available RCT data in a single model
Sources of SF-36 data health states during follow-up	No symptoms: Population norm SF-36. Severe symptoms and complications: Weighted av of pre-surgery SF-36 of 3 studies (Hasse CH and SH arms, Temple)[73, 109]. Utility of moderate symptoms 60% of difference between severe and no symptom. Utility of mild 33% of difference between moderate and no symptoms	No data found for utility of mild or moderate symptoms, though logically should be ordered. Explored as sensitivity analysis
Valuation of utility of health states during follow-up	SF-36 mapped to utility using a matching algorithm (Kind *et al*)[111]	Avoid having to make parametric assumptions about the relationship between SF-36 dimensions and utility
Source of resource use in hospital of the primary procedure	Length of stay: meta-analysis of 9 RCTs. Operating time: meta-analysis of 11 RCTs	Uses all the available RCT data
Time to development of symptoms and to reintervention	Surgery to recurrence: 44 days. Recurrence to outpatient: 138 days. Outpatient to re-surgery: 139 days	Clinical opinion that a) patients with recurrence usually try conservative therapy before surgery and b) waiting time in the NHS is an important consideration
Failure of reintervention	Patients who have recurrence of moderate or severe symptoms will ultimately have a successful reintervention	The model assumes that patients with re-surgery will have previously tried a sequence of more conservative therapies. Clinical opinion is that failure of patients who ultimately have re-surgery is very rare.

Table 6.10: Mean and standard errors of parameters used in the base-case of the model

Parameter	CH Mean (SE)	SH Mean (SE)	Sources
Recovery period 6 weeks			
Utility during the recovery period	0.758 (0.180)	0.767 (0.180)	Meta-analysis of pain scores; Currie[110]; Kind[111](a)
Time in operating theatre (mins)	29.2 (-)	15.5 (0.35)	Meta-analysis (b)
Length of stay in hospital (days)	2.66 (-)	1.43 (0.036)	Meta-analysis (b)
Cost per day in hospital	£256 (£75)	£256 (£75)	NHS 05/06[63]
Cost of staple gun per patient	-	£437	Manufacturer
Total hospital cost (mean)	923 (c)	931 (c)	
Long term post 6 weeks			
Probability of complication	0.024 (0.015)	0.017 (0.015)	Meta-analysis (b)
Probability of recurrent symptom	0.055 (0.026)	0.125 (0.026)	Meta-analysis(b)
Utility of severe symptom or complication	0.749 (0.069)	0.749 (0.069)	Meta-analysis (b); Kind[111]
Cost of RBL or sclerotherapy	£140	£140	NHS 05/06[63]
Cost of re-surgery	£923	£931	As cost of primary surgery

(a) meta-analysis described in Chapter 5

(b) meta-analysis described in Chapter 6

(c) distribution is determined by the joint distribution of other (fundamental) parameters

6.2.2 Parameter estimates for inclusion in the York economic model

This section presents the methods and data used to estimate the inputs to the base-case model shown in Table 6.10. The first part describes how utilities and costs were estimated during the recovery period. The second part describes the statistical model used to estimate the probabilities of complications and symptoms occurring after the recovery period, and shows how the utilities and costs of these health states were calculated.

6.2.2.1 The recovery period 0 to 6 weeks after surgery

Utility in the recovery period

Utilities are a means of valuing HRQoL. In order to be able to inform resource allocation decisions across a wide range of conditions, it is necessary to form an overall single morbidity index which reflects the preferences of the general public for that health state. This index can then be multiplied by the expected duration that the patient will spend in the health state to generate a QALY.

No data were found from RCTs which estimated utility during the first weeks post-operatively. Therefore the York model estimated utility during this period by indirect methods. Two types of data were found which relate to HRQoL in the recovery period. First, RCTs recorded mean VAS pain scores after SH and CH for up to 3 weeks. The meta-regression model described in Section 5.2.2.2 predicted VAS pain scores for each treatment group during the recovery period using data from 10 RCTs, and found evidence that SH was associated with 35% less pain than CH, during this period. In itself this does not offer sufficient information for decision-making, because it is not certain how a given reduction in pain should be valued in terms of utility.

Second, studies were found which recorded mean SF-36 dimension summary scores during this period. One RCT (Wilson *et al* 2002) [43] reported SF-36 but this was flawed and excluded from the analysis for reasons given in Section 6.1.2.2. The Health Outcomes Data Repository (HODaR) [110] recorded SF-36 and EQ-5D data for individuals 6 weeks after their inpatient episode at a Cardiff hospital, UK. Data were extracted for all patients who had undergone an excision of haemorrhoid procedure (OPCS4 code H511, H512, H518, H519). Results were found for 53 patients and are summarised in Table 6.11. It was assumed that all patients in the HODaR data had undergone CH.

Table 6.11: SF-36 and EQ-5D scores at 6 weeks[110]

SF-36 summary scores (8 dimensions)	HODaR CH Mean (SD)
Physical functioning	73.79 (46.94)
Role-Physical	50.43 (29.83)
Bodily Pain	**67.63 (26.99)**
General Health	57.76 (25.79)
Vitality	54.22 (31.36)
Social Functioning	74.52 (46.08)
Role-Emotional	66.08 (20.46)
Mental Health	73.75 (20.46)
EQ-5D index reported by HODaR	0.79 (0.26)

The York model combined data from VAS pain scores and SF-36 to estimate utility during the 6 week recovery period by indirect methods using a number of steps (Table 6.12). First, the SF-36 data were adjusted to estimate the values that might have been reported if patients had undergone SH. Second, the eight dimensions of the SF-36 for CH, and the adjusted scores for SH, were mapped to utility.

Table 6.12: Summary of the methods used by the EE-S and the York model base-case to estimate utility during the early post-operative period

Method	Estimate VAS	Estimate SF-36 at 6 weeks	Map VAS pain to SF-36	Change in other dimensions of the SF-36	Map SF-36 to utility
EE-S Model	1 RCT recording VAS every day for 3 weeks after SH and CH, extrapolated over 6 weeks (Van de Stadt[78])	1 RCT recording 4 of the 8 dimensions of the SF-36 at 6 weeks after SH and CH (Wilson[43])	Assume SF-36BP would have changed over 6 weeks according to a mapping between VAS and SF-36 BP (linear on a log-scale)	SF-36 Role physical score is 90 after SH and 95 after CH (Wilson[43])	Linear regression using dataset from a general practice (Brazier[102])
York model	Meta-regression to estimate proportionate treatment effect of SH (10 RCTs)	HODaR SF-36 data 6vweeks after surgery (Currie[110] represents average HRQoL during recovery period after CH	Assume 35% less pain on average corresponds with 35% reduction in SF-36BP after SH (on a log-odds scale)	Other dimensions of HODaR data are unchanged	Matching SF-36 dimensions to utility using Health Survey dataset (Kind[111])

To estimate the SF-36 scores after SH, it was assumed that the reduction in pain observed with the VAS scale would have an effect of similar magnitude, on average, on the SF-36 BP dimension. The average SF-36 BP dimension during the recovery period after CH surgery was reported by HODaR as 67/100 (Table 6.11). The statistical analysis of VAS in Section 5.2.2.2 found that SH was associated with 35% less pain (mean log-odds ratio of -0.4317, SE 0.045) than CH. It is not possible simply to change the SF-36 BP score by a given percentage because the SF-36 BP score must be bounded by 0 (worst) and 100 (best). If the mean BP score is thought of as a probability that pain is at a minimum (100), then a score of, say, 67/100 is equivalent to a probability that pain is not at the minimum of 0.33, or an odds of 0.33/0.67 = 0.49. If SH has 35% less pain, this translates to an odds that pain is not at a minimum of 0.49*(1-0.35) = 0.32, or a SF-36 BP score of 1- 0.32/(1+0.32) = 76/100. It was assumed that the other dimensions of the SF-36 were not changed by the decrease in the average BP score in the absence of evidence to the contrary (Table 6.13).

Table 6.13: SF-36 and EQ-5D scores at 6 weeks [110, 111]

SF-36 summary scores (8 dimensions)	HODaR CH mean	Adjusted HODaR SH mean
Physical functioning	73.79	73.79
Role-Physical	50.43	50.43
Bodily Pain	**67.63**	**76.23**
General Health	57.76	57.76
Vitality	54.22	54.22
Social Functioning	74.52	74.52
Role-Emotional	66.08	66.08
Mental Health	73.75	73.75
EQ-5D index reported by HODaR	0.79	N/A
EQ-5D index estimated by Kind *et al*.[111]	0.758 (SD 0.18)	0.770 (SD 0.18)

The eight dimensions of the SF-36 for CH, and the adjusted scores for SH, were then mapped to utility. Individual patient-level data were not available so using the Brazier SF-6D[103] scoring algorithm was not an option. Kind *et al* (2007)[111] have created a new approach to converting SF-36 data to utility data (full conference abstract Appendix 10.9). The Health Survey for England dataset collected SF-36 and EQ-5D for 16,000 adults. For a given set of 8 SF-36 dimensions, the 20 most closely matching individuals in the age range 46 to 65 years were selected on the basis of the root mean square, representing the average distance between the profiles across all dimensions. Mean and standard deviation of utility for that SF-36 score was then calculated by the mean EQ-5D TTO index of these 20 individuals. This method avoids having to make any parametric assumptions about the relationship between utility and the eight SF-36 dimensions which would be necessary in a regression analysis. Table 6.13 shows the estimated mean of the utility scores after CH and SH used in the model. Using the Kind *et al* (2007) approach,[111] the EQ-5D index score for the HODaR based SF-36 score for CH was 0.758 (SD = 0.180) or 0.770 (SD=0.18) for the adjusted HODaR score for SH. Table 6.13 shows a summary of the methods used to estimate utility during the early post-operative period, and a comparison with the methods used by EE-S.

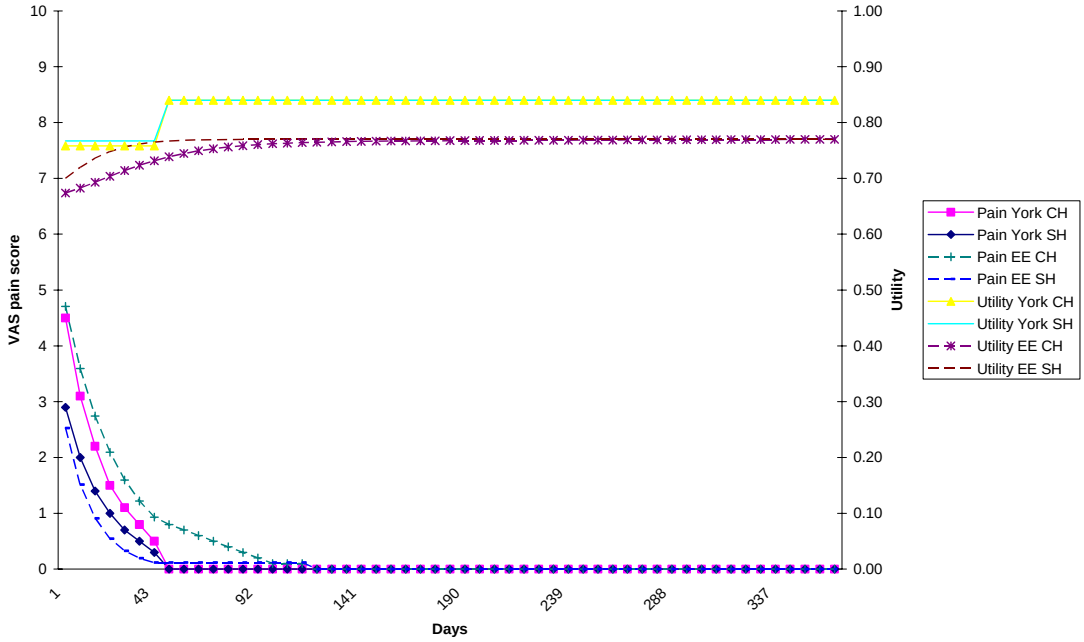
Table 6.14 and Figure 6.4 show predictions of VAS pain scores, SF-36 BP and utility for the York model. The corresponding values estimated by EE-S are shown for comparison. VAS pain and SF-36 data were used to estimate utility, which was an input to the economic models.

Table 6.14: Predictions of VAS pain, SF-36 bodily pain and utility during the first year after successful surgery, for the York and EE-S model scenarios

Days post surgery	VAS pain score				SF-36 BP dimension				Utility (a)			
	York		EE-S		York		EE-S		York		EE-S	
	CH	SH	CH	SH	CH	SH	CH	SH	CH	SH	CH	SH
1	4.5	2.9	4.7	2.5	68	76	8.4	21.9	0.76	0.77	0.67	0.70
8	3.1	2	3.6	1.5	68	76	13.7	34.3	0.76	0.77	0.68	0.72
15	2.2	1.4	2.7	0.9	68	76	19.9	44.8	0.76	0.77	0.69	0.74
22	1.5	1	2.1	0.5	68	76	26.5	52.6	0.76	0.77	0.70	0.75
29	1.1	0.7	1.6	0.3	68	76	33.0	57.9	0.76	0.77	0.71	0.76
36	0.8	0.5	1.2	0.2	68	76	39.0	61.3	0.76	0.77	0.72	0.76
43	0.5	0.3	0.9	0.1	68	76	44.3	63.5	0.76	0.77	0.73	0.76
113	0	0	0.1	0.0	76	76	65.1	66.9	0.84	0.84	0.76	0.77
183	0	0	0.0	0.0	76	76	66.8	66.9	0.84	0.84	0.77	0.77
365	0	0	0.0	0.0	76	76	66.9	66.9	0.84	0.84	0.77	0.77

(a) VAS pain and SF-36 data were used to estimate utility, which was an input to the economic model

Figure 6.4: Predicted VAS pain scores and utility of the early post operative period calculated in the York assessment model and the EE-S model (EE)



An assumption of the calculation of utility in the base-case is that the mean SF-36 dimensions reported by HODaR 6 weeks after surgery represent average HRQoL in the CH group during the recovery period. However, this may underestimate the loss of utility due to pain in the first few days after surgery when pain is most acute and consequently underestimate the relative difference in utility if SH reduces pain in this period. Therefore a sensitivity analysis was carried out using a simple alternative method of valuing pain in the first 2 weeks. Lee (2003)[112] reports the results of a regression of utility against VAS pain scores in a US population with chronic back pain. The study estimated that every increase in pain by one point was associated with a reduced utility of, on average, 0.078 (standard error not reported). This coefficient was multiplied by the predicted VAS pain score each day for the first 2 weeks and the product subtracted from the average utility estimated in the base-case for each treatment. There are many disadvantages with this approach, primarily that there is no reason to assume that the change in utility is linear with changes in VAS pain. Also, it could be argued that chronic back pain is a different type of pain than the acute pain felt by post-operative patients who have undergone haemorrhoidal surgery. Nevertheless this sensitivity analysis shows how results might be affected by a possible alternative method of valuing pain in the early post-operative period.

Resource use and costs in the early post operative period

The resource use and costs of surgery and hospital stay used in the base-case are shown in Table 6.15 at 2005/06 prices.

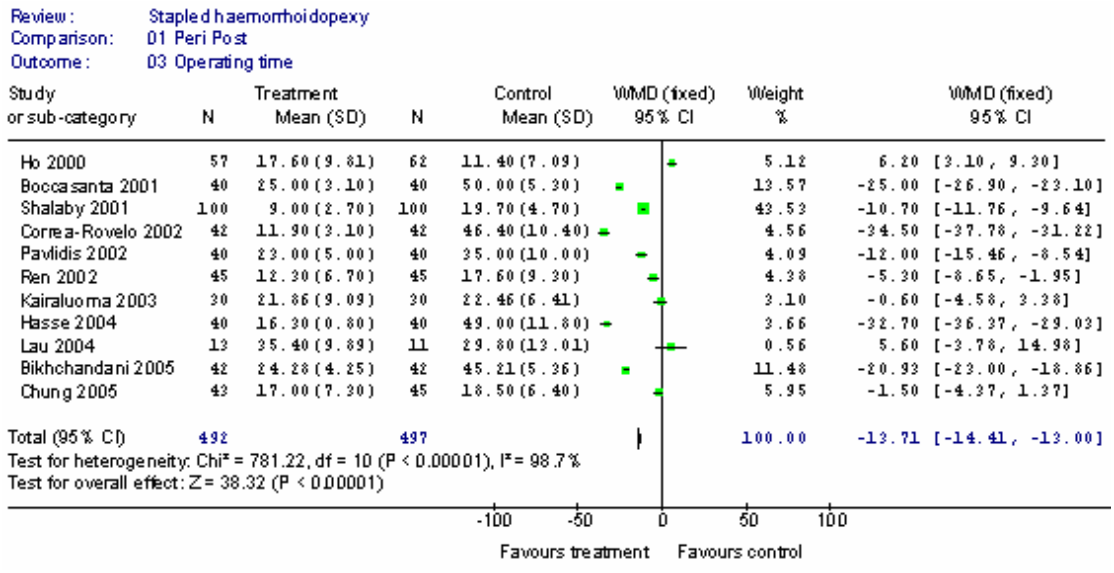
Table 6.15: Resource use and costs of surgery and hospital stay for CH and SH used in the base-case

Cost component	Resource use		Unit	Unit cost £,2005/6	Source of unit cost	Total cost = resource * unit cost £,2005/6	
Primary procedure	CH	SH				CH	SH
Staple gun	NA	1	Per gun	437	Endo-Ethicon	0	437
Theatre	29.21	15.50*	Per minute	8.27	Endo-Ethicon	242	128
Hospital stay	2.66	1.43**	Per day	256***	NHS Reference costs[63]	681	366
Total hospital cost (mean)						923	931

***** standard error for difference in theatre time = 0.35045
****** standard error for difference in length of hospital stay days = 0.036
*** Hospital stay costs, lower IQR = 194, upper IQR = 291

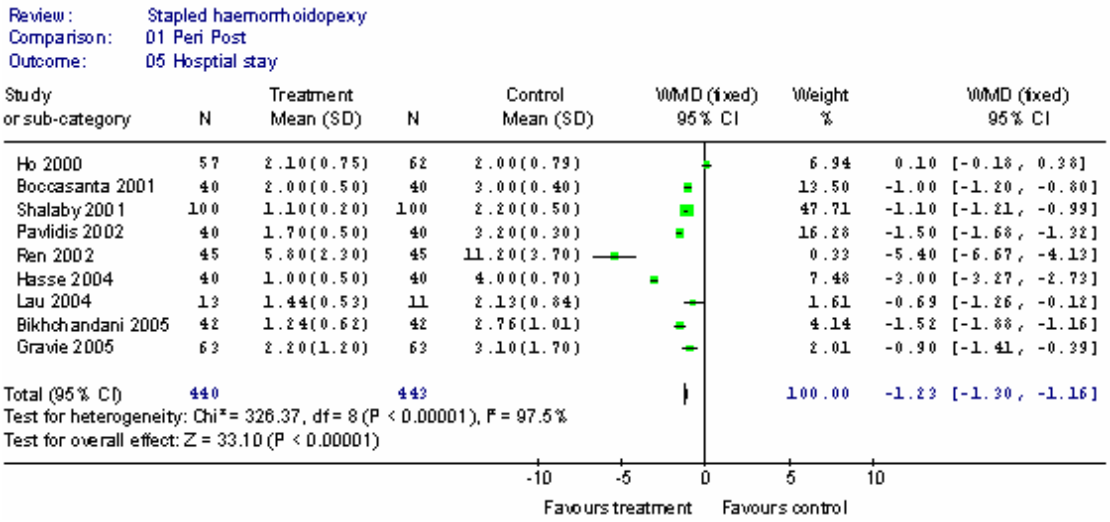
The mean surgery time and mean length of hospital stay were estimated by fixed effects meta-analyses. Section 5.2.2.12 and 5.2.2.13 noted that there was significant heterogeneity between these studies for both outcomes. Nevertheless, the economic evaluation required an estimate of these parameters. Fixed effects analyses were preferred despite the heterogeneity, because this method was found to give lower weight to outlier RCTs than random effects analyses. The meta-analyses assume that length of stay and theatre time are normally distributed. Sensitivity analyses were undertaken in the model using alternative assumptions. Data were included from all RCTs included in the clinical review which reported mean and standard deviation (11 RCTs operating time; 9 RCTs length of stay). Results are shown for operating time in Figure 6.5 and mean length of hospital stay in Figure 6.6. Both analyses demonstrated significant differences between the treatments (operating time WMD -13.7, 95%CI: -14.4 to -13.0, Mean length of stay -1.23; 95% CI: -1.31 to -1.16).

Figure 6.5: Mean difference in number of minutes (mins) operating time



Note: Negative values indicate a shorter mean time in operating theatre following SH

Figure 6.6: Mean difference in duration of hospital stay (days)



Note: Negative values indicate a shorter mean length of stay following SH

Unit costs of time in surgical theatre were taken from the EE-S economic evaluation, who undertook a detailed micro-costing study of the staff typically required for these kinds of surgical procedures. The mean cost of the staple gun and accessories was based on list prices provided by the manufacturer. The hotel cost per day in hospital was based on the mean cost per day of patients whose length of stay following "anus intermediate procedures without complications" exceeds an outlier "trim point" (NHS Reference Costs http://www.dh.gov.uk)[63]. Any costs that did not relate to the year 2005/06 were inflated based on the PSSRU unit costs HCHS pay and prices index[113]. The analyses undertaken in Chapter 5 did not find any major or statistically significant differences in peri-post-operative complications before six weeks and therefore these were not included in the model.

6.2.2.2 The medium and longer term (more than 6 weeks after surgery)

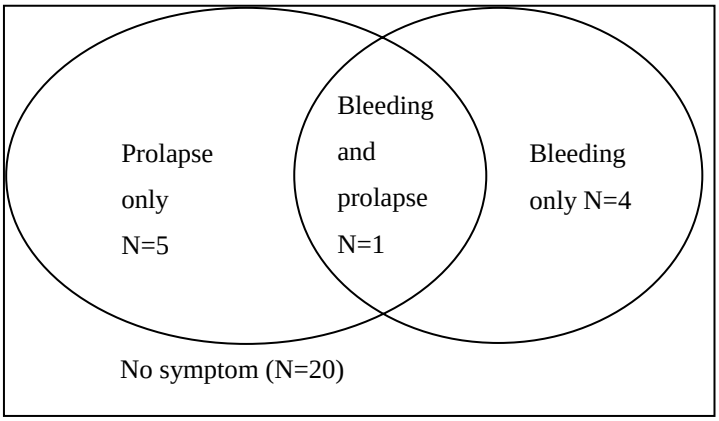
Chapter 5 identified the complications of surgery as incontinence, urgency, haemorrhoidal thrombosis, fissure, stenosis and fistula, and the symptoms of treatment failure as prolapse, bleeding, itching and persistent pain. The analyses of Chapter 5 estimated the odds ratios of observing each of these complications and symptoms. However, these estimates cannot be used directly in the economic model because patients can report more than one outcome at the same time as they are not mutually exclusive. Only a few studies identified the number of patients who were free of symptoms and complications. Therefore the probabilities of complications and symptoms to be used in the economic model were estimated in a separate analysis. First, the number of people in each study without any symptoms or complications was estimated. Second, symptoms and complications were classified into sets of mutually exclusive health states, as shown in Figure 6.3. Finally, the probability of each health state was estimated using a statistical model.

Estimating the number of people in each study without symptoms or complications
It was assumed that the categories of symptoms were independent in order to estimate the number of patients reporting symptoms in each trial. For example, if a trial reported that out of 30 people in one arm, 6 reported prolapse (outcome A) and 5 reported bleeding (outcome B), and bleeding and prolapse are independent, then the predicted number of people with one or more symptoms (prolapse and/or bleeding) would be 6 + 5 – 6*5/30 = 10 (Figure 6.7). The predicted number with no symptoms in this example would then be 30 - 10 = 20. It was assumed that the likelihood of experiencing both uncontrolled symptoms and complications was negligible, since complications are relatively rare anyway.

The assumption that symptoms are independent was validated by comparing the predicted against the actual number of symptoms in the ten trials where sufficient data were available (Figure 6.8). Data are shown for the 10 RCTs which reported the number of patients with one or more symptoms and also reported the numbers with each symptom separately. This shows that for most studies, the number of patients with one or more symptoms matches the number predicted by the model. One study (Hasse 2004)[73] was an outlier. This study also seemed to show a discrepancy in the

way symptoms were reported, stating there were 6 patients with prolapse but only 5 with symptoms in one arm. Therefore the trial was excluded from this part of the analysis.

Figure 6.7: Venn diagram to illustrate the assumption of independence

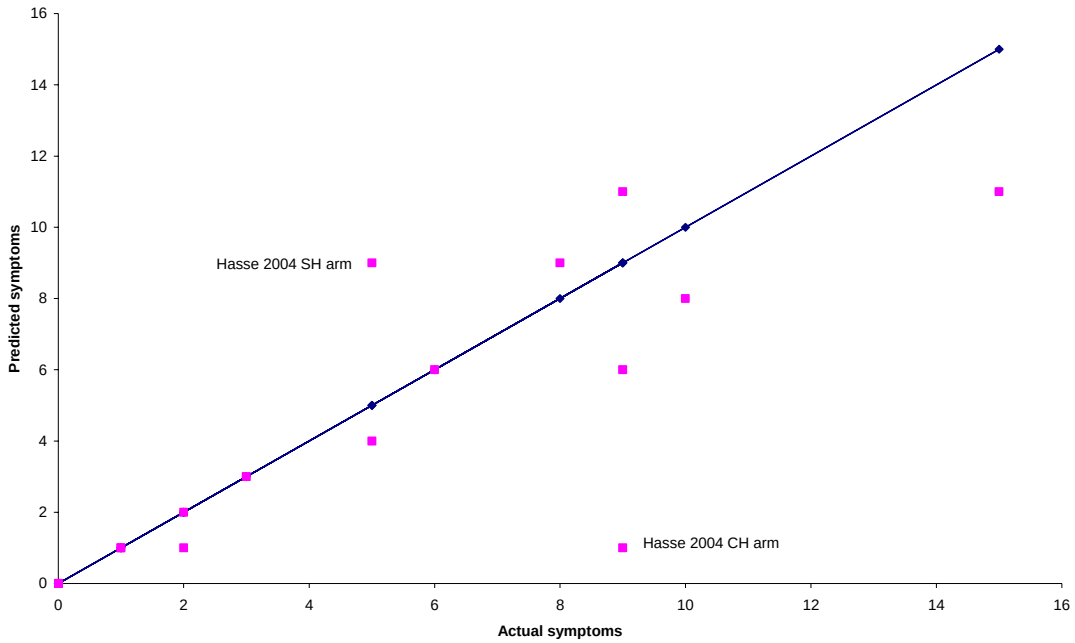


$$P(A \cup B) = P(A) + P(B) - P(A \cap B)$$

If A and B are independent then

$$P(A \cap B) = P(A) * P(B \mid A) = P(A) * P(B)$$

Figure 6.8: Actual number of patients with one or more symptoms at follow-up compared with the predicted number



The probabilities of complications and recurrent symptoms

Figure 6.3 shows the classification of complications and symptoms into mutually exclusive health states. The symptoms are classified as mild (requiring no further reintervention or conservative management), moderate (requiring RBL or sclerotherapy), and severe (requiring re-surgery). Complications are classified as non-serious (dilation for anal stenosis) or serious (incontinence or urgency persisting for at least one year). The number of patients with mild symptoms in each arm of each trial was calculated as follows: The number randomised (n) minus the number without symptoms or complications (calculated using the method above), minus the number with complications, minus the number with severe symptoms, minus the number with moderate symptoms. A statistical analysis was conducted to determine the probabilities of each of the health states at one year. Sixteen of the RCTs included in Chapter 5 provided sufficient data to be included in the statistical model. The reasons for exclusion of RCTs are listed in Table 6.16, and the data to be included in the statistical model Table 6.17.

Table 6.16: Reasons for exclusion of some RCTs or data from the statistical model of complications, symptoms and reinterventions during the follow-up period

Reason for exclusion from statistical model	Number of studies excluded	References
Did not report interventions	2	Ren (2002)[75] Chung (2005)[90]
Did not report symptoms	1	Docherty (2001)[76]
Data not reported in a useable format – discrepancy between individual symptoms and total symptoms	1	Hasse (2004)[73]
Long term follow-up of RCT reported as full manuscript or reported at multiple time points	Included time point nearest to 1 year	Ooi (2002)[69] Palimento (2003)[84] Senagore (2004)[89] Pavlidis (2002)[83]

Table 6.17: The number of patients with no complications or symptoms; complications; or recurrent symptoms, in the medium and long term, in each each treatment group of each study

Study	n	None	Complications		Symptoms			Treat group	Mean Follow-up (Years)
			Non-serious	Serious	Mild	Moderate	Severe		
Basdanis *et al* 2005[82]	50	47	0	0	3	0	0	SH	0.5
	40	40	0	0	0	0	0	CH	
Correa-Rovello 2002[94]	41	29	1	0	11	0	0	SH	0.5
	41	34	1	0	6	0	0	CH	
Cheetham *et al* 2003[77]	14	8	0	0	6	0	0	SH	0.7
	16	12	0	0	4	0	0	CH	
Boccasanta *et al* 2002[85]	40	38	2	0	0	0	0	SH	0.9
	40	35	3	0	2	0	0	CH	
Ortiz *et al* 2005[86]	15	3	0	2	5	0	5	SH	1.0
	16	11	0	3	2	0	0	CH	
Kairaluoma *et al* 2003[80]	30	18	1	3	1	4	3	SH	1.0
	30	28	0	1	0	1	0	CH	
Hetzer *et al* 2002[88]	20	19	0	0	0	1	0	SH	1.0
	20	19	0	0	0	1	0	CH	
Shalaby *et al* 2001[93]	95	92	2	0	0	0	1	SH	1.0
	80	73	5	0	0	0	2	CH	
Ascanelli *et al* 2005[74]	50	45	0	3	0	2	0	SH	1.0
	50	48	1	1	0	0	0	CH	
Sengaore *et al* 2004[89]	59	45	0	3	9	2	0	SH	1.0
	58	44	1	6	4	0	3	CH	
Pavlidis *et al* 2002[83]	40	39	0	1	0	0	0	SH	1.0
	40	39	0	1	0	0	0	CH	
Ortiz *et al* 2002[87]	27	16	0	2	6	0	3	SH	1.3
	28	23	0	4	1	0	0	CH	
Palimento *et al* 2003[84]	37	24	0	0	13	0	0	SH	1.5
	37	25	0	0	12	0	0	CH	
Ho *et al* 2000[61]	27	23	0	0	3	0	1	SH	1.5
	33	31	0	0	0	1	1	CH	
Gravie *et al* 2005[81]	52	48	0	0	4	0	0	SH	2.0
	57	56	0	0	1	0	0	CH	
Van de Stadt *et al* 2005[78]	20	8	0	0	8	0	4	SH	3.8
	20	10	2	0	8	0	0	CH	
Total	1223	1030 (84%)	19 (2%)	30 (2%)	109 (9%)	12 (<1%)	23 (2%)		

n: number randomised

Note: there were very few mild complications and therefore mild and moderate complications have been combined as "non-serious complications" in this table

Note: The definitions of mild, moderate and severe symptom, and serious complications, are given in Figure 6.3

The statistical model estimates the probabilities of each health state at one year in two steps[114]. In the first step, the health states were grouped into three broad categories: no adverse outcome, complications or symptoms. Complications and symptoms arise from distinct processes. Complications are a technical failure of surgery, which represents the safety of the technology, whereas control of symptoms represents the effectiveness of the technology. A multicategorical logit model was used to calculate the probabilities of a complication and of a symptom and the treatment effects (log-odds ratios). Random effects were used to take into account the effect of unobservable characteristics which might be both study and category-specific. For example, for complications this might include variations in the skill of the surgical teams between studies. For symptoms, there might be variations in patient characteristics or lifestyles making recurrence in particular studies more or less likely than average.

At the second step, the symptoms of haemorrhoids were categorised as mild, moderate or severe, conditional on a symptom having occurred. Within this higher level, these categories were considered homogenous; that is, there is a natural ordering of severity of the symptom. The second step was estimated by a cumulative logistic model. The model can also include a treatment effect parameter at this second step; that is, a difference between SH and CH in the mix of severities, given a patient has a recurrence of symptom.

Similarly, at the second step, the complications of surgery were classified as mild, moderate and serious. There were very few mild complications observed in the data, and therefore the categories of mild and moderate complications were combined and the model was only estimated for two categories: serious and non-serious complications.

Further details of the statistical model and the WinBUGS http://www.mrc-bsu.cam.ac.uk/bugs/ code are given in Appendix 10.10

6.2.2.3 Results of the statistical model to determine the probabilities of each health state after the first year

The coefficients of the statistical model are shown in Table 6.18.

Table 6.18: The coefficients of the statistical model to predict the probabilities of symptoms and complications at one year

	Complications Mean (SE)	Symptoms Mean (SE)
Step 1 coefficients		
Intercept (log scale)	-3.641 (0.617)	-2.820 (0.458)
Treatment effect (log odds ratio)	-0.296 (0.305)	0.895 (0.206)
Between-study standard error	1.765 (0.682)	1.611 (0.398)
Step 2 coefficients		
Threshold 1– not serious/serious complication	0.467 (0.294)	
Threshold 2- mild/not mild symptom		1.146 (0.196)
Threshold 3- not severe/severe symptom		-0.688 (0.284)

Step 1 is the probability of observing symptoms or complications or neither. Step 2 is the probability of observing a symptoms or complication of a given severity, should symptoms or complications occur. The positive sign on the treatment effect for symptoms at the first step is evidence that the probability of a symptom occurring is more likely after SH, consistent with the findings of Chapter 5. The treatment effect for complications was negative but the standard error was relatively high, indicating a trend for fewer complications after SH. This parameter did not reach statistical significance at the 5% level, which is consistent with the results for complications of surgery found in Chapter 5. Nevertheless, this treatment effect for complications at the first step was kept in the model and probabilistic sensitivity analysis was carried out in order to include both this trend for fewer complications and reflect the uncertainty around it. There was no evidence for a treatment effect at the second step for either symptoms or complications and this was not included in the model since, a priori, it was not expected that the mix of severities would differ between the treatments, given symptoms have occurred.

The predicted probabilities for the model by randomised treatment group for the first and second steps are shown in Table 6.19. Step 1 is the probability of observing symptoms or complications or neither. Step 2 is the probability of observing a symptoms or complication of a given severity, should symptoms or complications occur.

Table 6.19: The predicted probabilities of the York assessment group's statistical model

	CH Mean (SE)	SH Mean (SE)
Step 1 probabilities		
No adverse outcome	0.921	0.858
Complication	0.024 (0.015)	0.017 (0.015)
Symptom	0.055 (0.026)	0.125 (0.026)
Step 2 probabilities		
Non-serious complication	0.615 (0.068)	0.615 (0.068)
Serious complication	0.385	0.385
Mild symptom	0.759 (0.036)	0.759 (0.036)
Moderate symptom	0.161 (0.030)	0.161 (0.030)
Severe symptom	0.080	0.080

N/R not recorded N/A not included in the model. SE standard error

Utilities of health states in the long term

The utility of patients with severe uncontrolled symptoms was assumed to be the same as that reported on average before a haemorrhoid surgical procedure. A literature review was undertaken to identify studies which reported HRQoL for patients either before a haemorrhoid procedure or with uncontrolled severe symptoms, including both randomised and observational study designs. Wilson e al (2002) excluded because it did not report all the dimensions of the SF-36.[43] HODaR data were not suitable because it was conducted post-operatively.[110] The Narbuts study reported data at the same time point in two tables which gave different values.[115] Table 6.20 shows the results of Hasse (2004)[73] and Temple, (1995)[109]

The SF-36 measures HRQoL but does not estimate a preference-based utility suitable for use in economic evaluation. Patient-level data were not available therefore the Brazier *et al*.(2002) [103] SF-6D algorithm could not be used. Utility values were estimated from SF-36 mean summary scores for each of the studies in Table 6.20 using an algorithm developed by Kind *et al* (2007)[111](Appendix 10.9). The expected

utility of patients with severe symptoms is taken to be the weighted mean of the three data (Hasse 2004 CH and SH arms[73]; and Temple 1995[109] CH), using the reciprocal of the variance as weights. The utility of patients with no adverse outcomes or complications was assumed to be the population norm SF-36[109] valued as utility using the same algorithm. Table 6.21 shows the utility value used in the model, which are shown as decrements from the population norm utility.

Table 6.20: Mean utility of patients with haemorrhoid symptoms before surgery reported by studies identified by a review of the literature

SF-36 component	Temple[109] CH	Hasse[73] CH	Hasse[73] SH
Source country	**US**	**Germany**	**Germany**
Physical functioning	67	65	65
Role-Physical	40	65	65
Bodily Pain	59	65	62
General Health	62	58	50
Vitality	54	62	62
Social Functioning	59	62	58
Role-Emotional	67	69	65
Mental Health	67	73	73
Utility EQ-5D (P Kind algorithm)	0.744	0.755	0.759
Standard deviation	0.169	0.108	0.104
Weighted mean utility of 3 data		0.749 (SE 0.069)	

No data were found to estimate the utility of patients with mild outcomes or moderate outcomes. However, the utility of patients with moderate outcomes should be between severe and mild, and for mild outcomes utility should be between moderate and no symptom. Sensitivity analyses were used to evaluate different assumptions about the utility of moderate and mild symptoms, relative to severe symptoms and no symptoms.

Table 6.21: Utility values for health states in the long term follow-up period used in the York model

	Base-case Mean (SD)
Utility with no symptoms – population norm SF-36 [109] scored using Kind algorithm [111]	0.842 (0.128)
Severe symptoms and serious complications - weighted mean [73, 109]	0.749 (0.069)
Utility decrements from no symptoms	
Severe symptoms and serious complications	0.09 (a)
Moderate (assumed 60% of difference between severe and no symptom)	0.055 (a)
Mild (assumed 33% of the difference between moderate and no symptom)	0.018 (a)

(a) The distributions of the utility decrements compared to no symptoms are derived from the joint distributions of other (fundamental) parameters

Resource use and cost in the medium and long term

The York model used unit costs for a procedure undertaken during an outpatient visit (mean £149) to estimate the cost of RBL or sclerotherapy. [63]

Cost-effectiveness analysis

Standard decision rules were used to assess the most cost effective technology.[100] Mean costs and QALYs were calculated for each treatment option. If on average SH has greater cost and equal or lower QALYs then it is dominated by CH. If SH costs more and has greater QALYs, then SH will be cost effective if the ICER (incremental difference in mean costs divided by incremental difference in mean QALYs) is less than the threshold cost per additional health benefit. If SH is less costly and has less QALYs, then SH will be cost-effective if the ICER is greater than the threshold cost per QALY lost. A probabilistic sensitivity analysis was undertaken using the base-case model. Each parameter was assigned a distribution (Table 6.22) and cost-effectiveness results associated with simultaneously selecting random values from those distributions are recorded in a Monte-Carlo simulation of the model.

Table 6.22: Probability distributions assigned to parameters used in the base-case

Parameters	Distribution type	Mean (SD)	Source
Treatment effect for VAS pain score in the first 6 weeks (log scale)	Normal	-0.4317 (0.045)	Meta-analysis
Utility values			
Utility of CH procedure in the first 6 weeks (a)	Gamma	0.758 (0. 180)	Currie[110] Kind [111]
Utility after severe recurrence of symptom (a)	Gamma	0.749 (0. 069)	Temple[109] Hasse[73] Kind[111]
Utility without symptoms (a)	Gamma	0.842 (0. 128)	Temple[109] Kind [111]
Coefficients of model of probability of complications or recurrence of symptoms (log scale)			
Threshold 1	Normal	0.467 (0. 294)	Meta-analysis
Threshold 2	Normal	1.146 (0. 196)	
Threshold 3	Normal	-0.688 (0. 284)	
Treat effect symptom	Normal	-0.296 (0. 305)	
Treat effect complication	Normal	0.895 (0. 206)	
Intercept symptom	Normal	-3.641 (0. 617)	
Intercept complication	Normal	-2.820 (0. 458)	
Resource use			
Difference in minutes in operating theatre	Normal	-13.700 (0. 350)	Meta-analysis
Difference in days in hospital	Normal	-1.232 (0. 036)	Meta-analysis
Cost per day in hospital £	Gamma	256 (75)	NHS[63]

Note: The pdf of the gamma distribution is $f(x \mid \alpha, \beta) = \frac{1}{\beta^{\alpha}\Gamma(\alpha)} x^{\alpha-1} \exp(-x/\beta)$ with $\alpha = E[x]^2 / Var(x)$ and $\beta = Var(x) / E(x)$. The minimum value of the gamma distribution is 0 and the maximum is Inf therefore utility values were modelled as decrements from full health

6.2.3 Results of the York Economic Assessment

6.2.3.1 Base-case analysis

Figures 6.9 and 6.10 show the calculations made using the decision tree to estimate costs and QALYs for SH and CH respectively.

Figure 6.9: Calculations made to estimate costs and QALYs using the decision tree for CH

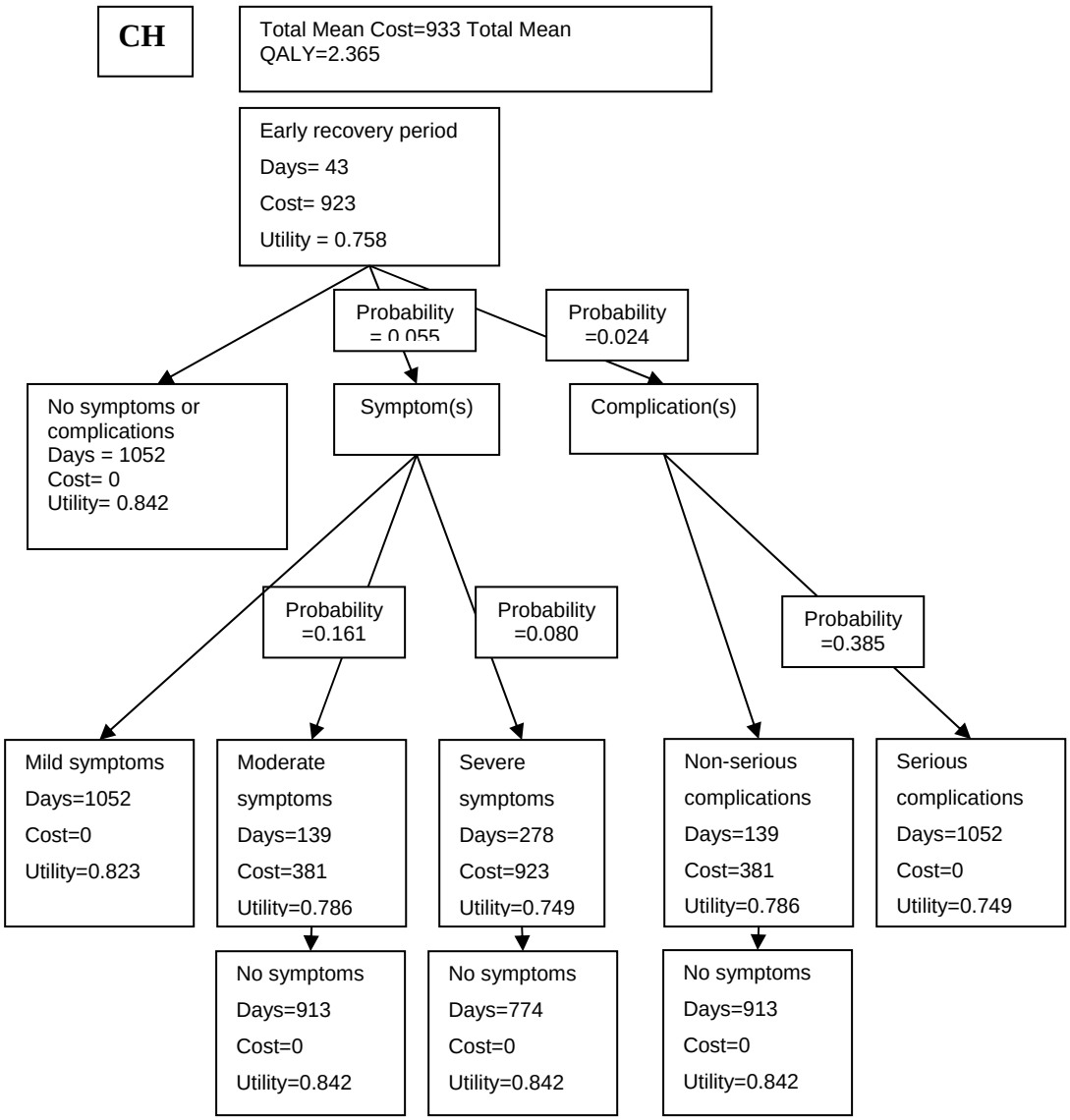


Figure 6.10: Calculations made to estimate costs and QALYs using the decision tree for SH

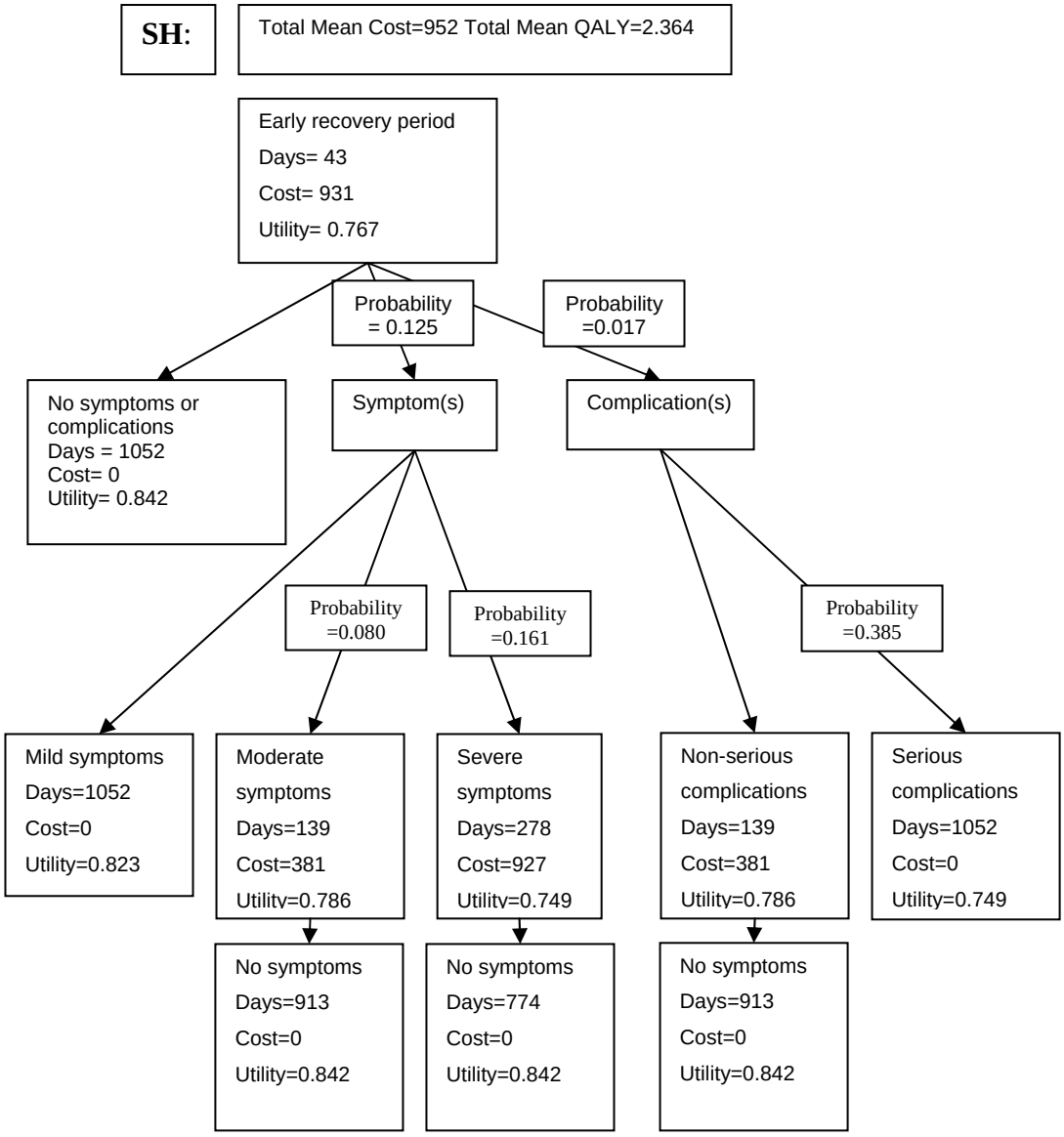


Table 6.23 shows the mean costs and QALYs of the base-case. In this scenario on average the difference in costs between the procedures was £19 and the difference in QALY was -0.001 over 3 years. CH dominates SH on average, but the difference in both cost and QALYs are very small.

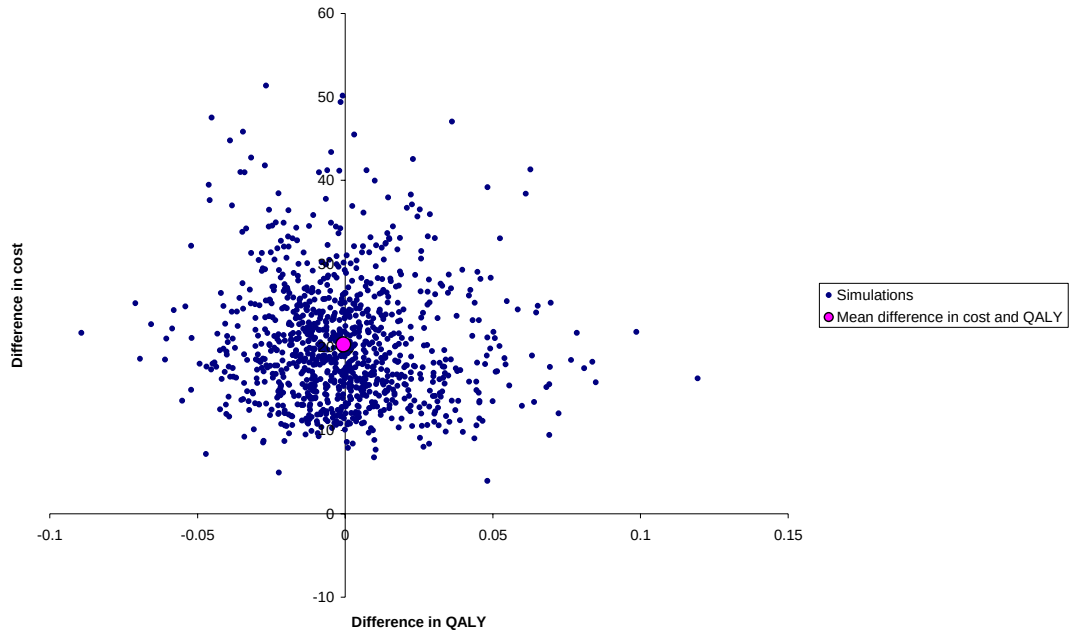
Table 6.23: Mean costs and QALYs calculated by the base-case of the York economic assessment

	CH	SH	Difference (95% CI)
Cost £	933	952	19 (15, 24)
QALY	2.366	2.364	-0.0014 (-0.0150, 0.0120)
ICER			CH dominates SH

95% confidence intervals are calculated using probabilistic sensitivity analysis

Figure 6.11 illustrates the joint distribution of incremental mean costs and incremental mean QALYs calculated using 1000 simulations in a probabilistic sensitivity analysis.

Figure 6.11: Cost-effectiveness plane based on a probabilistic sensitivity analysis using 1,000 simulations



6.2.3.2 Sensitivity analyses

There are considerable uncertainties over several of the model parameters, and results are shown as a set of scenarios. Table 6.24 describes and compares the assumptions used for each scenario and Table 6.25 shows the results for the base-case (scenario 2.0) and a set of univariate analyses (2.1 to 2.6).

Scenario 2.1 shows the effect of shorter waiting times (leaving time to recurrence unchanged); there is little difference compared with the base-case. Scenario 2.2 uses the method developed by the EE-S to value utility, and this shows a gain in QALYs for SH and SH is on average cost-effective at a threshold of £30,000 per QALY. The QALY gain is achieved mainly because the method values reductions in pain more highly during the recovery period. Assuming that recurrence of symptoms can appear in the second or third year and the probability is greater after SH, this increases the difference in QALYs between SH and CH (Scenario 2.3). Increasing the cost per day in hospital by 15% makes SH less costly than CH; cost-effective at a threshold of £30,000 per QALY lost (Scenario 2.4). Assuming that the length of time in theatre should be estimated by the RCT with the largest difference also makes SH less costly than CH overall; cost effective at a threshold of £30,000 per QALY lost (Scenario 2.5). Reducing the time horizon of the model (Scenario 2.6) assumes that there are no differences in recurrence rates after 1 year and that untreated complications and symptoms have no further effect on quality of life. Changing this assumption alone does not materially affect the results compared to the base-case. Using an alternative method to value utility during the first 2 weeks when pain may be greatest is more favourable to SH than the base-case but results are not cost-effective at a threshold of £30,000 per QALY.

Table 6.24: Description and comparison of the sensitivity analyses using the York economic model

	Method of estimation and extrapolation of VAS pain score	Method of valuation of utility in early post-operative period	Time horizon of model	Period over which patients are at risk of recurrence of symptoms	Health states	Sources of health data	Valuation of utility of health states	Source of resource use in hospital of the primary procedure	Time to development of symptoms and to reintervention	Failure of reintervention
2.0 York team Base-case	Average reduction in pain from CH to SH estimated by meta-regression of 10 RCTs	SF-36 mapped non-linearly to utility (P Kind method and dataset)	3 years	1 year	No symptoms; Symptoms: Mild, moderate + severe; Complications: non-serious and serious	No symptoms: Population norm SF-36. Severe symptoms and complications: Weighted av of pre-surgery SF-36 of 3 studies (Hasse, Temple). Utility of no symptoms > mild >moderate > severe	SF-36 mapped non-linearly to utility (P Kind method and dataset)	LOS: meta-analysis of 9 RCTs. Operating time: meta-analysis of 11 RCTs	Surgery to recurrence: 43 days. Recurrence to outpatient: 138 days. Outpatient to re-surgery: 139 days	All patients with recurrent symptoms are eventually treated successfully
2.1 2.0+Shorter waits	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	Surgery to recurrence: 43 days. Recurrence to outpatient: 30 days. Outpatient to re-surgery: 30 days	As 2.0
2.2 2.0+EE-Ss utility mapping	As 2.0	VAS mapped to SF-36BP (log-linear assumption). Other SF-36 dimensions from 1 study (Wilson). SF-36 mapped linearly to utility (J Brazier coefficients).	As 2.0	As 2.0	As 2.0	No symptoms: SF-36 dimensions after SH from 1 study (Wilson) scores,assuming no pain. Severe symptoms: SF-36 scores before SH from 1 study (Wilson). Utility of no symptoms > mild >moderate > severe	SF-36 dimensions mapped linearly to utility (J Brazier coefficients)	As 2.0	As 2.0	As 2.0

	Method of estimation and extrapolation of VAS pain score	**Method of valuation of utility in early post-operative period**	**Time horizon of model**	**Period over which patients are at risk of recurrence of symptoms**	**Health states**	**Sources of health data**	**Valuation of utility of health states**	**Source of resource use in hospital of the primary procedure**	**Time to development of symptoms and to reintervention**	**Failure of reintervention**
2.3 2.0+recurrence in yr 2&3	As 2.0	As 2.0	As 2.0	Probability of recurrence in year2&3 are half the probability in year 1	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0
2.4 2.0+increase in cost per day	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	15% greater cost per day in hospital	As 2.0	As 2.0
2.5 2.0+greater diff in operating time	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	Theatre time of most optimistic RCT	As 2.0	As 2.0
2.6 2.0+1 year time horizon	As 2.0	As 2.0	1 year	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0
2.8 2.0+alternative utility mapping	As 2.0	Utility in 1st 2 weeks valued using Lee algorithm	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0	As 2.0

Table 6.25: Mean difference in cost and QALY based on the sensitivity analyses

	Cost CH	Cost SH	Cost difference	QALY CH	QALY SH	QALY difference	ICER	Choice at £30k
2.0 York team Base-case	933	952	19	2.366	2.364	-0.001	Dom	CH
2.1 2.0+Shorter waits	933	952	19	2.361	2.36	-0.0009	Dom	CH
2.2 2.0+EE-Ss utility mapping	932	952	19	2.1695	2.171	0.00108	17662	**SH**
2.3 2.0+recurrence in yr 2&3	944	971	27	2.3632	2.36	-0.003	Dom	CH
2.4 2.0+increase in cost per day	1228	1113	-115	2.3656	2.364	-0.0014	83019	**SH**
2.5 2.0+greater diff in operating time	1076	923	-152	2.3656	2.364	-0.0014	110311	**SH**
2.6 2.0+1 year time horizon	932	952	19	0.8084	0.808	-0.0004	Dom	CH
2.8 2.0+alternative utility mapping	933	952	19	2.360	2.360	0.0004	43433	CH

Choice at £30K: The cost effective strategy if the threshold incremental cost-effectiveness ratio were £30,000 per QALY gained or lost. Therefore SH would be more cost effective if:

(a) Mean costs were less than CH and QALYs not worse

(b) Mean costs and QALYs were greater than CH and the ICER <£30,000 or

(c) Mean costs and QALYs were less than CH and the ICER >£30,000

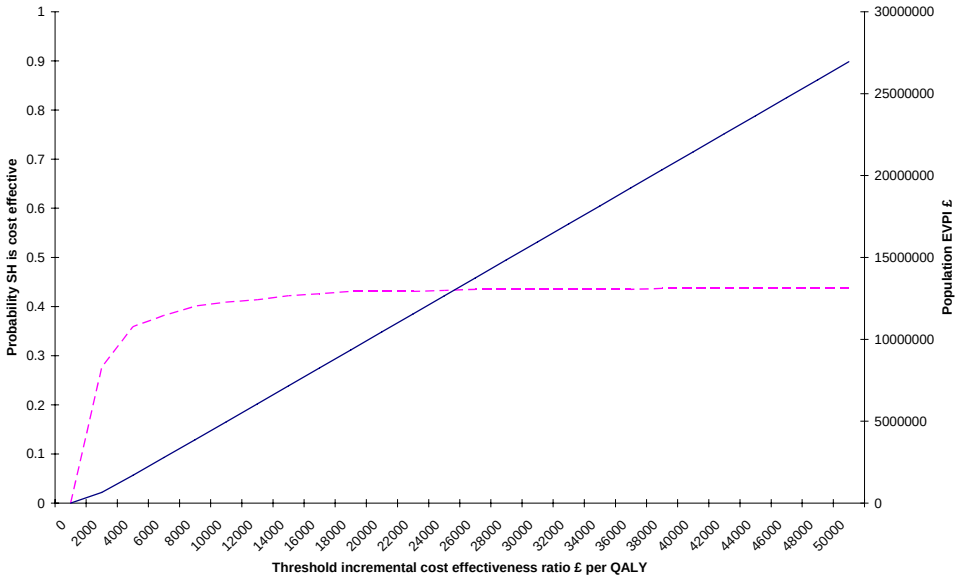
Dom = dominated

6.2.3.3 Probabilistic sensitivity analysis

A probabilistic sensitivity analysis was undertaken using 1000 simulations of the base-case model using the parameter distributions in Table 6.22. Confidence intervals for cost and QALYs are shown in Table 6.23 and the joint distribution of incremental costs and QALYs is shown in Figure 6.9. Figure 6.12 shows the probability that SH is cost-effective for a range of values of the threshold ICER. This shows that SH is cost-effective in 45% of the simulations if the willingness to pay for additional QALYs is £30,000. Figure 6.12 also shows the expected value of perfect information (EVPI) for a range of values of the threshold ICER, assuming an 8 year lifetime for the technology and an incidence of 8,000 patients per year who might benefit from either SH or CH. If the threshold is £30,000 per QALY then the population EVPI is about £16 million, indicating the maximum the health system would be willing to pay for perfect information, assuming the base-case model. However, the base-case model may underestimate the amount of uncertainty around the utility values since not all parameters in the model have been assigned an appropriate probability

distribution. For example, the model assumes that a 35% reduction in pain in the recovery period maps to an exactly 35% reduction in the SF-36BP score with no effect on the other dimensions of the SF-36.

Figure 6.12: Probability that SH is cost effective for a range of values of the threshold ICER (dashed line) and the expected value of perfect information (solid line)



6.2.4 Comparison of the EE-S model and the York model

This section compares the methods and data used by EE-S and the York model, and then shows how these differences affect the estimates of costs and QALYs in each model.

Table 6.26 summarises the differences in modelling methods used by EE-S with those used in the York economic assessment. Similarities in modelling methods between the models are omitted.

6.2.4.1 Utility scores in peri-post operative period

The EE-S model extrapolated RCT data to predict a considerable difference in utility arising from the difference in pain during the recovery period for about 120 days after

surgery. The model covered a one year timeframe and it was assumed that baseline pain diminished exponentially over this period. A year long time horizon was assumed on the basis that little evidence was found on any difference in treatment effects for SH and CH beyond one year. In addition, it was argued that beyond one year, the effect of any recurrent prolapse would dissipate and that any prolapse beyond that time was likely to be a new rather than a recurrent prolapse.

For the York model, the initial recovery period was estimated to continue up to around six weeks. VAS pain scores were only available up to 21 days (3 weeks).[78] A Bayesian meta-regression was undertaken which included all the VAS pain data for which mean scores and a measure of variance were available for SH and CH. It predicted that at three weeks VAS pain scores were less than 0.5 across each arm. The model assumed the pain score after SH was a constant proportion of the score after CH at all time points. These data, together with the early post-operative SF-36 data were used to calculate utilities up to six weeks post-operatively. The final time horizon of the York model was three years. Clinical advice suggested that there is a probability that symptoms can develop more than one year after surgery, and that this may differ between treatment groups. However, there were no published data about the long term recurrence after one year in those patients who did not have a recurrent prolapse at one year.

Table 6.26: Comparison of the modelling approaches used in the EE-S model and the York model

	Parameter	EE-S model	York base-case model
Early post operative period			
1	Duration of differences in post-operative utility across SH and CH arms	Up to 120 days	42 days
2	VAS pain score	Estimated from single study [78] Baseline pain diminished exponentially over 1 year	Expected VAS pain score estimated from a meta-regression of mean VAS, treatment group and time
3	Estimate SF-36 at 6 weeks post surgery	One RCT to estimate SF-36 after SH and CH [43]	HODaR data represent average SF-36 during the recovery period after CH. Assume pain after SH is reduced by the same magnitude as the VAS pain score. Other SF-36 dimensions unchanged
4	Assumptions about how SF-36 might have changed between 0 and 42 days	SF-36 bodily pain dimension as a non-linear function of the VAS score each day after SH and CH. Some other dimensions change a little	HODaR data represents average HRQoL over the whole post operative period after CH Other dimensions do not change
5	SF-36 summary scores map to utility	Cross sectional survey of people registered with a GP practice in Sheffield (Brazier dataset) Survey recorded SF-36 scores. Used dataset to estimate association between mean SF-36 dimensions (BP, PF, RF and GH) and SF-6D index	Matching of SF-36 summary scores to patients in Health Survey for England dataset (Kind *et al* [111])
6	Length of time in operating theatre	Meta-analysis of 6 RCTs	Meta-analysis of 11 RCTs
Medium and long term			
7	Length of stay	Expected proportion of day cases plus expected length of stay for patients who are not day cases	Meta-analysis of overall length of stay from 9 RCTs
8	Symptoms considered	Mild recurrence of prolapse Severe recurrence of prolapse	Mild symptoms Moderate symptoms Severe symptoms
9	Long term complications considered	None	Non serious complications Serious complications
10	Data used to estimate probability of recurrence of symptoms in first year	Subgroups of RCTs of patients with grade 3 at baseline	All RCTs
11	Statistical model of probability of long term success	Meta-analysis	Meta analysis

	Parameter	EE-S model	York base-case model
Medium and long term continued			
12	Treatments considered, given recurrence of symptoms	Self-treatment using conservative strategies Surgery	Self-treatment using conservative strategies Surgery Outpatient treatments
13	Statistical model of probability of intervention(s) given failure of initial surgery	Meta-analysis of proportion of re-surgery for patients with recurrent prolapse Include treatment effect (recurrence of symptoms more likely to be severe after SH)	Meta-analysis of treatments given failure No evidence found that the mix of severities differs by randomised treatment
14	Type of re-surgery	Repeat of same primary surgery	Expert opinion 50-50% following primary SH 100% CH following primary CH
15	Time from surgery to recurrence of symptom	120 days	43 days
16	Time from recurrence to re-surgery if severe	10 days	276 days
17	Time from recurrence to reintervention in outpatients if moderate	Not considered in model	138 days
18	Overall time horizon of model	1 year	3 years
19	Probability reintervention is successful	Surgery - as after primary surgery Self treatment - 0%	There is no possibility of second recurrence in this model
20	HRQoL with no symptoms or complications	Based mainly on SF-36 summary scores data from 1 study (Wilson [43]) at 7 weeks with some adjustments and extrapolation to 1 year	Use age-sex matched general population QOL as benchmark Kind *et al* 1999[116]
21	HRQoL with recurrence of severe symptoms (leading to re-surgery)	As symptoms pre-surgery (severe) based on utility valuation of baseline SF-36 scores from 1 study (Wilson [43])	As symptoms pre-surgery (severe) based on utility valuation of baseline SF-36 scores from 2 studies [73, 109]
22	HRQoL with recurrence of medium symptoms (leading to outpatient treatments)	No such health state in this model	Assume utility is 60% of the difference between severe and no symptoms
23	HRQoL with recurrence of mild symptoms (leading to no intervention, conservative medical management)	As symptoms pre-surgery (severe)	Assume utility is 33% of the difference between moderate and no symptoms

To estimate HRQoL in the SH and the CH arm at six weeks post-operatively, EE-S used the four physical health dimensions of the SF-36 from a single study (Wilson 2002).[43] This study included some patients who used a device that required an adaptor to make it suitable for SH, which was not used; the Autosuture arm was excluded from the clinical evaluation (Autosuture STRAM kit: Chapter 5) and so the York model used an alternative data source. The HODaR cohort dataset was used to estimate the SF-36 score for CH. (https://www.crc-limited.co.uk/portal/HODaR.html)

Underlying EE-S's estimates of the SF-36 at 6 weeks post-operatively is an assumption that the SF-36 BP dimension is a non-linear function of the daily VAS scores in the SH and CH arms. At this time the average physical functioning scores differed being 5 points higher (at 95) in the SH arm compared to 90 in the CH arm. Whilst the former score was assumed to remain constant, the score in the CH arm was assumed to increase linearly from 90 at 8 weeks to 95 at 12 months. The other two dimensions (i.e. RP and GH) were assumed to remain constant throughout the duration of the model.

In contrast, for the CH arm in the York model, an average SF-36 score was estimated which was constant across the entire post-operative period. Therefore it was assumed that 35% less pain on average maps to a 35% reduction in SF-36 BP (on a log-odds scale). In the absence of reliable data it was assumed that the scores for the other dimensions did not change.

Since directly measured utilities were not available, SF-36 scores were mapped to utility in the EE-S model using age-matched scores from a cross-sectional dataset of patients registered with a primary care practice in Sheffield.[103] These were used to estimate the association between the four physical health dimension scores and the SF-6D index, utility score. The York model applied the Kind *et al* (2007) approach to translate SF-36 scores to EQ-5D utilities).[111]

6.2.4.2 Outcomes in medium and longer term

In the EE-S model, the only adverse outcome of surgery that was considered was mild or severe symptoms associated with recurrent prolapse. The York model also considered recurrent prolapse and distinguished mild, moderate and severe symptoms. Symptoms included one or more of the following for each patient; prolapse, bleeding, bothersome skin tags, pain, itching and mucus and discharge. Complications included one or more of the following for each patient; anal stenosis, urgency and faecal incontinence.

In the EE-S model, to estimate the probability of recurrence of prolapse (and re-surgery due to prolapse) over the year, results from 13 papers were meta-analysed. The York economic model conducted a meta-analysis using 16 RCTs to estimate the probabilities in the first year of symptoms, complications and their severity, should they occur.

If symptoms (prolapse) did recur, in terms of reinterventions, the EE-S model assumed that either patients self-treated or underwent surgery. The York model also considered non-excisional treatments.

EE-S state that they used a meta-analysis to estimate the proportion of patients with severe symptoms but the source of this data was not clear from the report. The York model assessed the probability of reintervention given treatment failure from a meta-analysis of 16 RCTs. Table 6.27 compares the estimates of the probabilities of complications and recurrence of symptoms calculated by the York model and the EE-S model and the probabilities of reintervention given treatment failure. The mean estimated probability of a symptom estimated in the York model was 0.125 after SH and 0.055 after CH a difference of 0.07. In the EE-S model the probability of a symptom was 0.101 after SH and 0.026 after CH, a difference of 0.075. The York model included a probability of complications but the difference between the treatments was relatively small on average (0.007) and with high uncertainty. Therefore despite the differences in data and methods the models estimated similar results for these parameters. There was a more important difference however in the predicted mix of symptoms. The York model estimated that 76% of symptoms would

be mild on average. The EE-S model predicted that 73% of symptoms would be mild after CH but only 34% after SH.

Table 6.27: The predicted probabilities of the York assessment group's statistical model compared with the EE-S model

	York assessment		EE-S model	
	CH	SH	CH	SH
	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
Probabilities of complication or symptom				
No adverse outcome	0.921	0.858	0.974	0.899
Complication	0.024 (0.015)	0.017 (0.015)	N/A	N/A
Symptom	0.055 (0.026)	0.125 (0.026)	0.026 (N/R)	0.101 (N/A)
Mix of severities given complication or symptom				
Non-serious complication	0.615 (0.068)	0.615 (0.068)	N/A	N/A
Serious complication	0.385	0.385	N/A	N/A
Mild symptom	0.759 (0.036)	0.759 (0.036)	0.73 (N/R)	0.34 (N/A)
Moderate symptom	0.161 (0.030)	0.161 (0.030)	N/A	N/A
Severe symptom	0.080	0.080	0.27 (N/R)	0.66 (N/A)

N/R: Not recorded; N/A: Not included in the model; SE: standard error

Re-surgery in the EE-S model was a repeat of the initial surgery. The clinical evaluation found that it was possible for patients to undergo a second SH procedure if the first was unsuccessful. Following clinical opinion, it was assumed in the base-case that 50% of patients needing re-surgery following SH would undergo a repeat SH. Following initial CH, CH was repeated if re-surgery took place. The time from surgery to recurrence of symptom was four months in the EE-S model and 1.5 months in the York model. The full time horizons of the models were one year and three years for the EE-S and York models, respectively.

The proportion of patients in whom the reintervention was successful was 89.9% in the SH arm and 97.4% in the CH arm in the EE-S model. Based on clinical advice, the York model assumed that the probability of a second recurrent prolapse was very rare and it was not necessary to include this event; all reinterventions were assumed successful.

6.2.4.3 Resource use and cost estimates

As reported in Table 6.19 the York model used the EE-S cost estimates for the staple gun associated with SH and the unit cost of the theatre time in the absence of better available data. EE-S used the weighted average of two HRG codes (F92 and F93 (HRG code F92 - 'Anus - Intermediate Procedures >69' and F93 - 'Anus - Intermediate Procedures <70') from the Admitted Patient Care Tariff database. To calculate the average cost per day's stay excluding the cost of surgery, EE-S used the value '*per day long stay payment (for days exceeding trim point)*'. Both models assumed that the non-surgical hospital costs of a day case were equivalent to the hotel cost of a day on a ward.

The EE-S and the York model differed in the estimate used to measure theatre time. Both used meta-analyses of RCTs but differed in the exclusion and inclusion criteria applied. The EE-S meta-analysis comprised five studies (Bikhchandani 2005[92]; Chung 2005[90]; Pavlidis 2002 [83]; Racalbuto 2004[106]; Shalaby 2001[93]). The York model included the results of all those studies, with the exception of Racalbuto 2004[106] since this study was excluded from the review since SH was undertaken using CDH33: a type of circular stapler produced by EE-S that is not designed to perform a SH. The York model included an additional seven studies.[61, 73, 80, 85, 91] and [75, 93]

The EE-S and the York model differed in the methods and data used to estimate mean length of stay. EE-S calculated the expected proportion of day cases as well as the expected length of stay in patients who received inpatient care, that is, who were not discharged on the same day. The analysis relied upon data from non-randomised studies for estimating the probability that a procedure could be a day case. Results may be confounded if patients differed in characteristics apart from the intervention received. In contrast, the York model used the results of a fixed effects meta-analysis of nine RCTs to calculate the average length of day cases assuming a one day stay is equivalent to day case.[61, 73, 75, 81, 83, 85, 91-93] Two studies [106 105] which were incorporated in the EE-S analysis were excluded from the York meta-analysis since the CDH33 staple gun is not designed for SH.

To estimate the time spent in operating theatre, EE-S used a random effects meta-analysis based on five studies.[83, 90, 92, 93, 106]. The York model used the results of a fixed effect meta-analysis of eleven studies that were identified in the clinical effectiveness review (Chapter 5).Bikhchandani [92], Boccasanta [85], Chung [90], Correa-Rovelo [94], Hasse [73], Ho [61], Kairaluoma [80], Lau [91], Pavlidis [83], Ren [75], Shalaby [93] The results of a random effects model gave greater weight to the outlier study.[75]

6.2.4.4 Impact of these differences on results

This section describes how differences in methods and parameters affect the estimates of costs and QALYs in each model.

Table 6.28 shows a set of scenarios (labelled 1.0 to 1.9) which aim to show the key parameters which differ between the EE-S model and the York group's model. Scenario 1.0 shows the results of the EE-S model as stated in their submission. Other scenarios (1.1 to 1.9) show the effect of changing one or more of the parameters of the EE-Ss model which differed from the York group's model (Table 6.29). Scenarios 1.1 to 1.9 were calculated by using the York model, setting the parameters to take the values of the EE-S model, and then changing these in a set of univariate sensitivity analyses.

EE-S estimated that SH is cost effective at a threshold of £30,000 per QALY, but not at a threshold of £20,000. The single most influential variable in this model is the valuation of utility in the post-operative period. The EE-S model predicts VAS scores using the results of a single study (Van de Stadt).[78] These predictions are valued by first mapping VAS to SF-36BP assuming a log-linear relationship, assuming the other dimensions of the SF-36 are as reported by Wilson[43] and then mapping SF-36 to utility using a linear algorithm based on a dataset of HRQoL in a general population.[103] Utility scores are extrapolated up to one year, and the model predicted a measurable (>=0.01) difference in utility as a result of less post-surgical pain until about 120 days. Scenario 1.1 changes the EE-S model assuming that no measurable difference in utility persists after 43 days, following clinical advice that the recovery period lasts up to 6 weeks following surgery. Changing this assumption of the EE-S model and keeping all others unchanged reduced the mean difference in

Table 6.28: Scenarios (1.1 to 1.9) to show the effect of changing one or more of the parameters of the EE-Ss model which differed from the York group's model (Table 6.24)

	Method of estimation and extrapolation of VAS pain score	Method of valuation of utility in early post-operative period	Time horizon of model	Period over which patients are at risk of recurrence of symptoms	Health states	Sources of health data	Valuation of utility of health states	Source of resource use in hospital of the primary procedure	Time to development of symptoms and to reintervention	Failure of reintervention
1.0 EE-Ss model	1 RCT (Van de Stadt), extrapolated to 1 year. Differences in utility are predicted up to about 120 days	VAS mapped to SF-36BP (log-linear assumption). Other SF-36 dimensions from 1 study (Wilson). SF-36 mapped linearly to utility (J Brazier coefficients).	1 year	1 year	No symptoms/ mild symptoms/ severe symptoms	No symptoms: SF-36 dimensions after SH from 1 study (Wilson) scores,assuming no pain. Severe symptoms: SF-36 scores before SH from 1 study (Wilson). Mild symptoms = Severe	SF-36 dimensions mapped linearly to utility (J Brazier coefficients)	Prob(day case): LOS if not day case: Operating theatre time:meta-analysis (N RCTs)	Surgery to recurrence: 120 days. Recurrence to re-surgery: 10 days	Probability same as failure of primary intervention
1.1 Early post-op period 6 weeks	1 RCT (Van de Stadt), extrapolated to 6 weeks	As 1.0	As 1.0	As 1.0	As 1.0	As 1.0	As 1.0	As 1.0	As 1.0	All reinterventions are successful
1.2 As 1.1 + wait for re-surgery	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	Surgery to recurrence: 120 days. Recurrence to re-surgery: 139 days	As 1.1
1.3 1.1+Meta-analysis of VAS	Meta-regression (10 studies)	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1
1.4 1.1+Non-linear mapping of SF-36 to utility in early post op period	Average reduction in pain from CH to SH estimated by meta-regression	SF-36 mapped non-linearly to utility (P Kind method and dataset)	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1

	Method of estimation and extrapolation of VAS pain score	Method of valuation of utility in early post-operative period	Time horizon of model	Period over which patients are at risk of recurrence of symptoms	Health states	Sources of health data	Valuation of utility of health states	Source of resource use in hospital of the primary procedure	Time to development of symptoms and to reintervention	Failure of reinterventio n
1.5 1.1+Non-linear mapping of SF-36 to utility of health states	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	No symptoms: Population norm. Severe symptoms and complications: Weighted av of pre-surgery SF-36 of 3 studies (Hasse, Temple)	SF-36 mapped non-linearly to utility (P Kind method and dataset)	As 1.1	As 1.1	As 1.1
1.6 1.1+ other Health states	As 1.1	As 1.1	As 1.1	As 1.1	No symptoms; Symptoms: Mild, moderate + severe; Complications : non-serious and serious	Utility of symptoms: None> mild >moderate > severe	As 1.1	As 1.1	Surgery to recurrence: 43 days. Recurrence to outpatient: 138 days. Outpatient to re-surgery: 139 days	As 1.1
1.7 1.6+Non-linear utility mapping	As 1.1	As 1.1	As 1.1	As 1.1	No symptoms; Symptoms: Mild, moderate + severe; Complications : non-serious and serious	No symptoms: Population norm SF-36. Severe symptoms and complications: Weighted av of pre-surgery SF-36 of 3 studies (Hasse, Temple). Utility of no symptoms > mild >moderate > severe	SF-36 mapped non-linearly to utility (P Kind method and dataset)	As 1.1	Surgery to recurrence: 43 days. Recurrence to outpatient: 138 days. Outpatient to re-surgery: 139 days	As 1.1
1.8 1.1+3year time horizon	As 1.1	As 1.1	3 years	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1
1.9 1.1+alternative resource use	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	As 1.1	LOS: meta-analysis of N RCTs. Operating time: meta-analysis of N RCTs	As 1.1	As 1.1

QALYs predicted at one year from 0.008 to 0.003 and the ICER was increased from £23,000 to £50,000, which makes SH not cost effective at a threshold ICER of £30,000 per QALY. However, if length of stay in hospital and time in operating theatre were as estimated by the York model, rather than the EE-S model, then SH would be cost effective at a threshold ICER of £30,000 per QALY gained (Scenario 1.9).

Table 6.29 shows the mean difference in costs and QALYs calculated in each sensitivity analysis. Figure 6.13 shows these results graphically on the cost-effectiveness plane.

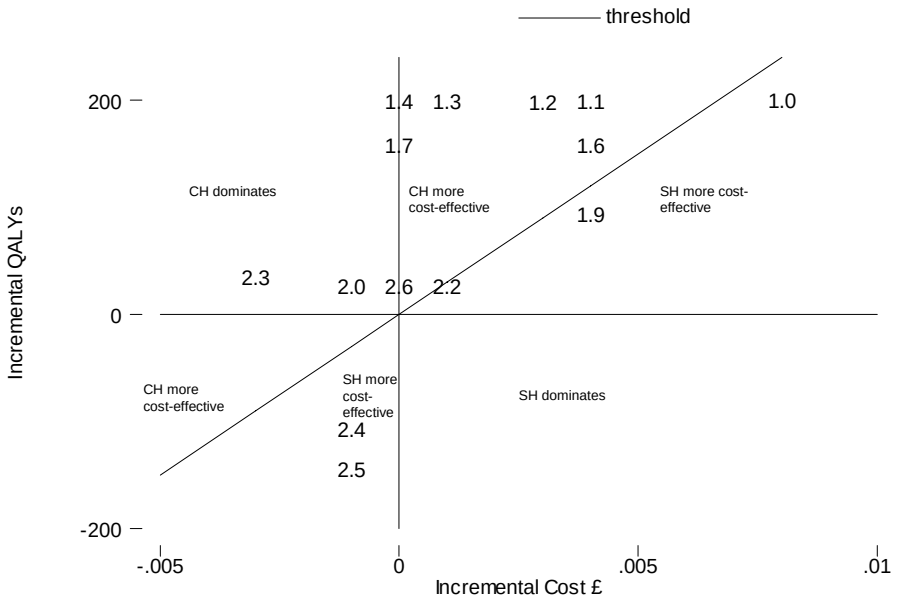
Table 6.29: Mean difference in cost and QALY based on the sensitivity analyses

		Cost CH	Cost SH	Cost difference	QALY CH	QALY SH	QALY difference	ICER	Choice at £30k
2.0	**York team Base-case**	933	952	19	2.366	2.364	-0.001	Dom	CH
2.1	**2.0+Shorter waits**	933	952	19	2.361	2.36	-0.0009	Dom	CH
2.2	**2.0+EE-Ss utility mapping**	932	952	19	2.1695	2.171	0.00108	17662	**SH**
2.3	**2.0+recurrence in yr 2&3**	944	971	27	2.3632	2.36	-0.003	Dom	CH
2.4	**2.0+increase in cost per day**	1228	1113	-115	2.3656	2.364	-0.0014	83019	**SH**
2.5	**2.0+greater diff in operating time**	1076	923	-152	2.3656	2.364	-0.0014	110311	**SH**
2.6	**2.0+1 year time horizon**	932	952	19	0.8084	0.808	-0.0004	Dom	CH
2.8	**2.0+alternative utility mapping**	933	952	19	2.360	2.360	0.0004	43433	CH
1.0	**EE-Ss model**	712	905	193	0.759	0.768	0.008	22931	**SH**
1.1	**Early post-op period 6 weeks**	709	901	192	0.742	0.746	0.004	50018	CH
1.2	**As 1.1 + wait for re-surgery**	709	900	191	0.743	0.747	0.003	60336	CH
1.3	**1.1+Meta-analysis of VAS**	709	901	192	0.743	0.745	0.001	156706	CH
1.4	**1.1+Non-linear mapping of SF-36 to utility in early post op period**	709	901	192	0.749	0.749	0.000	383985	CH
1.5	**1.1+Non-linear mapping of SF-36 to utility of health states**	709	901	192	0.804	0.807	0.003	57105	CH
1.6	**1.1 + other Health states**	710	862	151	0.742	0.746	0.004	37263	CH
1.7	**1.6+Non-linear utility mapping**	710	862	151	0.808	0.807	0.000	Dom	CH
1.8	**1.1+3year time horizon**	709	901	192	2.161	2.164	0.003	65837	CH
1.9	**1.1+alternative resource use**	830	916	86	0.742	0.746	0.004	22415	**SH**

Choice at £30K: The cost effective strategy if the threshold incremental cost-effectiveness ratio were £30,000 per QALY gained or lost. Therefore SH would be more cost effective if (a) Mean costs were less than CH and QALYs not worse (b) Mean costs and QALYs were greater than CH and the ICER < £30,000 or (c) Mean costs and QALYs were less than CH and the ICER > £30,000

Dom=dominated

Figure 6.13: Mean incremental cost and QALYs for each of the scenarios



Note: The line represents a threshold incremental cost-effectiveness ratio of £30,000 per QALY gained or lost. Scenarios below and to the right of the threshold are cost effective in favour of SH

Table 6.30 partitions the incremental costs and benefits according to how they arise in each model. Two scenarios are compared: the base-case of the York assessment (Scenario 2.0 of Table 6.24) and the EE-S model with the recovery period after the primary procedure limited to 6weeks and the assumption that all reinterventions for recurrent prolapse are successful (Scenario 1.1 of Table 6.28). Events in each of the models do not have the same duration. In the York model, patients can experience symptoms immediately after the end of the 6 week recovery period while in the EE-S model, symptoms recur after 4months (43 + 79 days). The York model has an overall time horizon of 3 years (1,095 days) while the EE-S model lasts one year. If severe symptoms recur, the York model assumes that patients will wait about 9 months (277 days) before being eventually resolved by surgical reintervention while the EE-S model assumes a wait of only 10 days.

The York model gives relatively less weight (measured in QALYs) to the difference in pain in the recovery period than the EE-S model. On the other hand, the York model predicts a greater difference in the number of recurrent symptoms, gives those symptoms a greater decrement in utility compared with full health than the EE-S

model, and assumes severe symptoms have a longer duration. In the York model the loss of health due to the greater number of recurrent symptoms after SH is offset slightly by a trend to more complications after CH. In both models, most of the costs are from the primary procedure. The EE-S model predicts a greater difference in the costs of treating reinterventions because, although there are fewer symptoms in total than in the York model, a greater proportion are assumed to be treated by re-surgery in the SH arm.

Table 6.30: Comparing costs & QALYs for SH & CH for each stage of the model

	York economic assessment							EE-S model						
		Costs			QALYs				Costs			QALYs		
	Days	CH	SH	Difference	CH	SH	Difference	Days	CH	SH	Difference	CH	SH	Difference
Primary procedure and 6 wk recovery period	43	919	927	8	0.087	0.088	0.0010	43	704	845	141	0.0806	0.0851	0.0045
All patients free of symptoms in period after recovery	1	0	0	0	0.002	0.002	0	79	0	0	0	0.1648	0.1648	0
Some patients have untreated complications or symptoms & may be waiting for outpatient visit or hospitalisation	138	0	0	0	0.312	0.311	-0.0006	0	0	0	0	0	0	0
Moderate symptoms and minor complications are successfully treated. Some patients continue with untreated mild symptoms or untreatable serious complications, or severe symptoms while waiting for hospitalisation	139	5	6	1	0.310	0.309	-0.0006	10	0	0	0	0.0208	0.0207	-0.0001
Severe symptoms are successfully treated in hospital and patients are in recovery for 6weeks. Some patients continue with mild symptoms or untreatable complications.	43	9	18	10	0.095	0.095	-0.0002	43	5	56	51	0.0891	0.0888	-0.0003
Some patients continue with mild symptoms or untreatable serious complications; all others have no symptoms	730	0	0	0	1.557	1.556	-0.0010	190	0	0	0	0.3870	0.3867	-0.0003
Totals	1095	933	951	19	2.366	2.364	-0.0014	365	709	901	192	0.7422	0.7460	0.0038

6.2.5 Overview of the economic assessment

The results of the York economic assessment do not allow a clear inference that, on average, one procedure is more cost-effective than the other. In the base-case there is only a small mean difference in costs (£19) and QALYs (-0.001) over three years and therefore the ICER is very sensitive to model assumptions. The probabilistic sensitivity analysis suggests that at a threshold ICER between £20,000 and £30,000 SH has a probability of being cost effective of 0.45.

A series of scenario analyses were carried out. The most sensitive assumptions were found to be:

- The length of the recovery period. The York model assumed that this would last a maximum of 6 weeks after which patients without complications or recurrence of symptoms would return to normal health
- The method used to estimate utility in the recovery period. The York model used a method that predicted a smaller difference in utility between SH and CH than the EE-S model
- Estimates of use of hospital resources (length of stay, theatre time, cost per day) in the recovery period. The York model estimated greater differences in costs between SH and CH than the EE-S model based on data from RCTs.

Although the decision problem overall is very sensitive to model assumptions and parameter values, some conclusions can be drawn from the analysis. There is reasonable evidence that SH is a less painful procedure than CH up to 3 weeks after surgery, and that pain recedes in both groups over this period. The probability of complications is low in both groups and differences do not reach statistical significance at the 5% level. Patients offered SH are more likely to experience symptoms during the follow-up period. These findings are consistent with the evidence from Chapter 5. The evidence from RCTs shows SH had a shorter length of stay in hospital and a shorter time in theatre than CH and these resource savings at least partly offset the greater cost of the device. However, these analyses of length of stay and time in surgery were limited by the assumption that these variables were

normally distributed and the heterogeneity between studies reporting these outcomes; furthermore these RCTs may not represent current practice in the NHS in England and Wales.

The parameter that most affects the results, and which is most uncertain, is how differences in pain during the early post-operative period should be valued in terms of utility. No evidence has been found to support this, and consequently the base-case uses a series of modelling assumptions. Arguably the weakest of these assumptions relates to the relationship between pain score measured on a VAS scale and the SF-36 summary scores. The base-case assumes that SF-36 data recorded at 6weeks after surgery represents the average HRQoL after CH during the recovery period, and that SH would have reduced pain but other dimensions of HRQoL would have been unchanged. This approach may underestimate the gain in utility after SH from less pain, especially in the first days after surgery when pain is most acute. Sensitivity analyses were carried out using various other methods to value pain. This analysis has also identified other key parameters which are uncertain, and which have an effect on the decision, as well as utility during the early post-operative period. No good quality data were found to estimate the utility of patients with different degrees of haemorrhoidal symptoms, nor for complications such as long term incontinence. The waiting times for outpatients and surgical procedures can affect the results, depending on the values taken by other parameters of the model, for example, the probabilities that symptoms recur and their severity. The York model assumed that patients would try conservative treatments first and, if re-surgery was required, would be placed on a waiting list. In principle waiting times are under the control of the health care system. Other parameters are uncertain but do not have a marked effect on the overall results, such as the probability of recurrence of symptoms in second or subsequent year. Other parameters might change the decision in certain scenarios, for example if the cost per day in hospital were about 20% higher than the base-case, then SH would be cost saving and cost-effective if the threshold ICER were £30,000 per QALY lost.

The only other economic evaluation in this patient group was the submission by EE-S which concluded that, on average, SH was marginally cost-effective, with an ICER of £22,000. EE-S conducted extensive sensitivity analyses and also found that estimates of the ICER were sensitive to model assumptions. The structure of the EE-S and the York models was broadly similar, though the York model included a wider definition of symptoms, complications of surgery, included both surgical and non-surgical reinterventions, and considered a longer time horizon.

The analysis so far, and its limitations, suggest further research should include RCTs which collect a generic HRQoL measure such as the EQ-5D or SF-36 at follow-up times close to the procedure and in the long term, to calculate an estimate of preference-based utility. Baseline data from a trial of this kind would also provide a better estimate of HRQoL and utility of patients with symptoms. Data were lacking which would enable an evaluation of the effectiveness and cost-effectiveness of the procedures for different grades of symptom at baseline. A meta-analysis using individual patient data from the existing RCTs might be an efficient way of evaluating benefits and resource use in these sub-groups.

The base-case York model suggests that SH offers benefits to patients and the health service during the post-operative period in some dimensions, such as less post-operative pain and less use of hospital resources, and possibly less risk of complications. However, these benefits are to a greater or lesser extent offset by a greater risk of return of symptoms and the cost of the device. It remains uncertain as to which procedure is cost-effective overall.

7 Assessment of Factors Relevant to the NHS and Other Parties

Learning curve

One area of concern when evaluating any new surgical procedure compared to an established procedure, is the learning curve involved. CH has been standard practice in the UK for a long time, with a large proportion of colorectal surgeons experienced in the technique. On the other hand, SH, is a relatively new technique, and therefore it might be expected that there would be a learning curve for surgeons conducting this procedure. It is therefore possible that when the technology is first introduced to a centre or across the NHS, outcomes following SH may be worse than they should be due to the inexperience of the surgeons. This seems to be substantiated by one included trial, which was conducted during the early post-introductory period, and which reported technical difficulties whilst conducting SH; this study did seem to report less favourable outcomes for Sh than did trials that did not report technical difficulties.[80]

Furthermore, Jongen (2006)[117](an uncontrolled observational study not include din our review) reported the complications and re-operation rates after SH for 654 patients. During this study they attempted to assess the impact of the learning curve associated with the SH technique, by comparing outcomes of patients undergoing SH during 1998 and 1999 to those conducted during the period 2000 to 2003. This study reported a significantly lower incidence of dehiscence, faecal retention and number of re-operations in the latter period, although there was a significant increase in the incidence of bleeding in the early post-operative period.

The training required in the use of the staple gun, is not expected to have major resource implications for the NHS.

Follow-up appointments

An issue beyond the scope of this review, but may be a consideration for decision makers, is the requirement for follow-up appointments. Routine follow-up six to twelve weeks post-surgery as standard procedure in many institutions, has recently been questioned; advising a patient to visit their general practitioner if they experience any recurrence of symptoms or signs of a complication may be adequate. Should these follow-up appointments be abandoned then there is potential for cost savings. Whether, such savings would be equal for SH and CH would need investigation.

Ability to work

Given the apparent reduction in both post-operative pain and convalescence time after SH, the impact upon the finances and careers of individuals must be considered. This may be particularly significant for those who are self-employed, therefore unsalaried and without the provision of statutory sick pay. The short-term gain in the ability to return to normal daily activities may be seen as a priority by this group of people.

8 Discussion

8.1 Statement of principal findings

8.1.1 Clinical evaluation

In the early post-operative period 95% of trials reported less pain following SH and analysis of the data revealed that by day 21 the pain reported following SH and CH was minimal, with no difference between the two techniques. Residual prolapse was more common after SH. There was no difference between SH and CH in the incidence of bleeding or post-operative complications. SH resulted in shorter operating times, hospital stay, time to first bowel movement, and time to normal activity.

In the short-term (>6 weeks to <1 year) prolapse was more common after SH. There was no difference in the number of patients complaining of pain between SH and CH. Significantly fewer wounds remained unhealed at 6 weeks after SH.

In the long-term (1 year and beyond) there was a significantly higher rate of prolapse after SH. There was no difference in the number of patients experiencing pain, or the incidence of bleeding, between SH and CH.

There was no difference in the total number of reinterventions, or reinterventions for pain, bleeding or complications, between SH and CH. A significantly greater number of reinterventions were undertaken after SH for prolapse at 12 months or longer.

Overall, there was no statistically significant difference in the rate of complications between SH and CH.

8.1.2 Economic evaluation

In the economic assessment it was found that CH and SH had very similar costs and QALYs. With respect to costs, the additional cost of the staple gun was largely offset by savings in operating time and hospital stay. With respect to QALYs, the superior

quality of life due to lower pain levels in the early recovery period with SH, were offset by the higher rate of recurrence in the longer-term, as compared with CH.

However, the costs and QALYs are very sensitive to model assumptions. The probabilistic sensitivity analysis showed that, at threshold ICER of between £20,000 and £30,000 per QALY, SH had a 45% probability of being cost-effective.

8.2 Strengths and limitations of the assessment

8.2.1 Strengths

We conducted a comprehensive and rigorous systematic review which addressed a clear research question using predefined inclusion criteria. Extensive literature searches were undertaken to locate all relevant studies, both published and unpublished, in any language. Efforts were made to contact authors to identify further studies and obtain additional information to ensure as many studies could be included in the meta-analyses as possible. The study selection, data extraction, and quality assessment were conducted in duplicate, reducing the potential for error and bias. Subgroups of interest were identified a priori and analyses pre-planned. Our review benefited from regular advice from a clinician experience in the techniques being evaluated, and the close collaboration between the clinical and economic teams.

When compared to other reviews, ours is the first to our knowledge to exclusively evaluate staple guns designed for SH, include all comparator excisional techniques involving scalpel, diathermy or scissors, and attempt to evaluate the technology across the full spectrum of non-emergency patients in which the procedure would be used in practice (II, III, and IV degree haemorrhoids). Previous reviews included studies evaluating: linear staplers;[57-59] circular staplers not specifically designed for SH;[30, 99, 106, 118] patients with thrombosed haemorrhoids/emergency procedures;[96, 97, 99, 119] or restricted the included studies to those using Milligan Morgan and/or Ferguson as the comparator techniques.[64, 99] We also included a more substantial body of evidence than previous reviews due to the inclusion of more recently published studies.

The economic assessment builds on, and uses data from, the clinical review. The economic model is fairly simple, but considers a wide range of outcomes following haemorrhoidal surgery, including pain during the early recovery period and the probability of various symptoms and complications over the follow-up period.

8.2.2 Limitations

By necessity, our review is limited by the available data. All included studies seemed to have some methodological flaws, however, poor reporting made the assessment of study quality difficult. Only three studies reported recruiting the patient spectrum considered representative; patients with II, III and IV degree haemorrhoids. However, these studies had other methodological flaws relating to allocation concealment, method of randomisation or blinding.[83, 91, 93] Several studies were small, providing limited data, and possibly recruited insufficient numbers to be adequately powered to detect rarer outcomes. There was also very limited data for long-term outcomes, and where longer-term outcomes were reported, these were often subject to high losses to follow-up, in one case nearly 50% at 18 months.[61, 69] When studies reported a mean value along with its associated SD, the SD was often very large due indicating that the data was skewed. Several studies reported median values rather than mean values, and a large proportion did not report a measure of variance, or provided only the range. Although the use of median values is appropriate for skewed data, it does limit the ability to include these studies in the meta-analyses, and therefore the pooled results were sometimes based on only a subset of studies.

The number of studies for some outcome measures was limited, particularly for long-term follow-up. In addition, the included studies were very heterogeneous for some outcomes, most notably when evaluating pain. Some of this heterogeneity could be explained by differences in patient characteristics, degree of haemorrhoids pre-surgery, the protocol for post-operative care, methods and time points for measuring the study outcomes, and length of follow up. This heterogeneity precluded pooling data for these outcomes. When the data were pooled, the source of the heterogeneity was investigated.

The main limitation of the economic study is the lack of directly observed utility data in the early recovery period. There is reasonable evidence that SH is a less painful procedure up to three weeks after surgery and that pain recedes in both groups over this period. However, in the absence of directly observed data, it is very difficult to express any difference between the procedures in terms of utilities. Both the manufacturer submission and the TAR group model used indirect methods to estimate utilities and all the approaches used require key assumptions to be made.

From the patient's perspective the choice of procedure depends greatly on the relative value he or she places on lower pain in the early recovery period, compared with a higher rate of symptoms in the longer term. Although the economic assessment, through its estimation of QALYs for both procedures, seeks to value these items for the patient population in general, it is likely that different individuals will have different trade-offs. This could be explored through further research, but, given the similarity in the cost of the two procedures, another approach would be to make both available. Individual patients could then make a choice based on their views about (i) intensity and length of pain the early recovery period (ii) the probability of the occurrence of various symptoms and complications following either procedure.

8.3 Uncertainties

One of the most important areas where information is lacking in respect to current practice is data for the PPH03 stapling gun (EE-S). All studies where the gun used could be determined used PPH01, which is no longer supplied in the UK. Therefore, we were unable to determine whether the improvements made to the currently available EE-S stapling gun - the provision of transparent accessories and the ability to adjust the closed staple height down to 0.75mm - have led to improved outcomes. In addition, we found no studies evaluating the Autosuture staple gun with the STRAM kit adaptor (Tyco Healthcare), therefore we are also unable to determine the relative effectiveness and safety of this equipment compared to the PPH01 staple gun (EE-S).

Another factor that is still uncertain is the relative reintervention rate between SH and CH. Given the higher rate of prolapse after SH, the already apparent increase in the

need for reintervention for prolapse, and the lack of long-term follow-up for most studies, it is possible that the reintervention rate has been underestimated.

Insufficient numbers of studies provided results separately for patients with different degree of haemorrhoids pre-surgery; reported the number of patients operated on as a day case procedure; reported the number of patients requiring conversion to a general anaesthetic when regional or local anaesthetic was planned or initially used; or included patients with co-morbid conditions to provide definitive conclusions as to the impact of these factors on outcomes. The limited data available suggests:

- Patients with comorbid conditions would require a longer duration of hospital stay, but other outcomes would not be adversely affected.
- Patients undergoing SH require a shorter hospital stay, and based on the reports of numbers of day cases and the ranges reported in other studies, are probably more likely to be day case procedures.
- The use of SH for IV degree haemorrhoids is not contra-indicated; and that there is no evidence that patients with III degree haemorrhoids are any more suited to SH than those with II or IV degree haemorrhoids.

As stated above, the main uncertainty in the economic assessment is in the measurement and valuation (in utility terms) of the pain experienced in the early recovery period. The methods used to estimate utilities, and the assumptions about the time period over which pain will be experienced, have a major impact on the ICER.

8.4 Other relevant factors

During the course of this review, we encountered several areas where primary research could assist in the assessment of the technologies under review. Primarily, we feel that improved reporting of studies, preferably using the CONSORT statement, would be beneficial. Areas that require clearer reporting include:

- The degree of pre-operative prolapse in the patients recruited.

- Any inclusion or exclusion criteria used during the selection of patients, to ensure that the population recruited is well defined, and generalisability of the results apparent.
- Detailed descriptions of the techniques use to allow repeatability.

The reporting of outcomes varied widely across the studies. The reporting of some outcomes in a differently, and standardisation of the measurement of outcomes, would have assisted the review of effectiveness of these technologies. For example:

- When reporting the number with prolapse post-operatively, the number with each degree of prolapse would be informative, to determine whether the severity of recurrent prolapse differs between SH and CH.
- Reporting of outcomes after initial surgery and repeated surgery separately.
- The number of procedures undertaken as day cases using a consistent definition of day case (i.e. discharge from hospital within 24 hours).
- Standardised reporting of outcomes. For example:
  - Pain: The number of days that analgesia was required was considered to be the most useful pain outcome, yet this was very poorly reported.
  - When using VAS scores, the same scale (10 mm) should be used across studies, and the mean VAS score on specified days post-operatively reported. Additional VAS scores such as maximal pain, the change from baseline, or difference in patient expectation could also be reported if appropriate for the aim of the study.
  - Bleeding: The numbers of patients bleeding peri-operatively and requiring interventions such as haemostatic sutures should be reported separately from those with post-operative bleeding.
  - Bleeding: It is preferable to know the number of patients with bleeding episodes and which of these patients required intervention, rather than the volume of blood lost or the number of bleeding episodes that does not indicate the number of patients involved.
  - The mean and standard deviation should be reported for continuous data. If data is skewed, a median and range is appropriate, however, a mean and SD is required to undertake a meta-analysis. Therefore when data is skewed both the median and mean could be reported.

- The time point at which each outcome has been assessed should be clear. Some studies stated outcomes in the text or listed outcomes in tables without specifying the time point at which they were measured making the classification of these results difficult.

One of the problems with this type of review is the subjective nature of the classification of the target condition. The use of the IV degree classification described by Nisar and Scholefield (2003)[4] is commonly used and is applied variably across studies. An alternative classification was suggested by Lunnis and Mann (2004)[19] which incorporated the degree of prolapse along with the principle presentation and additional symptoms. The consistent application of a less subjective classification of haemorrhoids would improve the evaluation of their management.

9 Conclusions

9.1 Implications for service provision

- SH was associated with less pain in the immediate post-operative period, however it was also associated with a higher rate of residual prolapse, prolapse in the longer term and reintervention for prolapse.
- There was no clear difference in the rate or type of complications associated with the two techniques.
- The absolute and relative rates of recurrence and reintervention, for SH and CH, are still uncertain.
- CH and SH had very similar costs and QALYs. The small difference in the overall cost of SH compared to CH (£19) arises, in the main, because the acquisition cost of the staple gun is offset by savings in hospital stay. However, the estimates are based on published data and may not necessarily reflect local circumstances. Therefore, when a switch to SH is being discussed, it is important that NHS managers assess the potential for shortening stays, by reducing the length of inpatient admissions or by increasing the proportion of day cases. It would also be important to assess whether these changes have occurred at a suitable time in the future. The economic assessment contained in this report was based on a staple gun price of £437. Should this price change in the future, this may change the conclusions of the economic analysis.
- Some training may be required in the use of the staple gun; this is not expected to have major resource implications for the NHS.
- Given the currently available clinical evidence and the results of the economic analysis, the decision as to whether SH or a CH is conducted, should primarily be based upon the priorities and preferences of the patient (reduced pain and rapid return to work/activities in the short-term, or reduced risk of recurrence in the longer-term), and the preference of the surgeon.

9.2 Recommendations for research

The results of this review make it clear that using SH rather than CH will afford patients some benefits in the short-term, but at an increased risk of recurrence and the need for reintervention in the longer-term. However, due to the lack of long-term data, the evidence currently available does not provide a clear insight into the magnitude of the increased rate of prolapse and reintervention. In order to gather this information, two strategies can be employed:

- An adequately powered, good quality RCT comparing SH with CH, recruiting patients with II, III and IV degree haemorrhoids, and having a minimum follow-up period of five years to ensure an adequate evaluation of the reintervention rate.
- A prospective register of patients undergoing initial haemorrhoidal surgery, with follow-up to determine surgical and non-surgical reinterventions required.

In addition, further research would be recommended in the following areas:

- Evaluation of the effectiveness of SH in patients with more severe disease (IV degree) and patients with co-morbid conditions.
- A review of all treatments for haemorrhoids (conservative, non-surgical and surgical) investigating and comparing reintervention rates.
- Research into utilities up to six months post-operatively.
- Exploration of the trade-offs of patients for short-term pain versus long term outcomes through a discrete choice experiment.
- Exploration into the ability of SH to reduce hospital stays, by shortening inpatient admissions or increasing the proportion of day cares, in a real practice setting.

10 Appendices

10.1 Literature search strategies

10.1.1 Clinical effectiveness

No search strategies were limited by date or language.
Where applicable, searches were limited to RCTs and systematic reviews.

10.1.1.1 Databases of Systematic Reviews

Cochrane Database of Systematic Reviews (CDSR)

Searched via: The Cochrane Library: http://www.library.nhs.uk/
Issue 3: 2006
Date Searched: 11/07/06
This search strategy retrieved 2 reviews (2 completed);
#1 MeSH descriptor Hemorrhoids explode all trees
#2 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid* or piles):ti,ab,kw
#3 (#1 OR #2)
#4 (stapl*):ti,ab,kw
#5 ((stapl*) near/5 (mucosectomy or anopexy or rectal or hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#6 ((circumferential or circular) near/5 (mucosectomy or anopexy or rectal or hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#7 mucoprolapsectomy:ti,ab,kw
#8 longo:ti,ab,kw
#9 ((procedure for prolaps*) near/2 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#10 PPH:ti,ab,kw
#11 (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12 (#3 AND #11)

Database of Abstracts of Reviews of Effects (DARE)

Searched via: CRD Internal Database
July 2006
Date Searched: 17/07/06
This search strategy retrieved 4 records;
S Hemorrhoids (subject headings exploded) or hemorrhoid or haemorrhoid or hemorhoid or haemorrhoid or piles (title & abstract)
S (staple or mucosectomy or anopexy or circumferential or circular or mucoprolapsectomy or Longo or (procedure for prolapse)) (title & abstract)
S s1 and s2

10.1.1.2 Health/Medical Related Databases

BIOSIS

Searched via: EDINA (discontinued 31/07/06)
Searched: 13/07/06
This search strategy retrieved 48 records;
(ti: ((hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles))) and ti: ((stapl* or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or Longo or PPH or (procedure for prolaps*)))

CENTRAL (Cochrane Central Register of Controlled Trials)

Searched via: The Cochrane Library: http://www.library.nhs.uk/
Issue 3: 2006
Date Searched: 11/07/06
This search strategy retrieved 74 records;
#1 MeSH descriptor Hemorrhoids explode all trees
#2 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid* or piles):ti,ab,kw
#3 (#1 OR #2)
#4 (stapl*):ti,ab,kw
#5 ((stapl*) near/5 (mucosectomy or anopexy or rectal or hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#6 ((circumferential or circular) near/5 (mucosectomy or anopexy or rectal or hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#7 mucoprolapsectomy:ti,ab,kw
#8 longo:ti,ab,kw
#9 ((procedure for prolaps*) near/2 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw
#10 PPH:ti,ab,kw
#11 (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
#12 (#3 AND #11)

Cumulative Index to Nursing and Allied Health Literature (CINAHL)

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to July Week 1 2006
Date Searched: 11/07/06
This search strategy retrieved no records;
1. exp Hemorrhoids/
2. (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab.
3. or/1-2
4. stapl$.ti,ab.
5. (stapl$ adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
6. ((circumferential or circular) adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
7. mucoprolapsectomy.ti,ab.
8. Longo.ti,ab.
9. (procedure for prolaps$ adj2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
10. PPH.ti,ab.
11. or/4-10
12. 3 and 11
13. exp clinical trials/
14. double-blind studies/
15. single-blind studies/
16. triple-blind studies/

17. clinical trial.pt.
18. random assignment/
19. (randomized or randomised or placebo or randomly).ab.
20. trial.ti.
21. or/13-20
22. 12 and 21
23. animals/ not (animals/ and humans/)
24. 22 not 23

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 27
Date Searched: 11/07/06
This search strategy retrieved 129 records.
1. exp Hemorrhoid/
2. (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab.
3. or/1-2
4. stapl$.ti,ab.
5. (stapl$ adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
6. ((circumferential or circular) adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
7. mucoprolapsectomy.ti,ab.
8. Longo.ti,ab.
9. (procedure for prolaps$ adj2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
10. PPH.ti,ab.
11. or/4-10
12. 3 and 11
13. controlled study/
14. exp clinical trial/
15. outcomes research/
16. randomized controlled trial/
17. (randomized or randomised or placebo or randomly).ab.
18. trial.ti.
19. or/13-18
20. 12 and 19
21. animals/ not (animals/ and humans/)
22. 20 not 2

Health Technology Assessment Database (HTA)

Searched via: CRD Internal Database
July 2006
Date Searched: 17/07/06.
This search retrieved 3 records.
S Hemorrhoids (subject headings exploded) or hemorrhoid or haemorrhoid or hemorhoid or haemorrhoid or piles (title & abstract)

S (staple or mucosectomy or anopexy or circumferential or circular or mucoprolapsectomy or Longo or (procedure for prolapse)) (title & abstract)
S s1 and s2

MEDLINE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to July Week 1 2006
Date Searched: 11/07/06
This search strategy retrieved 102 records;
1. exp Hemorrhoids/
2. (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab.
3. or/1-2
4. stapl$.ti,ab.
5. (stapl$ adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
6. ((circumferential or circular) adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
7. mucoprolapsectomy.ti,ab.
8. Longo.ti,ab.
9. (procedure for prolaps$ adj2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
10. PPH.ti,ab.
11. or/4-10
12. 3 and 11
13. clinical trial.pt.
14. randomized.ti,ab.
15. placebo.ti,ab.
16. dt.fs.
17. randomly.ti,ab.
18. groups.ti,ab.
19. or/13-18
20. 12 and 19
21. controlled.ab.
22. design.ab.
23. evidence.ab.
24. extraction.ab.
25. randomized controlled trials/
26. meta-analysis.pt.
27. review.pt.
28. sources.ab.
29. studies.ab.
30. or/21-29
31. (letter or editorial or comment).pt.
32. 30 not 31
33. 12 and 32
34. animals/ not (animals/ and humans/)
35. 20 not 34
36. 33 not 34

37. 35 or 36

MEDLINE In-Process, Other Non-Indexed Citations

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to July Week 1 2006
Date Searched: 11/07/06
This search strategy retrieved 7 records;
1. exp Hemorrhoids/
2. (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab.
3. or/1-2
4. stapl$.ti,ab.
5. (stapl$ adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
6. ((circumferential or circular) adj5 (mucosectomy or anopexy or rectal or hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
7. mucoprolapsectomy.ti,ab.
8. Longo.ti,ab.
9. (procedure for prolaps$ adj2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
10. PPH.ti,ab.
11. or/4-10
12. 3 and 11
13. clinical trial.pt.
14. randomized.ti,ab.
15. placebo.ti,ab.
16. dt.fs.
17. randomly.ti,ab.
18. groups.ti,ab.
19. or/13-18
20. 12 and 19
21. controlled.ab.
22. design.ab.
23. evidence.ab.
24. extraction.ab.
25. randomized controlled trials/
26. meta-analysis.pt.
27. review.pt.
28. sources.ab.
29. studies.ab.
30. or/21-29
31. (letter or editorial or comment).pt.
32. 30 not 31
33. 12 and 32
34. animals/ not (animals/ and humans/)
35. 20 not 34
36. 33 not 34
37. 35 or 36

Science Citation Index (SCI)

Searched via: Web of Knowledge: http://wos.mimas.ac.uk/
1956- Present
Date Searched: 12/07/06
This search strategy retrieved 212 records;
#1 TI=(hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles)
#2 TI=(stapl* or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or Longo or PPH)
#3 TI=(procedure for prolaps*)
#4 #1 and (#2 or #3)

10.1.1.3 Databases of Conference Proceedings

ISI Proceedings: science & technology

Searched via: Web of Knowledge: http://wos.mimas.ac.uk/
1990 – Present
Date Searched: 13/07/06
This search strategy retrieved 50 records;
#1 TI=(hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles)
#2 TI=(stapl* or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or Longo or PPH)
#3 TI=(procedure for prolaps*)
#4 #1 and (#2 or #3)

Zetoc Conferences

Searched via MIMAS: http://zetoc.mimas.ac.uk/
1993 – Present
Date Searched: 18/07/06
After within database de-duplication this series of individual search strings retrieved 10 records;
Haemorrhoid* AND stapl*
Haemorrhoid* AND PPH
Haemorrhoid* AND anopexy
Haemorrhoid* AND longo
Hemorrhoid* AND stapl*
Hemorrhoid* AND PPH
Hemorrhoid* AND anopexy
Hemorrhoid* AND longo

10.1.1.4 Databases for Ongoing and Recently Completed Research

ClinicalTrials.gov

Searched via: http://www.clinicaltrials.gov/
Searched: 13/07/06
This search retrieved no records;
hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles

MetaRegister of Controlled Trials

Searched via: http://www.controlled-trials.com/
Searched: 09/08/06
All registers (except clinicaltrials.gov and the National Research Register (NRR) which were searched directly) were selected.
This search retrieved 28 records;
(hemorrhoid% or haemorrhoid% or hemorhoid% or haemorhoid% or hemoroid% or haemorhoid% or piles) and (stapl% or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or Longo or PPH or (procedure for prolaps%))

National Research Register (NRR)

Searched via: http://www.update-software.com/national/
Issue 3: 2006
Date Searched: 17/07/06
This search retrieved 26 records;
#1. (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles)
#2. HEMORRHOIDS explode all trees (MeSH)
#3. (stapl* or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or longo or pph)
#4. (procedure next prolaps*)
#5. ((#1 or #2) and (#3 or #4))

10.1.1.5 Clinical Guidelines Resources

Clinical Evidence (June 2006 update)

Searched: 17/07/06
All chapters checked- no relevant chapters found.

Health Evidence Bulletin Wales (HEBW)

Searched via: http://hebw.cf.ac.uk
Searched: 17/07/06
All content checked- no relevant bulletins found.

National Guideline Clearinghouse (NGC)

Searched via: http://www.guideline.gov/
Searched: 17/07/06
Search strategy retrieved no guidelines;
(hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles) and (stapl* or mucosectomy or anopexy or rectal or circumferential or circular or mucoprolapsectomy or longo or pph)

National Institute for Health and Clinical Excellence (NICE)

Searched via: http://www.nice.org.uk/
Searched: 17/07/06
All publications checked- 1 relevant guideline found.

National Library for Health (NLH) Guidelines Finder

Searched via: http://www.library.nhs.uk/guidelinesfinder/
Searched: 17/07/06
Search strategy retrieved 1 guideline;
hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles

Scottish Intercollegiate Guidelines Network (SIGN)

Searched via: http://www.sign.ac.uk/
Searched: 17/07/06
All publications checked- no relevant guidelines found.

Turning Research Into Practice (TRIP+)

Searched via: http://www.tripdatabase.com/index.html
Searched: 17/07/06
Search strategy retrieved 4 guidelines;
hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles (title and text)

10.1.1.6 Websites

American Society of Colon and Rectal Surgeons (ASCRSA)

Searched via: http://ascrs.affiniscape.com/index.cfm
Searched: 18/07/06
All publications checked- no relevant studies or guidelines found.

Association of Coloproctology of Great Britain and Ireland (ACGBI)

Searched via: http://www.acpgbi.org.uk
Searched: 18/07/06
All publications checked- 1 relevant studies or guidelines found.

Association of Surgeons of Great Britain and Ireland (ASGBI)

Searched via: http://www.asgbi.org.uk/
Searched: 18/07/06
All publications checked- no relevant studies or guidelines found.

Digestive Disorders Foundation (DDF)

Searched via: http://www.digestivedisorders.org.uk
Searched: 18/07/06
All publications checked- no relevant studies or guidelines found.

Hemorrhoids File

Searched via: http://www.lifestages.com/health/hemorrho.html
Searched: 18/07/06
All publications checked- 71 relevant studies or guidelines found.

10.1.1.7 Key Journals

In order to select key journals for handsearching the Journal Citation Reports via ISI Web of Knowledge were checked. 139 journals are listed in the category 'Surgery' and these were sorted by 'Impact Factor' to help identify key journals in this area. General surgical journals and journals specific to this topic were identified. Additional journals were also identified through the results of initial searches that were carried out to develop the search strategy in the protocol. The list of journals identified was then checked with the clinical expert on the review, and a list of seven key journals for this topic was agreed as follows;

American Journal of Surgery (MEDLINE core journal)
British Journal of Surgery (MEDLINE core journal)
Colorectal Disease
Diseases of the Colon & Rectum
International Journal of Colorectal Disease
Journal of Gastrointestinal Surgery
Techniques in Coloproctology

All of the above journals are indexed on MEDLINE so studies would be identified through the electronic searches. Two (as marked) are 'core journals', so are fully indexed immediately on publication.

However, as the other journals listed were not core journals on MEDLINE, and as the CENTRAL database (which is populated through hand-searching) had not been updated for some time, it was decided to search issues of these five journals published during the last twelve months by hand, in order to ensure studies were not missed. This was feasible given the relatively small volume of literature in this specific subject area.

Bibliographic Records Retrieved

Databases of Systematic Reviews

Database	Host	Dates covered	Date searched	Records Retrieved
CDSR	Internet	Issue 3: 2006	11/07/06	2
DARE	CRD Internal Database	To July 2006	17/07/06	4

Health/Medical Related Databases

Database	Host	Dates covered	Date searched	Records Retrieved
BIOSIS	Internet	1993 – Present	13/07/06	48
CENTRAL	Internet	Issue 3: 2006	11/07/06	74
CINAHL	OvidWeb	1982 – July Week 1 2006	11/07/06	0
EMBASE	OvidWeb	1980 – 2006 Week 27	11/07/06	129
HTA	CRD Internal Database	To July 2006	17/07/06	3
MEDLINE	OvidWeb	1966 – July Week 1 2006	11/07/06	102
MEDLINE in process	OvidWeb	To 10 July 2006	11/07/06	7
SCI	Web of Science	1956 – Present	12/07/06	212

Databases of Conference Proceedings

Database	Host	Dates covered	Date searched	Records Retrieved
ISI Proceedings: Science and Technology	Web of Science	1990 - Present	13/07/06	50
Zetoc Conferences	MIMAS	1993 – Present	18/07/06	10

Databases for Ongoing and Recently Completed Research

Database	Host	Dates covered	Date searched	Records Retrieved
ClinicalTrials.gov	Internet	Present	13/07/06	0
MetaRegister of Controlled Trials	Internet	Present	13/07/06	28
NRR	Internet	Present	17/07/06	26

Clinical Guidelines Resources

Resource	Format	Dates covered	Date searched	Records Retrieved
Clinical Evidence	Book	Present	13/07/06	0
HEBW	Internet	Present	17/07/06	0
NGC	Internet	Present	17/07/06	0
NICE	Internet	Present	17/07/06	1
NLH	Internet	Present	17/07/06	1
SIGN	Internet	Present	17/07/06	0
TRIP+	Internet	Present	17/07/06	4

Websites

Resource	Format	Dates covered	Date searched	Records Retrieved
ASCRSA	Internet	Present	18/07/06	0
ACGBI	Internet	Present	18/07/06	1
ASGBI	Internet	Present	18/07/06	0
DDF	Internet	Present	18/07/06	0
Hemorrhoids File	Internet	Present	18/07/06	71

10.1.2 Cost-effectiveness

All search strategies were not limited by date or language.

10.1.2.1 Economic Databases

EconLit

Searched via: WebSPIRS: http//arc.uk.ovid.com/
1969 – 2006/06
Date Searched: 17/07/06
This search retrieved no records.
(hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles) in TITLE

Health Economics Evaluation Database (HEED)

Searched via: CD-ROM
July 2006
Date Searched: 17/07/06
This search strategy retrieved 6 records;
hemorrhoid* or haemorrhoid* or haemorhoid* or hemorhoid* or hemoroid* or piles
AND

stapl* or mucosectomy or circumferential or circular or anopexy or rectal or mucoprolapsectomy or longo or PPH or 'procedure for prolapse' or 'procedure for prolapsing'

IDEAS

Searched via: http://ideas.repec.org/
Current
Date Searched: 17/07/06
This search strategy retrieved no records;
(hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemorhoid* or piles) in long format records.

NHS Economic Evaluation Database (NHS EED)

Searched via: CRD Internal Database
July 2006
Date Searched: 17/07/06
This search strategy retrieved 5 records;
Hemorrhoids (subject headings exploded) or hemorrhoid or haemorrhoid or hemorhoid or haemorrhoid or piles (title & abstract)
And
(staple or mucosectomy or anopexy or circumferential or circular or mucoprolapsectomy or Longo or (procedure for prolapse)) (title & abstract)

Bibliographic Records Retrieved

Total Records Retrieved: 784
Records entered into the Endnote Library after de-duplication: 363

Database	Host	Dates covered	Date searched	Records Retrieved
EconLit	WebSPIRS	1969 – 2006/06	17/07/06	0
HEED	CD – ROM	To June 2006	17/07/06	6
IDEAS	RePEC	Present	17/07/06	0
NHS EED	Internet	To July 2006	17/07/06	5

10.1.3 Economic model

All search strategies were not limited by date or language.

10.1.3.1 Quality of Life

CINAHL - Cumulative Index to Nursing & Allied Health Literature

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to June Week 4 2006
Date Searched: 28/06/06
This search strategy retrieved 6 records;
1 exp hemorrhoids/ (180)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (176)
3 or/1-2 (241)
4 exp life tables/ (0)
5 "quality of life"/ (13042)
6 exp health status indicators/ (3268)

7 (utilit$ approac$ or health gain or hui or hui2 or hui 2 or hui3 or hui 3).ti,ab. (129)
8 (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab. (1)
9 (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab. (256)
10 (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab. (421)
11 (index of wellbeing or quality of wellbeing or qwb).ti,ab. (29)
12 (rating scale$ or multiattribute$ health ind$ or multi attribute$ health ind$$).ti,ab. (2250)
13 (health utillit$ index or health utilit$ indices).ti,ab. (1)
14 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab. (2)
15 (health utilit$ scale$ or classification of illness state$ or 15d or 15 d or 15 dimension).ti,ab. (53)
16 (health state$ utilit$ or 12d or 12 d or 12 dimension).ti,ab. (27)
17 well year$.ti,ab. (3)
18 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab. (26)
19 health utilit$ scale$.ti,ab. (0)
20 (qol or 5d or 5-d or 5 dimension or quality of life or euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab. (13476)
21 (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab. (246)
22 life year$ gain$.ti,ab. (63)
23 willingness to pay.ti,ab. (88)
24 (hye or hyes or health year$ equivalent$).ti,ab. (1)
25 (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab. (56)
26 theory utilit$.ti,ab. (2)
27 life table$.ti,ab. (186)
28 health state$.ti,ab. (310)
29 (sf36 or sf 36).ti,ab. (1188)
30 (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab. (524)
31 (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$ or 6d or 6-d or 6 dimension).ti,ab. (94)
32 hrqol.ti,ab. (378)
33 hrql.ti,ab. (173)
34 (health related quality adj2 life$).ti,ab. (1649)
35 or/4-34 (25169)
36 3 and 35 (6)

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 25
Date Searched: 28/06/06
This search strategy retrieved 67 records;
1 exp hemorrhoids/ (2146)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (2440)

3 or/1-2 (3091)
4 exp life tables/ (925)
5 "quality of life"/ (64887)
6 exp health status indicators/ (39768)
7 (utilit$ approac$ or health gain or hui or hui2 or hui 2 or hui3 or hui 3).ti,ab. (1008)
8 (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab. (23)
9 (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab. (2307)
10 (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab. (1910)
11 (index of wellbeing or quality of wellbeing or qwb).ti,ab. (98)
12 (rating scale$ or multiattribute$ health ind$ or multi attribute$ health ind$$).ti,ab. (15984)
13 (health utillit$ index or health utilit$ indices).ti,ab. (5)
14 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab. (7)
15 (health utilit$ scale$ or classification of illness state$ or 15d or 15 d or 15 dimension).ti,ab. (1587)
16 (health state$ utilit$ or 12d or 12 d or 12 dimension).ti,ab. (1074)
17 well year$.ti,ab. (102)
18 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab. (94)
19 health utilit$ scale$.ti,ab. (1)
20 (qol or 5d or 5-d or 5 dimension or quality of life or euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab. (56287)
21 (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab. (1897)
22 life year$ gain$.ti,ab. (663)
23 willingness to pay.ti,ab. (685)
24 (hye or hyes or health year$ equivalent$).ti,ab. (25)
25 (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab. (461)
26 theory utilit$.ti,ab. (18)
27 life table$.ti,ab. (4137)
28 health state$.ti,ab. (1417)
29 (sf36 or sf 36).ti,ab. (4595)
30 (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab. (1902)
31 (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$ or 6d or 6-d or 6 dimension).ti,ab. (2397)
32 hrqol.ti,ab. (1591)
33 hrql.ti,ab. (823)
34 (health related quality adj2 life$).ti,ab. (6031)
35 or/4-34 (148336)
36 3 and 35 (67)

MEDLINE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to June Week 2 2006
Date Searched: 28/06/06
This search strategy retrieved 111 records;

1 exp hemorrhoids/ (3001)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (3109)
3 or/1-2 (3935)
4 exp life tables/ (8370)
5 "quality of life"/ (55049)
6 exp health status indicators/ (85929)
7 (utilit$ approac$ or health gain or hui or hui2 or hui 2 or hui3 or hui 3).ti,ab. (641)
8 (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab. (17)
9 (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab. (2596)
10 (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab. (2022)
11 (index of wellbeing or quality of wellbeing or qwb).ti,ab. (107)
12 (rating scale$ or multiattribute$ health ind$ or multi attribute$ health ind$$).ti,ab. (16522)
13 (health utillit$ index or health utilit$ indices).ti,ab. (4)
14 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab. (5)
15 (health utilit$ scale$ or classification of illness state$ or 15d or 15 d or 15 dimension).ti,ab. (1854)
16 (health state$ utilit$ or 12d or 12 d or 12 dimension).ti,ab. (1348)
17 well year$.ti,ab. (18)
18 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab. (109)
19 health utilit$ scale$.ti,ab. (2)
20 (qol or 5d or 5-d or 5 dimension or quality of life or euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab. (62916)
21 (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab. (2026)
22 life year$ gain$.ti,ab. (688)
23 willingness to pay.ti,ab. (701)
24 (hye or hyes or health year$ equivalent$).ti,ab. (45)
25 (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab. (478)
26 theory utilit$.ti,ab. (4)
27 life table$.ti,ab. (5355)
28 health state$.ti,ab. (1685)
29 (sf36 or sf 36).ti,ab. (4669)
30 (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab. (1987)
31 (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$ or 6d or 6-d or 6 dimension).ti,ab. (2993)
32 hrqol.ti,ab. (1691)

33 hrql.ti,ab. (868)
34 (health related quality adj2 life$).ti,ab. (6441)
35 or/4-34 (199619)
36 3 and 35 (111)

PsycINFO

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to June Week 3 2006
Date Searched: 28/06/06
This search strategy retrieved no records;
1 exp hemorrhoids/ (0)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (107)
3 or/1-2 (107)
4 exp life tables/ (0)
5 "quality of life"/ (10405)
6 exp health status indicators/ (0)
7 (utilit$ approac$ or health gain or hui or hui2 or hui 2 or hui3 or hui 3).ti,ab. (326)
8 (health measurement$ scale$ or health measurement$ questionnaire$).ti,ab. (17)
9 (standard gamble$ or categor$ scal$ or linear scal$ or linear analog$ or visual scal$ or magnitude estimat$).ti,ab. (1615)
10 (time trade off$ or rosser$ classif$ or rosser$ matrix or rosser$ distress$ or hrqol).ti,ab. (598)
11 (index of wellbeing or quality of wellbeing or qwb).ti,ab. (43)
12 (rating scale$ or multiattribute$ health ind$ or multi attribute$ health ind$$).ti,ab. (21741)
13 (health utillit$ index or health utilit$ indices).ti,ab. (0)
14 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab. (13)
15 (health utilit$ scale$ or classification of illness state$ or 15d or 15 d or 15 dimension).ti,ab. (36)
16 (health state$ utilit$ or 12d or 12 d or 12 dimension).ti,ab. (40)
17 well year$.ti,ab. (41)
18 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab. (129)
19 health utilit$ scale$.ti,ab. (0)
20 (qol or 5d or 5-d or 5 dimension or quality of life or euro qual or euro qol or eq-5d or eq5d or eq 5d or euroqual or euroqol).ti,ab. (14408)
21 (qualy or qaly or qualys or qalys or quality adjusted life year$).ti,ab. (146)
22 life year$ gain$.ti,ab. (12)
23 willingness to pay.ti,ab. (242)
24 (hye or hyes or health year$ equivalent$).ti,ab. (3)
25 (person trade off$ or person tradeoff$ or time tradeoff$ or time trade off$).ti,ab. (85)
26 theory utilit$.ti,ab. (57)
27 life table$.ti,ab. (164)
28 health state$.ti,ab. (398)
29 (sf36 or sf 36).ti,ab. (1104)

30 (short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab. (410)
31 (sf 6d or sf6d or short form 6d or shortform 6d or sf six$ or shortform six$ or short form six$ or 6d or 6-d or 6 dimension).ti,ab. (68)
32 hrqol.ti,ab. (541)
33 hrql.ti,ab. (259)
34 (health related quality adj2 life$).ti,ab. (1763)
35 or/4-34 (40439)
36 3 and 35 (0)

Bibliographic Records Retrieved

Total records retrieved: 184
Records entered into the Endnote Library after de-duplication: 145

Resource	Search date	Records	After deduplication
CINAHL	28/06/06	6	6
EMBASE	28/06/06	67	63
MEDLINE	28/06/06	111	76
PSYCINFO	28/06/06	0	0

10.1.3.2 Incidence and Prevalence

CINAHL - Cumulative Index to Nursing & Allied Health Literature

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to July Week 4 2006
Date Searched: 01/08/06
This search strategy retrieved 5 records;
1 *Hemorrhoids/ (121)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (181)
3 or/1-2 (194)
4 (frequency of or occurence$ or incidence$ or prevalenc$ or rate of or rates of).ti. (8004)
5 incidence/ (4910)
6 prevalence/ (7290)
7 or/4-6 (16876)
8 3 and 7 (5)

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 30
Date Searched: 01/08/06
This search strategy retrieved 107 records;
1 *Hemorrhoids/ (1418)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (2455)
3 or/1-2 (2686)
4 (frequency of or occurence$ or incidence$ or prevalenc$ or rate of or rates of).ti. (148916)

5 incidence/ (74016)
6 prevalence/ (99213)
7 or/4-6 (280746)
8 3 and 7 (107)

MEDLINE and MEDLINE In Process

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to Present
Date Searched: 28/06/06
This search strategy retrieved 126 records;
1 *Hemorrhoids/ (2268)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (3247)
3 or/1-2 (3508)
4 (frequency of or occurence$ or incidence$ or prevalenc$ or rate of or rates of).ti. (124651)
5 incidence/ (102096)
6 prevalence/ (92655)
7 or/4-6 (267741)
8 3 and 7 (126)

Bibliographic Records Retrieved

Total records retrieved: 238
Records entered into the Endnote Library after de-duplication: 127

Resource	Search date	Records	After sift/ deduplication
CINAHL	01/08/06	5	0
EMBASE	01/08/06	107	41
MEDLINE	01/08/06	126	86

10.1.3.3 Open v Closed RCT search

CENTRAL (Cochrane Central Register of Controlled Trials)

Searched via: The Cochrane Library: http://www.library.nhs.uk/
Searched via: OvidWeb: http://gateway.ovid.com/athens
Date Searched: 014/09/06
This search strategy retrieved 27 records;
#1 (closed near/5 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw (37)
#2 (milligan morgan):ti,ab,kw (57)
#3 (open near/5 (hemorrhoid* or haemorrhoid* or hemorhoid* or haemorhoid* or hemoroid* or haemoroid*)):ti,ab,kw (31)
#4 (ferguson):ti,ab,kw (24)
#5 (#1 OR #2) (85)
#6 (#3 OR #4) (51)
#7 (#5 AND #6) (27)

CINAHL - Cumulative Index to Nursing & Allied Health Literature

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to July Week 4 2006
Date Searched: 01/08/06
This search strategy retrieved no records;
1. (closed adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
2. milligan morgan.ti,ab.
3. or/1-2
4. (open adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab.
5. ferguson.ti,ab.
6. or/4-5
7. 3 and 6
8. exp clinical trials/
9. double-blind studies/
10. single-blind studies/
11. triple-blind studies/
12. clinical trial.pt.
13. random assignment/
14. (randomized or randomised or placebo or randomly).ab.
15. trial.ti.
16. or/8-15
17. 7 and 16
18. animals/ not (animals/ and humans/)
19. 17 not 18

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 36
Date Searched: 14/09/06
This search strategy retrieved 28 records;
1 (closed adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (68)
2 milligan morgan.ti,ab. (81)
3 or/1-2 (140)
4 (open adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (57)
5 ferguson.ti,ab. (398)
6 or/4-5 (449)
7 3 and 6 (39)
8 controlled study/ (2244792)
9 exp clinical trial/ (403366)
10 outcomes research/ (56451)
11 randomized controlled trial/ (109221)
12 (randomized or randomised or placebo or randomly).ab. (281427)
13 trial.ti. (54347)
14 or/8-13 (2575036)
15 6 and 14 (118)

16 animals/ not (animals/ and humans/) (12831)
17 15 not 16 (118)
18 (closed adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (68)
19 milligan morgan.ti,ab. (81)
20 or/18-19 (140)
21 (open adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (57)
22 ferguson.ti,ab. (398)
23 or/21-22 (449)
24 20 and 23 (39)
25 controlled study/ (2244792)
26 exp clinical trial/ (403366)
27 outcomes research/ (56451)
28 randomized controlled trial/ (109221)
29 (randomized or randomised or placebo or randomly).ab. (281427)
30 trial.ti. (54347)
31 or/25-30 (2575036)
32 24 and 31 (28)
33 animals/ not (animals/ and humans/) (12831)
34 32 not 33 (28)

MEDLINE and MEDLINE In Process

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to Present
Date Searched: 14/09/06
This search strategy retrieved 36 records;
1 (closed adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (76)
2 milligan morgan.ti,ab. (112)
3 or/1-2 (182)
4 (open adj5 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$)).ti,ab. (66)
5 ferguson.ti,ab. (606)
6 or/4-5 (668)
7 3 and 6 (50)
8 clinical trial.pt. (457600)
9 randomized.ti,ab. (165432)
10 placebo.ti,ab. (102365)
11 dt.fs. (1202180)
12 randomly.ti,ab. (113511)
13 groups.ti,ab. (812649)
14 or/8-13 (2207668)
15 controlled.ab. (232118)
16 design.ab. (319691)
17 evidence.ab. (569560)
18 extraction.ab. (79583)
19 randomized controlled trials/ (48065)
20 meta-analysis.pt. (14237)

21 review.pt. (1262242)
22 sources.ab. (96654)
23 studies.ab. (1081853)
24 or/15-23 (3042062)
25 (letter or editorial or comment).pt. (840724)
26 24 not 25 (3008714)
27 7 and 14 (31)
28 7 and 26 (11)
29 27 or 28 (36)
30 animals/ not (animals/ and humans/) (3093553)
31 29 not 30 (36)

Bibliographic Records Retrieved

Total records retrieved: **82**
Records entered into the Endnote Library after de-duplication: 53

Resource	Search date	Records	After sift/ deduplication
Central	14/09/06	**27**	1
CINAHL	14/09/06	0	0
EMBASE	14/09/06	28	27
MEDLINE	14/09/06	36	25

10.1.3.4 Cohort studies of complications (all haemorrhoid surgeries)

CINAHL - Cumulative Index to Nursing & Allied Health Literature

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to October Week 1 2006
Date Searched: 12/10/06
This search strategy retrieved 6 records;
1 exp hemorrhoids/ (191)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$).ti,ab. (163)
3 or/1-2 (234)
4 exp colorectal surgery/ (0)
5 exp surgery/ (77760)
6 surg$.ti,ab. (41259)
7 or/4-6 (97445)
8 3 and 7 (52)
9 pain/ or pain measurement/ or postoperative pain/ (21972)
10 Sepsis/ (1726)
11 Fecal Incontinence/ or Urinary Incontinence/ (3731)
12 Pruritus/ (436)
13 exp Postoperative Complications/ (11907)
14 adverse healthcare event/ (590)
15 adverse drug event/ (653)
16 complication$.ti,ab. (18743)
17 pain.ti,ab. (38910)
18 prolaps$.ti,ab. (474)
19 bleed$.ti,ab. (3499)
20 sepsis.ti,ab. (1951)
21 (anal adj (fistula or stenos$ or fissure$)).ti,ab. (44)

22 (incontinen$ or urgen$).ti,ab. (6278)
23 (anastomotic adj stricture).ti,ab. (3)
24 (haemorrhoidal adj thrombosis).ti,ab. (0)
25 (itching or pruritis).ti,ab. (313)
26 (complication$ or reoccur$ or reintervention$ or reoperat$ or retreat$ or redo).ti,ab. (19357)
27 ((further or repeat) adj (surgery or treatment or procedure$)).ti,ab. (243)
28 (safe or safety or side effect$ or undesirable effect$ or treatment emergent or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or event or events or outcome or outcomes))).ti,ab. (45088)
29 or/9-28 (120154)
30 Prospective studies/ (50171)
31 exp case control studies/ (11399)
32 Correlational studies/ (6996)
33 Nonconcurrent prospective studies/ (21)
34 Cross sectional studies/ (17538)
35 (cohort adj (study or studies)).tw. (5078)
36 (Follow up adj (study or studies)).tw. (1576)
37 (observational adj (study or studies)).tw. (2238)
38 or/30-37 (83206)
39 29 and 38 (14531)
40 8 and 39 (6)
41 animals/ not (animals/ and humans/) (755)
42 40 not 41 (6)

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 40
Date Searched: 14/09/06
This search strategy retrieved 378 records;
1 exp hemorrhoid/ (2189)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$).ti,ab. (2080)
3 or/1-2 (2768)
4 exp colorectal surgery/ (4231)
5 exp surgery/ (1238854)
6 surg$.ti,ab. (605688)
7 or/4-6 (1440365)
8 3 and 7 (1573)
9 pain/ or pain assessment/ or postoperative pain/ (86492)
10 Sepsis/ (33338)
11 feces incontinence/ or Urinary Incontinence/ (15422)
12 Pruritus/ (20170)
13 exp Postoperative Complication/ (178245)
14 complication/ (14941)
15 exp adverse drug reaction/ (159357)
16 exp side effect/ (128464)
17 complication$.ti,ab. (285497)
18 pain.ti,ab. (194221)

19 prolaps$.ti,ab. (9288)
20 bleed$.ti,ab. (68810)
21 sepsis.ti,ab. (32440)
22 (anal adj (fistula or stenos$ or fissure$)).ti,ab. (1157)
23 (incontinen$ or urgen$).ti,ab. (38291)
24 (anastomotic adj stricture).ti,ab. (498)
25 (haemorrhoidal adj thrombosis).ti,ab. (2)
26 (itching or pruritis).ti,ab. (4116)
27 (complication$ or reoccur$ or reintervention$ or reoperat$ or retreat$ or redo).ti,ab. (298016)
28 ((further or repeat) adj (surgery or treatment or procedure$)).ti,ab. (6408)
29 (safe or safety or side effect$ or undesirable effect$ or treatment emergent or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or event or events or outcome or outcomes))).ti,ab. (480317)
30 co.fs. (591895)
31 to.fs. (238238)
32 ae.fs. (394173)
33 or/9-32 (1877582)
34 major clinical study/ (1072258)
35 Clinical study/ (13614)
36 Case control study/ (14464)
37 Family study/ (6820)
38 Longitudinal study/ (13873)
39 Retrospective study/ (70829)
40 Cohort analysis/ (37038)
41 prospective study/ (59551)
42 (Cohort adj (study or studies)).mp. (25566)
43 (Case control adj (study or studies)).tw. (26865)
44 (follow up adj (study or studies)).tw. (19698)
45 (observational adj (study or studies)).tw. (12266)
46 (epidemiologic$ adj (study or studies)).tw. (29363)
47 (cross sectional adj (study or studies)).tw. (18216)
48 or/34-47 (1216848)
49 randomized controlled trials/ (110088)
50 48 not 49 (1156281)
51 33 and 50 (353839)
52 8 and 51 (378)
53 animals/ not (animals/ and humans/) (12832)
54 52 not 53 (378)

MEDLINE and MEDLINE In Process

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to Present
Date Searched: 12/10/06
This search strategy retrieved 264 records;
1 exp hemorrhoids/ (3065)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$).ti,ab. (2905)
3 or/1-2 (3787)
4 exp colorectal surgery/ (892)

5 exp surgery/ (22731)
6 surg$.ti,ab. (821995)
7 or/4-6 (831536)
8 3 and 7 (1053)
9 pain/ or pain measurement/ or pain, postoperative/ (111903)
10 Sepsis/ (9104)
11 Fecal Incontinence/ or Urinary Incontinence/ (17745)
12 Pruritus/ (5354)
13 exp Postoperative Complications/ (300473)
14 complication/ (0)
15 complication$.ti,ab. (361430)
16 exp drug toxicity/ (14319)
17 pain.ti,ab. (230277)
18 prolaps$.ti,ab. (13207)
19 bleed$.ti,ab. (85602)
20 sepsis.ti,ab. (39656)
21 (anal adj (fistula or stenos$ or fissure$)).ti,ab. (1327)
22 (incontinen$ or urgen$).ti,ab. (48755)
23 (anastomotic adj stricture).ti,ab. (562)
24 (haemorrhoidal adj thrombosis).ti,ab. (2)
25 (itching or pruritis).ti,ab. (3945)
26 (complication$ or reoccur$ or reintervention$ or reoperat$ or retreat$ or redo).ti,ab. (377945)
27 ((further or repeat) adj (surgery or treatment or procedure$)).ti,ab. (7632)
28 (safe or safety or side effect$ or undesirable effect$ or treatment emergent or tolerability or toxicity or adrs or (adverse adj2 (effect or effects or reaction or reactions or outcome or outcomes))).ti,ab. (546926)
29 ae.fs. (968095)
30 co.fs. (1148816)
31 po.fs. (49864)
32 de.fs. (1822105)
33 or/9-32 (4473133)
34 Epidemiologic studies/ (3577)
35 exp case control studies/ (343600)
36 exp cohort studies/ (615580)
37 Case control.tw. (36994)
38 (cohort adj (study or studies)).tw. (29425)
39 Cohort analy$.tw. (1560)
40 (Follow up adj (study or studies)).tw. (25761)
41 (observational adj (study or studies)).tw. (13624)
42 Longitudinal.tw. (72633)
43 Retrospective.tw. (133775)
44 Cross sectional.tw. (67433)
45 Cross-sectional studies/ (72643)
46 or/34-45 (1066266)
47 33 and 46 (482167)
48 8 and 47 (264)
49 animals/ not (animals/ and humans/) (3120839)
50 48 not 49 (264)

Bibliographic Records Retrieved

Total records retrieved: 648
Records entered into the Endnote Library after de-duplication: 531

Resource	Search date	Records	After sift/ deduplication
CINAHL	12/10/06	6	4
EMBASE	12/10/06	378	277
MEDLINE	12/10/06	264	250

10.1.3.5 Length of stay (all haemorrhoid surgeries)

CINAHL - Cumulative Index to Nursing & Allied Health Literature

Searched via: OvidWeb: http://gateway.ovid.com/athens
1982 to November Week 3 2006
Date Searched: 23/11/06
This search strategy retrieved 14 records;
1 Hemorrhoids/ (195)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (184)
3 or/1-2 (257)
4 "Length of Stay"/ (6168)
5 ((hospital or length or duration) adj3 stay).ti,ab. (5301)
6 time to discharge.ti,ab. (27)
7 patient discharge/ (3202)
8 (time adj3 in hospital).ti,ab. (98)
9 day case$.ti,ab. (203)
10 "ambulatory surgery"/ (2327)
11 or/4-10 (14028)
12 3 and 11 (14)

EMBASE

Searched via: OvidWeb: http://gateway.ovid.com/athens
1980 to 2006 Week 46
Date Searched: 23/11/06
This search strategy retrieved 209 records;
1 Hemorrhoid/ (2206)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (2513)
3 or/1-2 (3185)
4 "Length of Stay"/ (18305)
5 ((hospital or length or duration) adj3 stay).ti,ab. (30261)
6 time to discharge.ti,ab. (319)
7 (time adj3 in hospital).ti,ab. (576)
8 day case$.ti,ab. (1663)
9 "ambulatory surgery"/ (3829)
10 or/4-9 (42691)
11 3 and 10 (209)

MEDLINE and MEDLINE In Process

Searched via: OvidWeb: http://gateway.ovid.com/athens
1966 to Present
Date Searched: 23/11/06
This search strategy retrieved 275 records;
1 *Hemorrhoids/ (2347)
2 (hemorrhoid$ or haemorrhoid$ or hemorhoid$ or haemorhoid$ or hemoroid$ or haemoroid$ or piles).ti,ab. (3381)
3 or/1-2 (3644)
4 "Length of Stay"/ (36099)
5 ((hospital or length or duration) adj3 stay).ti,ab. (37522)
6 time to discharge.ti,ab. (346)
7 (time adj3 in hospital).ti,ab. (702)
8 day case$.ti,ab. (1843)
9 "ambulatory surgery"/ (7763)
10 or/4-9 (67405)
11 3 and 10 (275)

Bibliographic Records Retrieved

Total records retrieved: 498
Records entered into the Endnote Library after de-duplication: 353

Resource	Search date	Records	After sift/ deduplication
CINAHL	23/11/06	14	7
EMBASE	23/11/06	209	84
MEDLINE	23/11/06	275	262

10.2 Data extraction form

Study details	Peri-/post-operative outcomes (up to 6 weeks)	Subsequent time points
First author	Mean (SD) minutes operating time	Withdrawals/loss to follow-up
Date of publication	Mean (SD) days hospital stay	Number of patients experiencing pain
Country in which study was conducted	VAS score - nearest to 3 days post-operation or mean of first 7 days	Number of patients with controlled symptoms
Number of participants	VAS score - nearest to 14 days; not a mean of first 14 days	Number of patients with bleeding
Number Male	Number of patients requiring additional IM or oral analgesia	Number of patients with prolapse
Mean age (range) of participants	Number of patients with post-operative bleeding episode	Number of patients with recurrence of haemorrhoidal disease
Number with II, III and IV degree haemorrhoids	Number of patients with a bleeding episode requiring intervention	Number of patients with wound or systemic infection
Number randomised to SH and CH	Mean (SD) days to first bowel movement	Number of patients with incontinence
Stapler gun used	Mean (SD) days to normal activity	Number of patients with urgency
Type of conventional surgery used	Number of patients with wound or systemic infection	Number of patients with haemorrhoidal thrombosis
Type of anaesthesia for stapled	Number of patients with wounds healed at 6 and 12 weeks	Number of patients with submucosal haematoma
Type of anaesthesia for conventional	Number of patients with controlled symptoms	Number of patients with anal stenosis/ anastomotic stricture
Duration of follow-up	Number of patients with residual prolapse	Number of patients with anal fissure
Prior treatment undertaken	Number of patients with urinary retention	Number of patients with anal fistula
Inclusion/exclusion of patients with co-morbid conditions	Number of patients with incontinence	Number of patients with rectovaginal fistula
	Number of patients with urgency	Number of patients with pelvic/perianal sepsis
	Number of patients with haemorrhoidal thrombosis	Number of patients with itching/pruritis
	Number of patients with submucosal haematoma	Number of patients with mucus/slime discharge
	Number of patients with anal stenosis/ anastomotic stricture	Total number of reinterventions per arm of trial
	Number of patients with anal fissure	Number of patients requiring reintervention for prolapse
	Number of patients with anal fistula	Number of patients requiring reintervention for bleeding
	Number of patients with rectovaginal fistula	Number of patients requiring reintervention for pain
	Number of patients with pelvic/perianal sepsis	Number of patients requiring removal of skin tags
	Number of patients with itching/pruritis	Number of patients requiring stapled haemorrhoidopexy
	Number of patients with mucus/slime discharge	Number of patients requiring conventional haemorrhoidectomy
	Mortality	Number of patients requiring RBL
	Overall patient satisfaction	Number of patients requiring injection sclerotherapy
		Number of patients requiring other surgery
		Quality of Life
		Overall patient satisfaction

10.3 Quality assessment

10.3.1 Clinical effectiveness RCTs

The results of the quality assessment for each study. Studies were scored as Yes (Y), No (N) or Unclear (UC) in relation to whether they satisfied each criterion, or the criterion was deemed not applicable (NA).

Study	1. Number randomised reported?	2. Randomisation method appropriate?	3. Allocation concealment adequate?	4. Groups similar at baseline?	5. Study described as double blind?	6a. Patients blinded?	6b. Assessors blinded?	6c. Carers blinded?	7. Were the same surgeons performing both types of operation?	7a. If Yes to 7: Were the surgeons experienced in both operations?	7b. If No to 7: Were the surgeons considered experts at their respective operations?	8. Was a power calculation reported?	9. Were selection/eligibility criteria reported?	10. Was the population recruited representative?	11. Was loss to follow-up reported?	12. Were at least 80% of those randomised followed-up at the final time point?
Ascanelli (2005)[74]	Y	N	N	UC	N	UC	UC	UC	UC	NA	NA	N	Y	N	N	UC
Basdanis (2005)[82]	Y	UC	Y	Y	N	Y	UC	UC	UC	NA	NA	N	N	N	Y	Y
Bikhchandani (2005)[92]	Y	UC	Y	Y	N	UC	UC	UC	UC	N	N	N	Y	N	Y	Y
Boccasanta (2001)[85]	Y	Y	Y	Y	Y	UC	UC	UC	UC	UC	UC	N	Y	N	Y	Y
Cheetham (2003)[77]	Y	Y	Y	Y	N	UC	UC	UC	UC	NA	NA	Y	Y	UC	Y	Y
Chung (2005)[90]	Y	UC	Y	Y	N	UC	Y	UC	Y	UC	UC	Y	Y	N	Y	Y
Correa-Rovelo (2002)[94]	Y	Y	UC	Y	N	UC	Y	UC	UC	UC	UC	N	Y	N	Y	Y
Docherty (2001)[76]	Y	UC	UC	UC	N	UC	UC	UC	UC	UC	UC	UC	N	UC	Y	UC
Gravie (2005)[81]	Y	UC	UC	Y	N	N	UC	UC	UC	NA	NA	N	Y	UC	Y	Y
Hasse (2004)[73]	Y	Y	Y	Y	N	UC	UC	UC	Y	UC	NA	Y	Y	N	Y	Y
Hetzer (2002)[88]	Y	UC	UC	Y	N	UC	UC	UC	Y	Y	NA	N	Y	N	Y	Y
Ho (2000)[61, 69]	Y	UC	Y	Y	N	UC	Y	UC	UC	Y	NA	N	Y	N	Y	N
Kairaluoma (2003)[80]	Y	UC	Y	Y	N	UC	UC	UC	Y	Y	NA	N	Y	N	Y	Y
Kraemer (2005)[28]	Y	Y	UC	Y	N	UC	UC	UC	Y	Y	NA	Y	N	UC	Y	Y
Krska (2003)[79]	Y	UC	UC	UC	N	UC	UC	UC	UC	UC	UC	N	Y	N	Y	Y
Lau (2004)[91]	N	UC	Y	Y	N	UC	UC	UC	UC	NA	NA	Y	Y	UC	Y	Y
Ortiz (2002)[87]	Y	Y	UC	Y	N	UC	Y	UC	Y	Y	NA	Y	Y	N	Y	Y
Ortiz (2005)[86]	Y	Y	UC	Y	N	UC	UC	UC	Y	Y	NA	N	Y	N	Y	Y
Palimento (2003)[68, 84]	Y	Y	UC	Y	N	UC	UC	UC	UC	NA	NA	Y	Y	N	Y	Y
Pavlidis (2002)[83]	Y	UC	UC	Y	N	UC	Y	UC	Y	Y	NA	N	N	Y	UC	UC
Ren (2002)[75]	Y	UC	UC	UC	UC	UC	UC	UC	UC	NA	NA	N	N	N	N	UC
Schmidt (2002)[72]	Y	N	UC	N	N	UC	UC	UC	UC	NA	NA	N	N	N	Y	Y
Senagore (2004)[89]	Y	Y	Y	Y	N	UC	UC	UC	UC	Y	NA	Y	Y	N	Y	N
Shalaby (2001)[93]	Y	Y	UC	N	N	UC	UC	UC	Y	UC	UC	N	N	Y	Y	Y
Thaha (2004)[70, 71]	Y	UC	UC	UC	N	UC	UC	UC	UC	NA	NA	N	N	UC	UC	UC
Van de Stadt (2005)[78]	Y	UC	UC	Y	N	UC	UC	UC	Y	Y	NA	N	Y	N	Y	Y
Wilson (2002)[43]	N	UC	UC	Y	N	UC	UC	UC	UC	UC	UC	Y	N	N	Y	Y

Guidelines for completing the quality assessment

1. Was the number of participants randomised stated?

Yes: Number of people randomised to each arm of the trial was reported

No: Only the total number of participants was reported

Unclear: Only the number that actually received each treatment was reported

2. Was the method of randomisation appropriate?

Yes: Computer generated random numbers or the use of random number tables

No: Any other method of randomisation

Unclear: The study stated that randomisation occurred, but did not report the method

3. Was allocation concealment adequate?

Yes: Any robust method that would not allow the patient status to influence the allocation of surgical procedure

No: Other methods of allocation concealment

Unclear: Either allocation was concealed but the method was not reported, or the concealment of allocation was not reported

4. Were the treatment groups comparable at baseline?

Yes: There were no significant differences between the participants of the treatment arms at baseline

No: There were significant differences between the participants of the treatment arms at baseline

Unclear: Baseline characteristics were not reported

5. Was the study reported as being at least double blind?

Yes: The study was reported as being double or triple blind

No: The study did not report whether it was double blind or not

6. Patients blinded?

Yes: Patients were blinded to surgical procedure

No: Patients were not blinded to surgical procedure

Unclear: Blinding of patients was not reported

7. Outcome assessors blinded?

Yes: Outcome assessors were blinded to surgical procedure

No: Outcome assessors were not blinded to surgical procedure

Unclear: Blinding of outcome assessors was not reported

8. Care givers blinded?

Yes: Care givers were blinded to surgical procedure

No: Care givers were not blinded to surgical procedure

Unclear: Blinding of care givers was not reported

9. Same surgeon(s) used for SH and CH?

Yes: The surgeons involved in the study undertook both SH and CH procedures

No: One (or more) surgeon undertook only SH, another (others) undertook only CH

Unclear: Which surgeons undertook surgery was not reported

9a. If Qu. 9 yes: Were the surgeons experienced in both techniques?

Yes: The surgeons were reported as being experienced in both techniques

Unclear: The experience of the surgeons was not reported

Not applicable: Answer to 9 was No

9b. If Qu. 9 no: Were the surgeons considered expert in the technique they undertook?

Yes: The surgeons were reported as being experts in their respective technique

Unclear: The expertise of the surgeons was not reported

Not applicable: Answer to 9 was Yes

10. Power calculation used?

Yes: Power calculation used

No: Power calculation not used, or it's use was not reported

11. Selection/eligibility criteria reported?

Yes: Selection/eligibility criteria were reported

No: Selection/eligibility criteria were not reported

12. Representative population recruited?

Yes: Recruitment of a consecutive sample of patients presenting with prolapsed haemorrhoids who were candidates for surgery, or all patients presenting with prolapsed haemorrhoids who were candidates for surgery were included in the study.

No: A non-consecutive sample of patients recruited, or some people were unacceptably excluded who would be considered for haemorrhoidectomy in practice (i.e. people with II or IV degree)

Unclear: Recruitment details were not reported

13. Loss to follow-up reported/explained?

Yes: Loss to follow-up reported/explained

No: Loss to follow-up not reported/explained

14. Were at least 80% of those randomised followed-up?

Yes: At least 80% followed-up at the final time point reported

No: <80% followed-up at the final time point reported

Unclear: Loss to follow-up was not reported

10.3.2 Economic evaluation

The results of the quality assessment of Farinetti, 2000 [65], scored as Yes (Y), No (N), Not applicable (NA), NU = Not undertaken, P=Partial, or U=Uncertain.

Study question	
Were costs & effects examined	N
Alternatives compared	Y
Viewpoint/s clearly stated	Y
Selection of alternatives	
All relevant alternatives compared	Y
For the alternatives compared were all clearly described	Y
Rationale for choosing the alternative programmes compared is stated	Y
Form of evaluation	
Choice of form of economic evaluation is justified in relation to questions addressed	Y
If a cost-minimisation analysis is chosen, have equivalent outcomes been adequately demonstrated	N
Effectiveness data	
The source of effectiveness estimates used are stated	NA
Effectiveness data from RCT or review of RCTs	NA
Potential biases identified	NA
Details of method of synthesis or meta-analysis of estimates are given	NA
Costs	
All the important & relevant resource use included	Y
All the important & relevant resource use measured accurately	Y
Appropriate unit costs estimated	Y
Unit costs reported separately from resource use data	Y
If productivity costs were included, were they treated separately from other costs	NU
The year & country to which unit costs apply is stated with appropriate adjustments for inflation &/or currency conversion	N
Benefit measurement & valuation	
The primary outcome measure for the economic evaluation is clearly stated	NA
Methods to value health states & other benefits are stated	NA
Details of the individuals from whom valuations were obtained are given	NA
Decision modelling	
Details of any model used are given	NU
The choice of model used & the key input parameters on which it is based are adequately detailed & justified	NA
All model outputs described adequately	NA
Discounting	
Discount rate used for both costs & benefits	NA
Do discount rates accord with NHS guidance	NA
Stochastic analysis of patient-level data	
Details of statistical tests & confidence intervals are given for stochastic data	NU
Uncertainty around cost-effectiveness estimates expressed	NA
Sensitivity analysis used to assess uncertainty in non-stochastic variables and analytic methods	NA
Stochastic analysis of decision models	
Are all appropriate input parameters included with uncertainty?	
Is second-order uncertainty (uncertainty in means) included rather than first order uncertainty (uncertainty between patients)	NA
Are the probability distributions adequately detailed & appropriate?	NA
Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs) & analytic decisions (e.g. methods to handle missing data)	NA
Deterministic analysis	
The approach to sensitivity analysis is given	NU
The choice of variables for sensitivity analysis is justified	NA
The ranges over which the variables are varied are stated	NA
Presentation of results	
Incremental analysis is reported using appropriate decision rules	Y
Major outcomes are presented in a disaggregated as well as an aggregated form	NU
Applicable to the UK setting	N

10.4 Bayesian meta-regression of VAS pain scores

The relationship between VAS pain score, days from primary surgery and treatment was explored further using Bayesian meta-regression. All RCTs were that reported mean VAS score at one or more time points during the post operative period were included. The mean responses yit of study i at time t were assumed to be normally distributed yit ~ N(mu it, sigma^2 w it). Different functional forms for the mean response mu it were tested, and compared using deviance information criteria.

Model 1: Mu it = b0 i + b1* Treat + b2 * Time + b3* Treat* Time

Model 2: Log(mu it) = b0 i + b1* Treat + b2*Time

The slope coefficients b1, b2 and b3 were assumed constant and the intercepts b0 i were assumed to vary independently from one trial to another drawn from a common normal distribution with mean E(b0 i) = b and Var(b0 i) = sigma^2 b. The unobservable deviations between the population mean baseline VAS score b and the trial specific realisations b i may be interpreted as effects of unobserved characteristics, which might include among other things the selection of participants, the skill of the surgeons or the administration of the VAS instrument. The within-study sample standard deviation sigma w it was not reported in every trial i or at every time point t. This missing data were imputed by treating them as parameters in the model to be estimated, assuming the standard deviations sigma w it were independently and identically distributed random variables with uninformative uniform priors. Using a Bayesian perspective, the slope coefficients were given uninformative normal priors and the between-study standard deviation was given an uninformative uniform prior. The intercept represents the mean VAS score in the CH group at day 5. The coefficients for the linear and log-linear model are not directly comparable. The exponential of the parameters in the log-linear model have a multiplicative effect on the predicted VAS score whereas the parameters in the linear model have an additive effect.

The results are shown for each functional form of the model in Table 10.1. Both models show that pain declines over time and that the SH procedure is less painful on average. The functional form which fits the observed data best according to the DIC is model 1, the linear model with an interaction term between time from procedure and treatment group. This model predicts that VAS pain is on average 3.0 in the SH group and 5.3 in the CH group at day 1, decreasing to less than 0.5 (on a scale of 0 to 10) in both groups at 21 days. It is therefore not meaningful to extrapolate to time points beyond this date using this model. The between study standard error is high (more) indicating that the studies are heterogeneous for this outcome.

Table 10.1: Results of the meta-regression of VAS pain score during the post-operative period

	Model 1: linear		Model 2: log-linear		
	Mean	**SE**	**Mean**	**SE**	**Exp(coefficient)**
Population mean	4.367	.582	1.294	0.211	3.647
Treatment	-1.891	.1895	-.4317	.0452	0.649
Days	-.2516	.0354	-.0506	.0054	0.951
Days * Treat	.109	.0373	NA	NA	NA
Between –study standard error	1.663	.5172	.6135	.1931	NA
DIC	179		201		NA

10.5 Data extraction tables

10.5.1 Clinical effectiveness RCTs

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Ascanelli (2005)[74] Country: Italy Trial dates: Start: 2001 Finish: 2003 Language: Italian	Total: 100 SH: 50 CH: 50 % Loss to follow-up at final time point: Not reported	Age: Range: 30-73 Number male 21	Grades included II+III Grade II: Not reported Grade III: Not reported Grade IV: Not reported	Stapling gun: Mechanical suture Comparator: M&M + diathermy Anaesthesia: SH: Combination CH: Combination	**Post-operative** Bleeding: Intervention required <4 days SH: 0/50; CH: 0/50 Analgesics: Opioid oral SH: 2/50; CH: 4/50 10 pt VAS score up to 7 days: SH: Mean: 2; CH: Mean: 7 (estimated from figure) 10 pt VAS score at 10 to 15 days: SH: Mean: 0; CH: Mean: 3 (estimated from figure) Operating time (minutes): SH: Mean: 22 Range: 18-38; CH: Mean: 35 Range: 30-45 Duration of stay (days): SH: Mean: 0.75 Range: 0.25-1.67; CH: Mean: 0.92 Range: 0.25-2 Time to normal activity (days): SH: Range: 10-25; CH: Range: 20-45 **12 months** Bleeding: SH: 2/50; CH: 0/50 Urgency: SH: 3/50; CH: 0/50 Anal stenosis/anastomotic stricture: SH: 0/50; CH: 1/50 Incontinence: SH: 0/50; CH: 1/50 Reintervention Total: SH: 2/50; CH: 0/50 Reintervention Bleeding: SH: 2/50; CH: 0/50 Reintervention Sclerotherapy: SH: 2/50; CH: 0/50 **Additional outcomes reported in the study** None

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Basdanis (2005)[82] Country: Greece Trial dates: Start: 2000 Finish: 2002 Language: English	Total: 95 SH: 50 CH: 45 % Loss to follow-up at final time point:5%	Age: Range: 22-72 Number male 54	Grades included III+IV Grade III: 73 Grade IV: 22	Stapling gun: PPH 01 Comparator: M&M + diathermy and ligasure Anaesthesia: SH: Combination CH: Combination	**Post-operative** All bleeding <4 days SH: 10/50; CH: 21/45 All bleeding >10 days SH: 0/50; CH: 1/45 Bleeding: Intervention required <4 days SH: 1/50; CH: 1/45 Itching/pruritis: SH: 2/50; CH: 1/45 Pelvic/perianal sepsis/septic shock: SH: 0/50; CH: 0/45 Urinary retention: SH: 7/50; CH: 5/45 Wounds healed at 6 weeks: SH: 50/50; CH: 45/45 10 pt VAS score up to 7 days: SH: Median: 3 Range: 1-6; CH: Median: 6 Range: 3-7 Operating time (minutes): SH: Median: 15 Range: 8-17; CH: Median: 13 Range: 9.2-16.1 Duration of stay (days): SH: SH: Mean: 1.6 Range: 1-2; CH: Mean: 2.1 Range: 2-3 Time to normal activity (days): SH: Mean: 6.3 SD: 1.5; CH: Mean: 9.8 SD: 1.9 **>6 weeks and < 1 year** Prolapse: SH: 3/50; CH: 0/40 Pelvic/perianal sepsis SH: 0/50; CH: 0/40 Rectovaginal fistula SH: 0/50; CH: 0/40 **Additional outcomes reported in the study** Maximal VAS pain score 24 hours after surgery Pain at stool evacuation 24 hours and 1 week after surgery Mean use of intravenous diclofenac 24 hours after surgery Median VAS pain score 8 hours post operation Number of patients with tenderness to digital rectal examination Faecal impaction requiring enema immeidately post-operatively and one month post surgery. Authors state that follow-up occurred at 12 and 24 months, however, no results from these follow-up times other than the recurrence in the stapled group were reported

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Bikhchandani (2005)[92] Country: India Trial dates: Start: 2001 Finish: 2003 Language: English	Total: 84 SH: 42 CH: 42 % Loss to follow-up at final time point: 6%	Age: Mean: 47 Variance Not reported Number male 70	Grades included III+IV Grade III: 71 Grade IV: 13	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Regional CH: Regional 2 required conversion to general - not specified if these were undergoing SH or CH	**Post-operative** Bleeding: Intervention required <4 days SH: 1/42; CH: 1/42 Infection: Systemic SH: 1/42; CH: 0/42 Pelvic/perianal sepsis/septic shock: SH: 0/42; CH: 0/42 Residual prolapse: SH: 2/42; CH: 0/42 Urinary retention: SH: 5/42; CH: 7/42 10 pt VAS score up to 7 days: SH: Mean: 1.52 SD: 1.43; CH: Mean: 4.5 SD: 2.11 10 pt VAS score at 10 to 15 days: SH: Mean: 0.21 SD: 0.52; CH: Mean: 1.05 SD: 1.21 Operating time (minutes): SH: Mean: 24.28 SD: 4.25; CH: Mean: 45.21 SD: 5.36 Duration of stay (days): SH: Mean: 1.24 SD: 0.62; CH: Mean: 2.76 SD: 1.01 Time to first bowel movement (days): SH: Mean: 2.16 SD: 0.79; CH: Mean: 2.33 SD: 0.79 Time to normal activity (days): SH: Mean: 8.12 SD: 2.48; CH: Mean: 17.62 SD: 5.59 >6 weeks and < 1 year Anal stenosis/anastomotic stricture SH: 0/39; CH: 0/40 Incontinence SH: 3/39; CH: 4/40 Pain SH: 0/39; CH: 5/40 Pelvic/perianal sepsis SH: 0/39; CH: 0/40 Rectovaginal fistula SH: 0/39; CH: 0/40 **Additional outcomes reported in the study** Mean VAS score at first bowel motion Mean doses of analgesics Mean blood loss (ml) Number of patients with skin tags and increased fequency of stools

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Boccasanta (2001)[85, 120] Country: Italy Trial dates: Start: 1996 Finish: 1999 Language: English	Total: 80 SH: 40 CH: 40 % Loss to follow-up at final time point: Not reported	Age: Mean: 51 Range: 21-92 Number male 33	Grades included IV Grade IV: 80	Stapling gun: PPH 01 Comparator: M&M + HLB Anaesthesia: SH: Combination CH: Combination	**Post-operative** Bleeding: All bleeding <4 days SH: 2/40; CH: 3/40 Bleeding: Intervention required <4 days SH: 0/40; CH: 2/40 Urinary retention: SH: 2/40; CH: 2/40 Haemorrhoidal thrombosis: SH: 2/40; CH: 6/40 10 pt VAS score up to 7 days: SH: Mean: 4; CH: Mean: 6.5 (estimated from figure) 10 pt VAS score at 10 to 15 days: SH: Mean: 2.7; CH: Mean: 3.8 (estimated from figure) Operating time (minutes): SH: Mean: 25 SD: 3.1; CH: Mean: 50 SD: 5.3 Duration of stay (days): SH: Mean: 2 SD: 0.5; CH: Mean: 3 SD: 0.4 Time to normal activity (days): SH: Mean: 8 SD: 0.9; CH: Mean: 15 SD: 1.4 **>6 weeks and < 1 year** Prolapse: SH: 0/40; CH: 0/40 Bleeding: SH: 0/40; CH: 2/40 Anal stenosis/anastomotic stricture: SH: 2/40; CH: 3/40 Incontinence: SH: 1/40; CH: 1/40 Reintervention: Total SH: 2/40; CH: 3/40 **Additional outcomes reported in the study** Number of patients scoring >5 on VAS scale Monometry: mean resting pressure (mm Hg), squeeze pressure (mm Hg), maximum tolerable volume(mm Hg), rectal inhibitory reflex (mm Hg). Number of patients with skin tags

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Cheetham (2003)[77, 121] Country: UK Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 31 SH: 15 CH: 16 % Loss to follow-up at final time point: 3%	Age: Range: 26-72 Number male 22	Grades included Not reported States that all participants had symptomatic prolapsing haemorrhoids	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General	**Post-operative** Residual prolapse: SH: 2/15; CH: 0/16 Urinary retention: SH: 0/15; CH: 0/16 Symptoms controlled: >10 days SH: 8/15; CH: 11/16 Anal fissure: SH: 1/15; CH: 0/16 Bleeding: All bleeding >10 days SH: 4/15; CH: 1/16 Bleeding: Intervention required <4 days SH: 2/15; CH: 0/16 Day cases: SH: 12/15; CH: 14/16 Analgesics: Injections (not specified/combination) SH: 2/15; CH: 0/16 Wounds healed at 6 weeks: SH: 15/15; CH: 14/16 Wounds healed at 12 weeks: SH: 15/15; CH: 15/16 10 pt VAS score up to 7 days: SH: Median: 2.8; CH: Median: 7 (converted from 100 point scale; estimated from figure) 10 pt VAS score at 10 to 15 days: SH: Median: 0.7; CH: Median: 2.3 Time to normal activity (days): SH: Median: 10 Range: 3-38; CH: Median: 14 Range: 3-21 **>6 weeks and < 1 year** Prolapse: SH: 2/14; CH: 1/16 Bleeding: SH: 4/14; CH: 3/16 Pain: SH: 7/14; CH: 2/16 Urgency: SH: 3/14; CH: 0/16 Symptoms controlled: SH: 5/14; CH: 11/16 **Additional outcomes reported in the study** Median maximal pain and expectation VAS score Number of patients with symptomatic external haemorrhoids

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Chung (2005)[90] Country: China Trial dates: Start: 2001 Finish: 2003 Language: English	Total: 88 SH: 43 CH: 45 % Loss to follow-up at final time point: 0%	Age: Mean: 45.7 Variance Not reported Number male 59	Grades included III Grade III: 88	Stapling gun: PPH 01 Comparator: M&M + Harmonic Scalpel Anaesthesia: SH: Combination CH: Combination	**Post-operative** Bleeding: All bleeding <4 days SH: 1/43; CH: 2/45 Bleeding: Intervention required <4 days SH: 1/43; CH: 1/45 Faecal incontinence: SH: 0/43; CH: 0/45 Haemorrhoidal thrombosis: SH: 2/43; CH: 0/45 Infection: Systemic SH: 0/43; CH: 0/45 Infection: Wound SH: 0/43; CH: 0/45 Urgency: SH: 0/43; CH: 0/45 Urinary retention: SH: 3/43; CH: 2/45 10 pt VAS score up to 7 days: SH: Median: 1.5 Range: 0.7-6.0; CH: Median: 3.5 Range: 1.9-6.0 Operating time (minutes): SH: Mean: 17 SD: 7.3; CH: Mean: 18.5 SD: 6.4 Time to first bowel movement (days): SH: Median: Range: 1-3; CH: Median: 2 Range: 1-4 Duration of stay (days): SH: Median: 1 Range: 1-5; CH: Median: 3 Range: 2-5 Time to normal activity (days): SH: Mean: 6.7 SD: 4.3; CH: Mean: 15.6 SD: 6.0 **>6 weeks and < 1 year** Incontinence: SH: 0/43; CH: 0/45 Symptoms controlled: SH: 41/43; CH: 43/45 Urgency: SH: 0/43; CH: 0/45 **Additional outcomes reported in the study** Mean blood loss (cc)

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Correa-Rovelo (2002)[94] Country: Mexico Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 84 SH: 42 CH: 42 % Loss to follow-up at final time point: 2%	Age: Mean: 45.15 Range: 27-77 Number male 41	Grades included III+IV Grade III: 60 Grade IV 24	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Combination CH: Regional	**Post-operative** Bleeding: All bleeding <4 days SH: 1/42; CH: 0/42 Bleeding: All bleeding >10 days SH: 14/42; CH: 23/42 Bleeding: Intervention required <4 days SH: 1/42; CH: 0/42 Faecal incontinence: SH: 0/42; CH: 1/42 Anal stenosis/anastomotic stricture: SH: 1/42; CH: 1/42 Haemorrhoidal thrombosis: SH: 0/42; CH: 0/42 Itching/pruritis: SH: 1/42; CH: 2/42 Symptoms controlled: >10 days SH: 31/41; CH: 28/41 Analgesics: Other injections SH: 21/42; CH: 42/42 Urgency: SH: 0/42; CH: 1/42 Urinary retention: SH: 1/42; CH: 3/42 Wounds healed at 6 weeks: SH: 41/41; CH: 37/41 10 pt VAS score up to 7 days: SH: Mean: 2.8 SD: 1.4; CH: Mean: 5.5 SD: 1.4 10 pt VAS score at 10 to 15 days: SH: Mean: 1. SD: 1.4; CH: Mean: 3.7 SD: 1.5 Operating time (minutes): SH: Mean: 11.9 SD: 3.1; CH: Mean: 46.4 SD: 10.4 Time to first bowel movement (days): SH: Mean: 1.1 SD: 0.3; CH: Mean: 1.43 SD: 0.59 Time to normal activity (days): SH: Mean: 6.1 SD: 3.5; CH: Mean: 15.2 SD: 4.8 **>6 weeks and < 1 year** Prolapse: SH: 1/41; CH: 0/41 Pain: SH: 2/41; CH: 3/41 Bleeding: SH: 8/41; CH: 2/41 Anal stenosis/anastomotic stricture: SH: 1/41; CH: 1/41 Incontinence: SH: 0/41; CH: 2/41 Haemorrhoidal thrombosis: SH: 0/41; CH: 0/41 Itching/pruritis: SH: 2/41; CH: 4/41 Symptoms controlled: SH: 32/41; CH: 35/41 Reintervention Total: SH: 1/41; CH: 0/41 Reintervention Prolapse: SH: 1/41; CH: 0/41 Reintervention Bleeding: SH: 1/41; CH: 0/41 Reintervention RBL: SH: 1/41; CH: 0/41 **Additional outcomes reported in the study** Mean maximum pain score during first 24h Mean and SD and range days taking ketorolac Number of patients with submucosal haemotoma, faecal impaction, skin tags; dyspareunia; Number of patients willing to undergo same surgery

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Docherty (2001)[76] Country: UK Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 46 SH: 26 CH: 20 % Loss to follow-up at final time point: Not reported	Age: Not reported Number male Not reported	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** All bleeding <4 days SH: 0/26; CH: 2/20 Bleeding: Intervention required <4 days SH: 0/26; CH: 2/20 Urinary retention: SH: 3/26; CH: 4/20 **12 months** Reintervention Total: SH: 5/26; CH: 4/20 Reintervention CH: SH: 4/26; CH: 0/20 Reintervention RBL: SH: 1/26; CH: 1/20 **Additional outcomes reported in the study** None
Gravie (2005)[81] Country: France Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 126 SH: 63 CH: 63 % Loss to follow-up at final time point: 13.5%	Age: Mean: 47.5 Variance Not reported Number male Not reported	Grades included Not reported Stated that 85% had reducable prolapse, 5% had non-reducible and 5 patients had no prolapse	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** Analgesics: Opioid injections SH: 11/63; CH: 24/63 Analgesics: Oral (not specified/combination) SH: 62/63; CH: 62/63 Duration of stay (days): SH: Mean: 2.2 SD: 1.2; CH: Mean: 3.1 SD: 1.7 Time to first bowel movement (days): SH: Mean: 1.6 SD: 1; CH: Mean: 2.1 SD: 1.1 Time to normal activity (days): SH: SH: Mean: 14 SD: 10; CH: Mean: 24 SD: 13 **>6 weeks and < 1 year** Reintervention: Bleeding SH: 2/63; CH: 0/63 Reintervention CH: SH: 1/63; CH: 0/63 Reintervention: Total SH: 3/63; CH: 3/63 **2 years** Prolapse: SH: 4/52; CH: 1/57 Reintervention: Total SH: 0/52; CH: 0/57 **Additional outcomes reported in the study** Mean consumption of analgesics, VAS score on defecation, comparability of VAS scores at different times of day. Proportion of patients with improved symptoms (pain, bleeding, itching, urgency, constipation, incontinence and tenesmus) Proportion of patients for which the intervention was effective for skin tags and external, hypertrophic haemorrhoids Number of patients with fecaloma; tenesmus and problems discrimitating gas and stool

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Hasse (2004)[73] Country: Germany Trial dates: Start: 1998 Finish: 2001 Language: German	Total: 80 SH: 40 CH: 40 % Loss to follow-up at final time point: 5%	Age: Mean: 47.1 Variance: Not reported Number male 39	Grades included III Grade III: 80	Stapling gun: PPH 01 Comparator: Fransler and Anderson Anaesthesia: SH: General CH: General	**Post-operative** Bleeding: Intervention required <4 days SH: 3/40; CH: 1/40 Anal stenosis/anastomotic stricture: SH: 3/40; CH: 0/40 Symptoms controlled: >10 days SH: 31/40; CH: 28/40 Wounds healed at 6 weeks: SH: 38/40; CH: 19/40 Operating time (minutes): SH: Mean: 16.3 SD: 0.; CH: Mean: 49 SD: 11.8 Duration of stay (days): SH: Mean: 1 SD: 0.5; CH: Mean: 4 SD: 0.7 Time to normal activity (days): SH: Mean: 11.2 SD: 7.1; CH: Mean: 21.2 SD: 9.2 **>6 weeks and < 1 year** Symptoms controlled: SH: 32/38; CH: 21/38 **12 months** Prolapse: SH: 6/38; CH: 0/38 Bleeding: SH: 3/38; CH: 1/38 Symptoms controlled: SH: 33/38; CH: 29/38 **Additional outcomes reported in the study** None

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Hetzer (2002)[88] Country: Switzerland Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 40 SH: 20 CH: 20 % Loss to follow-up at final time point: 0%	Age: Mean: 47.6 Range: 28-74 Number male 29	Grades included II+III Grade II: 12 Grade III: 28	Stapling gun: PPH 01 Comparator: Ferguson Anaesthesia: SH: Combination CH: Combination	**Post-operative** All bleeding <4 days SH: 2/20; CH: 0/20 Bleeding: Intervention required <4 days SH: 2/20; CH: 0/20 Faecal incontinence: SH: 0/20; CH: 0/20 Haemorrhoidal thrombosis: SH: 1/20; CH: 0/20 Mortality: SH: 0/20; CH: 0/20 Urinary retention: SH: 0/20; CH: 1/20 10 pt VAS score up to 7 days: SH: Mean: 0.8 Range: 0-3; CH: Mean: 5.4 Range: 1-9 Wounds healed at 6 weeks: SH: 20/20; CH: 16/20 Wounds healed at 12 weeks: SH: 20/20; CH: 16/20 Operating time (minutes): SH: Median: 30 Range: 15-45; CH: Median: 43 Range: 25-60 Duration of stay (days): SH: Mean: 2.4 Range: 1-4; CH: Mean: 2.1 Range: 1-4 Time to normal activity (days): SH: Mean: 6.7 Range: 2-14; CH: Mean: 20.7 Range: 7-45 **12 months** Pain: SH: 0/20; CH: 0/20 Prolapse: SH: 1/20; CH: 1/20 Anal stenosis/anastomotic stricture: SH: 0/20; CH: 0/20 Faecal incontinence: SH: 0/20; CH: 0/20 Reintervention: Total SH: 1/20; CH: 1/20 Reintervention: Prolapse SH: 1/20; CH: 1/20 Reintervention: RBL SH: 1/20; CH: 1/20 **Additional outcomes reported in the study** Histologic examinations of resected specimens Williams incontinence score

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Ho (2000)[61, 69] Country: Singapore Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 119 SH: 57 CH: 62 % Loss to follow-up at final time point: 49.5%	Age: Mean: 48.6 Variance Not reported Number male 59	Grades included II+III Grade II: Not reported Grade III: Not reported Grade IV: Not reported	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General	**Post-operative** All bleeding <4 days SH: 2/57; CH: 0/62 All bleeding >10 days SH: 19/57; CH: 33/62 Bleeding: Intervention required <4 days SH: 0/57; CH: 0/62 Bleeding: Intervention required >10 days SH: 0/57; CH: 3/62 Anal stenosis/anastomotic stricture: SH: 5/57; CH: 5/62 Faecal incontinence: SH: 0/57; CH: 2/62 Urinary retention: SH: 1/57; CH: 0/62 Haemorrhoidal thrombosis: SH: 1/57; CH: 0/62 Infection: Systemic SH: 0/57; CH: 1/62 Itching/pruritis: SH: 5/57; CH: 11/62 Mucus/slime discharge: SH: 0/57; CH: 3/62 Pelvic/perianal sepsis/septic shock: SH: 0/57; CH: 0/62 Wounds healed at 6 weeks: SH: 57/57; CH: 53/62 Wounds healed at 12 weeks: SH: 57/57; CH: 62/62 Pain: 10 pt VAS score up to 7 days: SH: Mean: 4.5 SE: 0.4; CH: Mean: 5 SE: 0.4 Pain: 10 pt VAS score at 10 to 15 days: SH: Mean: 3.8 SE: 0.5; CH: Mean: 4.8 SE: 0.4 Operating time (minutes): SH: Mean: 17.6 SE: 1.3; CH: Mean: 11.4 SE: 0.9 Duration of stay (days): SH: Mean: 2.1 SE: 0.1; CH: Mean: 2 SE: 0.1 Time to normal activity (days): SH: Mean: 17.1 SE: 1.9; CH: Mean: 22.9 SE: 1.8 **>6 weeks and < 1 year** Pain: SH: 1/57; CH: 3/62 Bleeding: SH: 1/57; CH: 2/62 Incontinence: SH: 0/57; CH: 1/62 Itching/pruritis: SH: 2/57; CH: 2/62 Pelvic/perianal sepsis: SH: 0/57; CH: 0/62 **18 months** Pain: SH: 1/27; CH: 1/33 Prolapse: SH: 3/27; CH: 1/33 Itching/pruritis: SH: 1/27; CH: 2/33 Reintervention Total: SH: 2/27; CH: 4/33 Reintervention CH: SH: 1/27; CH: 1/33 Reintervention RBL: SH: 0/27; CH: 1/33 **Additional outcomes reported in the study** Maximum pain score in hosp, and 2, and 6 weeks and at bowel movement Number of patients with tenderness at DRE; perception of skin tags; observer noted skin tags; faecal impaction; who had a bowel movement prior to discharge Mean and SE bowel movements/week

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Kairaluoma (2003)[80] Country: Finland Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 60 SH: 30 CH: 30 % Loss to follow-up at final time point: 0%	Age: Range: 17-65 Number male 32	Grades included III Grade III: 60	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General	**Post-operative** Anal stenosis/anastomotic stricture: SH: 1/30; CH: 1/30 All bleeding <4 days SH: 2/30; CH: 0/30 All bleeding >10 days SH: 10/30; CH: 2/30 Bleeding: Intervention required <4 days SH: 2/30; CH: 0/30 Day cases: SH: 30/30; CH: 30/30 Infection: Systemic SH: 1/30; CH: 1/30 Faecal incontinence: SH: 4/30; CH: 2/30 Residual prolapse: SH: 12/30; CH: 1/30 Symptoms controlled: >10 days SH: 15/30; CH: 27/30 10 pt VAS score up to 7 days: SH: Median: 3.36; CH: Median: 5.88 (estimated from figure) 10 pt VAS score at 10 to 15 days: SH: Median: 0; CH: Median: 1.47 (estimated from figure) Operating time (minutes): SH: Mean: 21.86 SD: 9.09; CH: Mean: 22.46 SD: 6.409 Time to normal activity (days): SH: Median: 8 Range: 1-21; CH: Median: 14 Range: 1-33 **12 months** Prolapse: SH: 5/30; CH: 0/30 Bleeding: SH: 4/30; CH: 1/30 Incontinence: SH: 3/30; CH: 1/30 Pain: SH: 0/30; CH: 0/30 Symptoms controlled: SH: 22/30; CH: 28/30 Reintervention: Total SH: 8/30; CH: 1/30 Reintervention: Prolapse SH: 7/30; CH: 1/30 Reintervention: Bleeding SH: 7/30; CH: 1/30 Reintervention: CH SH: 4/30; CH: 0/30 Reintervention: RBL SH: 3/30; CH: 1/30 Reintervention: Skin tag removal SH: 1/30; CH: 0/30 **Additional outcomes reported in the study** Number of patients constipation; feeling a lump; feeling of incompleteness on defecation; or feeling a blockage

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Kraemer (2005)[28] Country: Germany Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 50 SH: 25 CH: 25 % Loss to follow-up at final time point: 0%	Age: Range: 28-82 Number male 27	Grades included III+IV Grade III: 46 Grade IV: 4	Stapling gun: PPH 01 Comparator: M&M + ligasure. Fransler-Arnold segmental plastic reconstruction in 6 patients Anaesthesia: SH: Combination CH: Combination	**Post-operatvie** Anal fissure: SH: 0/25; CH: 1/25 Anal stenosis/anastomotic stricture: SH: 0/25; CH: 1/25 All bleeding <4 days SH: 0/25; CH: 1/25 All bleeding >10 days SH: 3/25; CH: 4/25 Faecal incontinence: SH: 0/25; CH: 0/25 Itching/pruritis: SH: 2/25; CH: 1/25 Analgesics: Opioid injections SH: 1/25; CH: 0/25 Analgesics: Oral (not specified/combination) SH: 25/25; CH: 25/25 Residual prolapse: SH: 2/25; CH: 0/25 Symptoms controlled: >10 days SH: 21/25; CH: 21/25 Urinary retention: SH: 4/25; CH: 2/25 Duration of stay (days): SH: Mean: 4 Range: 2-10; CH: Mean: 5 Range: 2-10 Operating time (minutes): SH: Mean: 21 Range: 6-54; CH: Mean: 26 Range: 10-80 Pain: 10 pt VAS score up to 7 days:: SH: Mean: 4.2; CH: Mean: 3.7 Pain: 10 pt VAS score at 10 to 15 days:: SH: Mean: 2.3; CH: Mean: 2.4 Time to first bowel movement (days): SH: Mean: 2 Range: 1-4; CH: Mean: 3 Range: 1-5 **Additional outcomes reported in the study** None

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Krska (2003)[79] Country: Czech Republic Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 50 SH: 25 CH: 25 % Loss to follow-up at final time point: 0%	Age: Mean: 50.8 Variance Not reported Number male 37	Grades included III Grade III: 50	Stapling gun: Not reported Comparator: M&M Anaesthesia: SH: Regional CH: Regional	**Post-operative** Anal fissure: SH: 0/25; CH: 0/25 Anal stenosis/anastomotic stricture: SH: 0/25; CH: 0/25 Faecal incontinence: SH: 0/25; CH: 0/25 Haemorrhoidal thrombosis: SH: 0/25; CH: 0/25 Infection: Systemic SH: 0/25; CH: 0/25 Infection: Wound SH: 0/25; CH: 0/25 Mortality: SH: 0/25; CH: 0/25 Pelvic/perianal sepsis/septic shock: SH: 0/25; CH: 0/25 Residual prolapse: SH: 0/25; CH: 0/25 Urgency: SH: 0/25; CH: 0/25 Urinary retention: SH: 0/25; CH: 0/25 10 pt VAS score up to 7 days: SH: Mean: 4; CH: Mean: 7.4 (converted from a 5 point scale) Bleeding: All bleeding <4 days SH: 0/25; CH: 1/25 Bleeding: Intervention required <4 days SH: 0/25; CH: 1/25 Duration of stay (days): SH: Mean: 3.5; CH: Mean: 6.2 Operating time (minutes): SH: Mean: 28; CH: Mean: 46 Time to normal activity (days): SH: Mean: 12; CH: Mean: 25.3 **Additional outcomes reported in the study** None
Lau (2004)[91] Country: Hong Kong Trial dates: Start: 2001 Finish: 2002 Language: English	Total: 24 SH: 13 CH: 11 % Loss to follow-up at final time point: 0%	Age: Mean: 49.1 Variance: Not reported Number male 11	Grades included II-IV Grade II: 13 Grade III: 6 Grade IV: 4 1 patient not classified	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: General CH: General	**Post-operative** Residual prolapse: SH: 6/13; CH: 1/11 All bleeding <4 days SH: 0/13; CH: 0/11 Bleeding: Intervention required <4 days SH: 0/13; CH: 0/11 Faecal incontinence: SH: 0/13; CH: 0/11 Itching/pruritis: SH: 1/13; CH: 4/11 Urinary retention: SH: 0/13; CH: 1/11 10 pt VAS score up to 7 days: SH: 3.5 SD: 2.5; CH: Mean: 2.6 SD: 1.5 Operating time (minutes): SH: Mean: 35.4 SD: 9.89; CH: Mean: 29.8 SD: 13.01 Duration of stay (days): SH: Mean: 1.44 SD: 0.53; CH: Mean: 2.13 SD: 0.84 **Additional outcomes reported in the study** None

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Ortiz (2002)[87] Country: Spain Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 55 SH: 27 CH: 28 % Loss to follow-up at final time point: 0%	Age: Mean: 47.6 Variance Not reported Number male 32	Grades included III+IV Grade III: 29 Grade IV: 26	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional	**Post-operative** Residual prolapse: SH: 0/27; CH: 0/28 Bleeding: Intervention required <4 days SH: 0/27; CH: 1/28 Haemorrhoidal thrombosis: SH: 1/27; CH: 0/28 Infection: Wound SH: 1/27; CH: 1/28 Analgesics: Injections (not specified/combination) SH: 3/27; CH: 5/28 Analgesics: Oral (not specified/combination) SH: 27/27; CH: 28/28 Urinary retention: SH: 6/27; CH: 10/28 Operating time (minutes): SH: Mean: 19 Range: 14-35; CH: Mean: 33.5 Range: 15-90 Time to first bowel movement (days): SH: Mean: 2.9 Range: 0-5; CH: Mean: 3.2 Range: 1-6 Time to normal activity (days): SH: Mean: 23.1 Range: 0-98; CH: Mean: 26.6 Range: 0-112 **16 months** Prolapse: SH: 7/27; CH: 0/28 Pain: SH: 1/27; CH: 0/28 Bleeding: SH: 2/27; CH: 1/28 Incontinence: SH: 0/27; CH: 0/28 Urgency: SH: 2/27; CH: 4/28 Anal stenosis/anastomotic stricture: SH: 0/27; CH: 0/28 Itching/pruritis: SH: 3/27; CH: 2/28 Reintervention Total: SH: 3/27; CH: 0/28 Reintervention Prolapse: SH: 3/27; CH: 0/28 Reintervention CH: SH: 3/27; CH: 0/28 **Additional outcomes reported in the study** Number of patients with difficulty evacuating or skin tags

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Ortiz (2005)[86] Country: Spain Trial dates: Start: 2001 Finish: 2002 Language: English	Total: 31 SH: 15 CH: 16 % Loss to follow-up at final time point: 0%	Age: Mean: 48 Range: 28-69 Number male 19	Grades included IV Grade IV: 31	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional	**Post-operatvie** Residual prolapse: SH: 0/15; CH: 0/16 Bleeding: Intervention required <4 days SH: 0/15; CH: 1/16 Analgesics: Opioid injections SH: 1/15; CH: 2/16 Haemorrhoidal thrombosis: SH: 1/15; CH: 0/16 Operating time (minutes): SH: Mean: 24 Range: 15-37; CH: Mean: 39 Range: 10-90 Time to first bowel movement (days): SH: Mean: 3.14 Range: 1-5; CH: Mean: 3.5 Range: 1-6 Time to first bowel movement (days): SH: Mean: 1.6 SD: 1; CH: Mean: 2.1 SD: 1.1 **12 months** Pain: SH: 0/15; CH: 0/16 Prolapse: SH: 8/15; CH: 0/16 Bleeding: SH: 1/15; CH: 1/16 Incontinence: SH: 0/15; CH: 0/16 Itching/pruritis: SH: 6/15; CH: 1/16 Urgency: SH: 2/15; CH: 3/16 Reintervention: Total SH: 5/15; CH: 0/16 Reintervention: Prolapse SH: 5/15; CH: 0/16 Reintervention CH: SH: 5/15; CH: 0/16 **Additional outcomes reported in the study** Mean and range pain scores over first 14 days (100mm VAS scale) Number of patients needing haemostatic sutures and number of stitches required Number of patients with skin tags or tenesmus

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Palimento (2003)[68, 84] Country: Italy Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 74 SH: 37 CH: 37 % Loss to follow-up at final time point: 0%	Age: Range: 25-84 Number male 47	Grades included III+IV Grade III: 34 Grade IV: 40	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional	**Post-operative** All bleeding <4 days SH: 2/37; CH: 1/37 Bleeding: Intervention required <4 days SH: 1/37; CH: 1/37 Urinary retention: SH: 5/37; CH: 8/37 10 pt VAS score up to 7 days: SH: Median: 3 Range: 1-6; CH: Median: 5 Range: 3-7 Operating time (minutes): SH: Median: 25 Range: 15-49; CH: Median: 30 Range: 20-44 Time to normal activity (days): SH: Median: 28 Range: 12-40; CH: Median: 34 Range: 16-50 **18 months** Bleeding: SH: 8/37; CH: 5/37 Incontinence: SH: 0/37; CH: 0/37 Pain: SH: 6/37; CH: 7/37 **5 years** Prolapse: SH: 0/31; CH: 0/29 Pain: SH: 4/37; CH: 3/37 Bleeding: SH: 3/37; CH: 2/37 Anal stenosis/anastomotic stricture: SH: 0/31; CH: 0/29 Incontinence: SH: 0/37; CH: 0/37 **Additional outcomes reported in the study** Median and range use of diclofenac and symptom severity score at 4 weeks Number of days to pain-free defecation

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Pavlidis (2002)[83] Country: Greece Trial dates: Start: 1999 Finish: 2000 Language: English	Total: 80 SH: 40 CH: 40 % Loss to follow-up at final time point: Not reported	Age: Mean: 47.5 Range: 29-75 Number male 47	Grades included II-IV Grade II: 16 Grade III: 55 Grade IV: 9	Stapling gun: PPH 01 Comparator: M&M + diathermy Anaesthesia: SH: Regional CH: Regional	**Post-operative** Bleeding: Intervention required <4 days SH: 3/40; CH: 2/40 Faecal incontinence: SH: 0/40; CH: 1/40 10 pt VAS score up to 7 days: SH: Mean: 0.7 SD: 0.2; CH: Mean: 2.4 SD: 0.5 Operating time (minutes): SH: Mean: 23 SD: 5; CH: Mean: 35 SD: 10 Duration of stay (days): SH: Mean: 1.7 SD: 0.5; CH: Mean: 3.2 SD: 0.3 **>6 weeks and < 1 year** Bleeding: SH: 0/40; CH: 0/40 Anal stenosis/anastomotic stricture: SH: 0/40; CH: 0/40 Haemorrhoidal thrombosis: SH: 0/40; CH: 0/40 Prolapse: SH: 0/40; CH: 0/40 Pain: SH: 0/40; CH: 0/40 Incontinence: SH: 0/40; CH: 0/40 Urgency: SH: 0/40; CH: 0/40 Itching/pruritis: SH: 0/40; CH: 0/40 Pelvic/perianal sepsis: SH: 0/40; CH: 0/40 Rectovaginal fistula: SH: 0/40; CH: 0/40 Symptoms controlled: SH: 40/40; CH: 40/40 Reintervention: Total SH: 0/40; CH: 0/40 Reintervention: Prolapse SH: 0/40; CH: 0/40 Reintervention: Pain SH: 0/40; CH: 0/40 Reintervention: Bleeding SH: 0/40; CH: 0/40 Reintervention: CH SH: 0/40; CH: 0/40 Reintervention: RBL SH: 0/40; CH: 0/40 Reintervention: Sclerotherapy SH: 0/40; CH: 0/40 Reintervention: SH SH: 0/40; CH: 0/40 Reintervention: Skin tag removal SH: 0/40; CH: 0/40 Reintervention: Surgery SH: 0/40; CH: 0/40 **12 months** Prolapse: SH: 0/40; CH: 0/40 Pain: SH: 0/40; CH: 0/40 Bleeding: SH: 0/40; CH: 0/40 Incontinence: SH: 1/40; CH: 1/40 Urgency: SH: 0/40; CH: 0/40 Anal stenosis/anastomotic stricture: SH: 0/40; CH: 0/40 Haemorrhoidal thrombosis: SH: 0/40; CH: 0/40 Itching/pruritis: SH: 0/40; CH: 0/40 Pelvic/perianal sepsis: SH: 0/40; CH: 0/40

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Pavlidis (2002)[83] (continued)					Rectovaginal fistula: SH: 0/40; CH: 0/40 Symptoms controlled: SH: 40/40; CH: 40/40 Reintervention Total: SH: 0/40; CH: 0/40 Reintervention Prolapse: SH: 0/40; CH: 0/40 Reintervention Pain: SH: 0/40; CH: 0/40 Reintervention Bleeding: SH: 0/40; CH: 0/40 Reintervention CH: SH: 0/40; CH: 0/40 Reintervention RBL: SH: 0/40; CH: 0/40 Reintervention Sclerotherapy: SH: 0/40; CH: 0/40 Reintervention SH: SH: 0/40; CH: 0/40 Reintervention Skin tag removal: SH: 0/40; CH: 0/40 Reintervention Surgery: SH: 0/40; CH: 0/40 **Additional outcomes reported in the study** Mean consumption of epidural morphine
Ren (2002)[75] Country: China Trial dates: Start: Not reported Finish: Not reported Language: Chinese	Total: 90 SH: 45 CH: 45 % Loss to follow-up at final time point: Not reported	Age: Range: 29-82 Number male 60	Grades included III+IV Grade III: 68 Grade IV: 22	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: General CH: General	**Post-operative** All bleeding <4 days SH: 28/45; CH: 0/45 Anal stenosis/anastomotic stricture: SH: 0/45; CH: 0/45 Faecal incontinence: SH: 6/45; CH: 7/45 Analgesics: Injections (not specified/combination) SH: 6/45; CH: 17/45 Wounds healed at 6 weeks: SH: 45/45; CH: 42/45 10 pt VAS score up to 7 days: SH: Mean: 2.2 SD: 0.4; CH: Mean: 6.4 SD: 2.1 (state a scale -5 to +5 used, but seem so give results for 0-10 point scale) Operating time (minutes): SH: Mean: 12.3 SD: 6.7; CH: Mean: 17.6 SD: 9.3 Duration of stay (days): SH: Mean: 5.8 SD: 2.3; CH: Mean: 11.2 SD: 3.7 Time to normal activity (days): SH: Mean: 7.9 SD: 3.2; CH: Mean: 14.2 SD: 6.5 **>6 weeks and < 1 year** Symptoms controlled: SH: 40/45; CH: 37/45 **Additional outcomes reported in the study** Number of patients requiring addition sutures peri-operatively o Number of patients with 'external swelling' (translation: 'papillae')

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Schmidt (2002)[72] Country: Germany Trial dates: Start: 1998 Finish: 2000 Language: German	Total: 152 SH: 72 CH: 80 % Loss to follow-up at final time point: 0%	Age: Range: 24-91 Number male 94	Grades included III+IV Grade III: 123 Grade IV: 29	Stapling gun: Not reported Parks and Fransler-Arnold Anaesthesia: 105 had regional 47 had general	**Post-operative** All bleeding <4 days SH: 3/72; CH: 6/80 Bleeding: Intervention required <4 days SH: 0/72; CH: 1/80 Faecal incontinence: SH: 0/72; CH: 3/80 Urinary retention: SH: 8/72; CH: 16/80 10 pt VAS score up to 7 days: SH: Mean: 1.83; CH: Mean: 3.74 Operating time (minutes): SH: Mean: 21.65; CH: Mean: 52.98 Duration of stay (days): SH: Mean: 3.04 Range: 1-8; CH: Mean: 6.14 Range: 3-9 Time to normal activity (days): SH: Mean: 6.2; CH: Mean: 14.5 **Additional outcomes reported in the study** None

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Senagore (2004)[89] Country: USA Trial dates: Start: 2001 Finish: 2002 Language: English	Total: 156 SH: 77 CH: 79 % Loss to follow-up at final time point: 25%	Age: Mean: 49.5 Range: 23-78 Number male 107	Grades included III Grade III: 156	Stapling gun: PPH 01 Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** All bleeding <4 days SH: 7/77; CH: 4/79 Anal fissure: SH: 0/77; CH: 2/79 Anal stenosis/anastomotic stricture: SH: 2/77; CH: 0/79 Day cases: SH: 73/74; CH: 75/77 Faecal incontinence: SH: 3/77; CH: 4/79 Infection: Wound SH: 0/77; CH: 1/79 Infection: Systemic SH: 0/77; CH: 4/79 Itching/pruritis: SH: 3/77; CH: 3/79 Analgesics: Oral (not specified/combination) SH: 53/77; CH: 65/79 Urinary retention: SH: 10/77; CH: 6/79 Urgency: SH: 0/77; CH: 1/79 Wounds healed at 6 weeks: SH: 77/77; CH: 73/79 10 pt VAS score up to 7 days: SH: Mean: 5; CH: Mean: 6.25 (estimated from figures) 10 pt VAS score at 10 to 15 days: SH: Mean: 2; CH: Mean: 3 (estimated from figures) Operating time (minutes): SH: Mean: 31; CH: Mean: 35 Duration of stay (days): SH: Range: 0-2; CH: Range: 0-2 Time to first bowel movement (days): SH: Mean: 1.4 95% CI: 1-1.8; CH: Mean: 2 95% CI: 1.6-2.5 **>6 weeks and < 1 year** Prolapse: SH: 5/77; CH: 0/79 Bleeding: SH: 10/77; CH: 17/79 Incontinence: SH: 3/77; CH: 10/79 Symptoms controlled: SH: 63/77; CH: 51/79 **12 months** Prolapse: SH: 2/59; CH: 2/58 Bleeding: SH: 9/59; CH: 6/58 Incontinence: SH: 3/59; CH: 6/58 Symptoms controlled: SH: 44/59; CH: 48/58 Reintervention Total: SH: 2/59; CH: 4/58 Reintervention RBL: SH: 2/59; CH: 0/58 Reintervention Skin tag removal: SH: 0/59; CH: 1/58 Reintervention Surgery: SH: 0/59; CH: 3/58 **Additional outcomes reported in the study** Number of patients scoring no, mild, mod, severe and max pain at first bowel movement Mean 10 point VAS pain scores on bowel movement and change in VAS score 0-14 days Number of patients with emesis/vomiting; abdominal distension; dysurea; inflammation/burning; constipation or chills % patients with new or worsening symptoms

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Shalaby (2001)[93] Country: Saudi Arabia Trial dates: Start: 1997 Finish: 1998 Language: English	Total: 200 SH: 100 CH: 100 % Loss to follow-up at final time point: 12.5%	Age: Point estimate Mean: 46.6 SD: 13.1 Number male 124	Grades included II-IV Grade II: 23 Grade III: 62 Grade IV: 77 A further 37 patients were described as having prolapse 1 patient not classified	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: General CH: General	**Post-operative** Residual prolapse: SH: 1/100; CH: 2/100 Anal fissure: SH: 1/100; CH: 0/100 Bleeding: Intervention required <4 days SH: 1/100; CH: 2/100 Urinary retention: SH: 7/100; CH: 14/100 Haemorrhoidal thrombosis: SH: 3/100; CH: 3/100 Analgesics: Injections (not specified/combination) SH: 49/100; CH: 100/100 10 pt VAS score up to 7 days: SH: Mean: 2.5 SD: 1.3; CH: Mean: 7.6 SD: 0.7 Days to healing Mean: 7 SD: 1.2; CH: Mean: 30.5 SD: 5.8 Operating time (minutes): SH: Mean: 9 SD: 2.7; CH: Mean: 19.7 SD: 4.7 SE: Duration of stay (days): SH: Mean: 1.1 SD: 0.2; CH: Mean: 2.2 SD: 0.5 Time to normal activity (days): SH: Mean: 8.2 SD: 1.9; CH: Mean: 53.9 SD: 5.8 **12 months** Prolapse: SH: 1/95; CH: 2/80 Incontinence: SH: 0/95; CH: 0/80 Anal stenosis/anastomotic stricture: SH: 2/95; CH: 5/80 Reintervention: Total SH: 3/95; CH: 5/80 Reintervention SH: SH: 1/95; CH: 0/80 Reintervention Surgery: SH: 1/95; CH: 2/80 **Additional outcomes reported in the study** Mean VAS scores at first motion and number of doses of analgesia per day Number of patients with skin tags, tenesmus; feeling a lump; feeling of incompleteness on defecation or feeling a blockage
Thaha (2003)[71] Country: UK Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 90 SH: 48 CH: 42 % Loss to follow-up at final time point: 0%	Age: Median: 50 Range: 24-81 Number male 52	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** Pain: 10 pt VAS score up to 7 days: SH: Mean: 1.9 SD: 1.58; CH: Mean: 3.1 SD: 1.97 **Additional outcomes reported in the study** Accumulative VAS score, mean VAS score at first bowel movement Time to first bowel movement (stated no difference: data not provided)

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Thaha (2004)[70] Country: UK Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 182 SH: 91 CH: 91 % Loss to follow-up at final time point: 0%	Age: Median: 50 Range: 24-81 Number male 103	Grades included Not reported	Stapling gun: Not reported Comparator: Ferguson Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** Time to normal activity (days): SH: Mean: 14; CH: Mean: 14 **Additional outcomes reported in the study** Days of analgesia intake Days to become pain-free

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Van de Stadt (2005)[78] Country: Belgium Trial dates: Start: 2000 Finish: 2001 Language: English	Total: 40 SH: 20 CH: 20 % Loss to follow-up at final time point: 0%	Age: Mean: 48 Range: 19-78 Number male 29	Grades included II+III Grade II: Not reported Grade III: Not reported Grade IV: Not reported	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Combination CH: Combination Only 1 patient in each arm of the trial did not have general anaesthesia	**Post-operative** Anal fissure: SH: 1/20; CH: 2/20 Anal stenosis/anastomotic stricture: SH: 0/20; CH: 2/20 Bleeding: Intervention required <4 days SH: 0/20; CH: 1/20 Day cases: SH: 5/20; CH: 0/20 Haemorrhoidal thrombosis: SH: 2/20; CH: 0/20 Urinary retention: SH: 2/20; CH: 0/20 Wounds healed at 6 weeks: SH: 19/20; CH: 14/20 Wounds healed at 12 weeks: SH: 20/20; CH: 20/20 10 pt VAS score up to 7 days: SH: Mean: 2.6; CH: Mean: 4.7 10 pt VAS score at 10 to 15 days: SH: Mean: 1.5; CH: Mean: 2.8 Operating time (minutes): SH: Mean: 22.2; CH: Mean: 25.7 Duration of stay (days): SH: Mean: 1.5; CH: Mean: 2.25 **>6 weeks and < 1 year** Incontinence: SH: 2/20; CH: 0/20 Urgency: SH: 2/20; CH: 2/20 **46 months** Prolapse: SH: 5/20; CH: 0/20 Pain: SH: 6/20; CH: 3/20 Bleeding: SH: 5/20; CH: 6/20 Anal stenosis/anastomotic stricture: SH: 0/20; CH: 2/20 Haemorrhoidal thrombosis: SH: 1/20; CH: 0/20 Incontinence: SH: 0/20; CH: 0/20 Itching/pruritis: SH: 4/20; CH: 1/20 Urgency: SH: 0/20; CH: 0/20 Reintervention Tota:l SH: 4/20; CH: 0/20 Reintervention Prolapse: SH: 4/20; CH: 0/20 Reintervention Pain: SH: 0/20; CH: 0/20 Reintervention Bleeding: SH: 0/20; CH: 0/20 Reintervention Surgery: SH: 4/20; CH: 0/20 **Additional outcomes reported in the study** 10 mm VAS score at defecation Anal manometry Number of patients with hypertrophic healing and persistent sympthomatic skin tags

	Participants				
Study	**Number**	**Population**	**Degree of haemorrhoids**	**Interventions**	**Results**
Wilson (2002)[43, 122-124] Country: UK Trial dates: Start: Not reported Finish: Not reported Language: English	Total: 62 SH: 32 CH: 30 % Loss to follow-up at final time point: 0%	Age: Range: 40-67 Number male Not reported	Grades included III Grade III: 62	Stapling gun: PPH 01 Comparator: M&M Anaesthesia: SH: Not reported CH: Not reported	**Post-operative** Analgesics: Injections (not specified/combination) SH: 0/32; CH: 0/30 Bleeding: All bleeding <4 days SH: 2/32; CH: 0/30 Bleeding: Intervention required <4 days SH: 2/32; CH: 0/30 Urinary retention: SH: 10/32; CH: 0/30 Operating time (minutes): SH Median: 12; CH: Median: 18 Duration of stay (days): SH: Median: 1 Range: 0.9-2; CH: Median: 1.9 Range: 1-2 Time to first bowel movement (days): SH: Median: 1 Range: 1-3; CH: Median: 1 Range: 1-2 Time to normal activity (days): SH: Median: 14; CH: Median: 18 **Additional outcomes reported in the study** Median and IQR number of injections and tablets use and blood loss; 27 patients included in a thrid arm who had haemorrhoidopexy using Autosuture (Tyco). were excluded

10.5.2 Economic evaluation

Surname of first author, date of publication	Farinetti, 2000 [65]
Type of economic evaluation	Cost analysis
Currency used, year	Lire, year not specified but assumed to be 1998. Conversion rate used 1 Italian Lira = 0.0003427 British Pound http://www.oanda.com/convert/classic
Study design	Prospective, matched-controlled study
Perspective	Not specified but likely to be the health care system
Participants	35 patients in each arm of the study with similar ages, sex and severity of haemorrhoids
Setting, country of study	Secondary care, single centre, Italy
Intervention group	Circular stapler, Endo Ethicon CDH33 (SH)
Control group	Milligan Morgan technique (CH)
Resources used	Pre-admission outpatient appointment, surgery, inpatient stay
Source of effectiveness data	Effectiveness data was not included
Length of follow up	Until discharged from hospital
Source of resource use data	A survey conducted within a single hospital. However only fixed estimates were provided
Source of unit cost data	National government, micro-costing and regional government costs
Link between cost & effectiveness data	Not applicable
Clinical outcomes measured & methods of valuation used	Not reported
Outcome results/ adverse events	Not reported
Cost data handled appropriately	Resource use was not reported separately from costs
Cost results	Pre-admission outpatient appointment = Lire 100,900 (SH) vs. Lire 100,900 (CH). = £35 (SH) vs. £35 (CH) Surgery = Lire 896,992 (SH) vs. Lire 300,067 (CH). = £307 (SH) vs. £103 (CH) Inpatient stay = Lire 600,000 (SH) vs. Lire 120,000 (CH). = £206 (SH) vs. £412 (CH) Total costs = Approx Lire 1,600,000 for either type of surgery = ££550
Sub-group analysis	None
Modelling summary	Not undertaken
Direction of result with appropriate quadrant location	Not applicable
Statistical analysis for patient-level stochastic data	Not undertaken
Appropriateness of statistical analysis	Not undertaken
Uncertainty around cost-effectiveness expressed & appropriateness of method of dealing with uncertainty around this	Not undertaken
Sensitivity analysis & appropriateness	Not undertaken
Modelling inputs & techniques appropriate	Not undertaken
Author's conclusions	The cost of either operations is very similar, however stapled haemorrhoidectomy has the advantage of management savings in terms of shorter inpatient stays following surgery. The authors suggest that stapled haemorrhoidectomy is also associated with faster physical recovery, less need for subsequent outpatient appointments and more opportunities for earlier returns to work by patients
Comments	No assessment of uncertainty or variation in costs and resource use. No assessment of day case. Very limited generalisability of results to the UK setting.

10.6 Table of excluded studies with rationale

Staple gun evaluated (at least in some patients) not designed for haemorroidopexy[1]

Insufficient information for inclusion[2]

Not a randomised control trial[3]

None of the outcomes to be evaluated in the review were reported in the paper[4]

Abbasakoor (2000)[57]**1**	Kirsch (2001)[62]**3**
Au-Yong (2004)[98]**1**	Levanon (2000)[125]**3**
Baker (2002)[126]**1**	Martinsons (2004)[127]**2**
Basdanis (2000)[128]**3**	Mattana (2006)[129]**3**
Chen (2006)[130]**3**	Maw (2003)[131]**4**
Dell'Abate (2005)[132]**3**	Mehigan (2000)[133]**1**
Ebert (2002)[134]**3**	Mehigan (2000)[135]**1**
Eissen (2000)[136]**3**	Mischinger (2001)[137]**2**
Favetta (2000)[138]**3**	Nastro (2004)[139]**3**
Ganio (2001)[118]**1**	O'Bichere (2000)[140]**1**
Gautam (2004)[141]**3**	Pinheiro Regadas (2005)[142]**1**
Gentile (2002)[143]**3**	Racalbuto (2004)[106]**1**
Goulimaris (2002)[144]**3**	Ranko (2004)[145]**3**
Hainsworth (2002)[146]**2**	Rowsell (2000)[105]**1**
Hancke (2004)[58]**1**	Schenkenbach (2001)[147]**3**
Helmy (2000)[148]**1**	Smyth (2003)[149]**1**
Hemmingway (1998)[150]**1**	Souza (2001)[151]**2**
Kang (2004)[152]**3**	Staude (1999)[153]**2**
Khalil (2000)[59]**1**	Staude (2000)[154]**2**
Kirsch (2000)[155]**3**	Staude (2001)[156]**2**
Kirsch (2001)[157]**3**	

10.7 Sensitivity analyses

Visual inspection of the forest plots showed no apparent effect of the comparator CH technique used, or the inclusion of results from studies that did not specify the stapling gun used, on the results for any outcome. Therefore sensitivity analyses were not undertaken to investigate these factors.

Loss to follow-up

Four studies had a high loss to follow-up at the final time point and four studies reporting outcomes beyond 6 weeks did not report losses to follow-up (Table 10.2).

Table 10.2: Trials that either did not report the loss to follow-up, or reported a high loss to follow-up at the final time point.

Study	Follow-up period	Language	Abstract or full paper?	Losses reported?	% loss to follow-up
Shalaby (2001)[93]	12 months	English	Full paper	Yes	12.5
Senagore (2004)[89]	12 months	English	Full paper	Yes	25
Ho (2000)[61, 69]	18 months	English	Full paper	Yes	49.5
Gravie (2005)[81]	2 years	English	Full paper	Yes	13.5
Ren (2002)[75]	4 months	English	Full paper	No	?
Ascanelli (2005)[74]	12 months	Italian	Full paper	No	?
Pavlidis (2002)[83]	12 months	English	Full paper	No	?
Docherty (2001)[76]	12 months	English	Abstract	No	?

To determine the effect of these studies on the results of the meta-analyses of primary outcomes, those not reporting the loss to follow-up were removed from the analyses, and high losses to follow-up were subject to best case, worst case analyses. The study by Ren (2002)[75] did not contribute to any of the analyses of primary outcomes beyond 6 weeks. The results of the sensitivity analyses for data at 12 months are given in Table 10.3, and at longer-term follow-up in Table 10.4.

Table 10.3 demonstrates excluding studies that did not report loss to follow-up, and assuming best case and worst case scenarios for patients lost to follow-up where this rate was high, did not alter the overall conclusion in relation to the number of patient complaining of bleeding at 12 months; there was no significant difference between SH and CH, with no significant heterogeneity between studies.

There was also no significant difference in the number of patients complaining of prolapse at 12 months between SH and CH. However, the worst case scenario resulted in significant heterogeneity between studies.

Table 10.3: Results of the sensitivity analyses for outcomes at 12 months

Number of patients complaining of bleeding at 12 months

Overall results[73, 74, 80, 83, 86, 89]	OR 2.09 (95% CI: 0.91, 4.83, p=0.08) Heterogeneity: p=0.85, I^2=0%
Studies not reporting loss to follow-up excluded[74, 83]	OR 1.95 (95% CI: 0.82, 4.64, p=0.13) Heterogeneity: p=0.80, I^2=0%
Losses to follow-up: best case[89]	OR 1.98 (95% CI: 0.84, 4.66, p=0.12) Heterogeneity: p=0.81, I^2=0%
Losses to follow-up: worst case[89]	OR 1.24 (95% CI: 0.68, 2.26, p=0.48) Heterogeneity: p=0.54, I^2=0%

Number of patients complaining of prolapse at 12 months

Overall results[73, 80, 83, 86, 88, 89, 93]	OR 3.20 (95% CI: 0.71, 14.45, p=0.40) Heterogeneity: p=0.08, I^2=48.8%
Losses to follow-up: best case[89, 93]	OR 3.30 (95% CI: 0.76, 14.30, p=0.11) Heterogeneity: p=0.10, I^2=46%
Losses to follow-up: worst case[89, 93]	OR 2.09 (95% CI: 0.49, 8.94, p=0.32) Heterogeneity: p<0.001, I^2=77%

Table 10.4 shows that assuming best case and worst case scenarios for all patients lost to follow-up where this rate was high, did not alter the overall conclusion in relation to the number of patient complaining of pain beyond 12 months; there was no significant difference between SH and CH. However, with a worst case scenario there was statistically significant heterogeneity between studies.

The significantly higher rate of prolapse beyond 12 months was still evident with both a best case and worst case scenario; there remained no significant heterogeneity between the studies for either analysis.

Table 10.4: Results of the sensitivity analyses for outcomes beyond 12 months

Number of patients complaining of pain at 16 to 24 months

Overall results[61, 84, 87]	OR 1.03 (95% CI: 0.37, 2.88, p=0.95) Heterogeneity: p=0.73, I^2=0%
Losses to follow-up: best case[61, 87]	OR 1.02 (95% CI: 0.37, 2.83, p=0.98) Heterogeneity: p=0.10, I^2=46%
Losses to follow-up: worst case[61, 87]	OR 1.19 (95% CI: 0.65, 2.17, p=0.58) Heterogeneity: p<0.001, I^2=79.4%

Number of patients reporting prolapse at 16 to 24 months

Overall results[61, 81, 87]	OR 7.26 (95% CI: 1.86, 28.35, p=0.004) Heterogeneity: p=0.64, I^2=0%
Losses to follow-up: best case[61, 81]	OR 6.40 (95% CI: 1.67, 24.56, p=0.007) Heterogeneity: p=0.56, I^2=0%
Losses to follow-up: worst case[61, 81]	OR 2.17 (95% CI: 1.25, 3.75, p=0.006) Heterogeneity: p=0.17, I^2=43%

VAS pain score during the early post-operative period

The underpowered trial by Lau (2004)[91] conducted in Hong Kong, which recruited a high proportion of patients (57%) with II degree haemorrhoids, and had the longest operating time, seemed to be responsible for much of the heterogeneity for this outcome (Figure 10.1). When this study was removed from the analysis the significant heterogeneity was not reduced (Figure 10.2).

Figure 10.1: The mean post-operative VAS pain score when all studies that provided sufficient data were included in the analysis

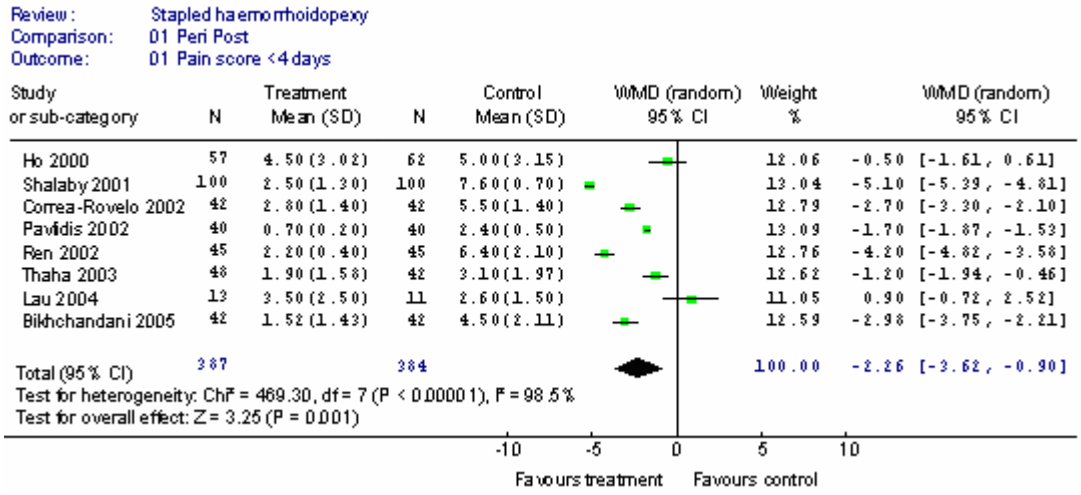
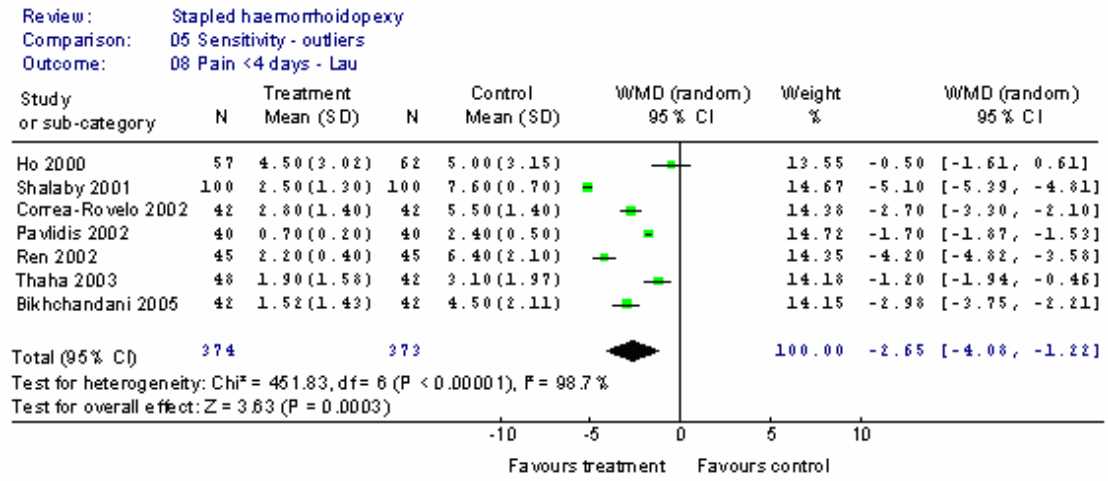
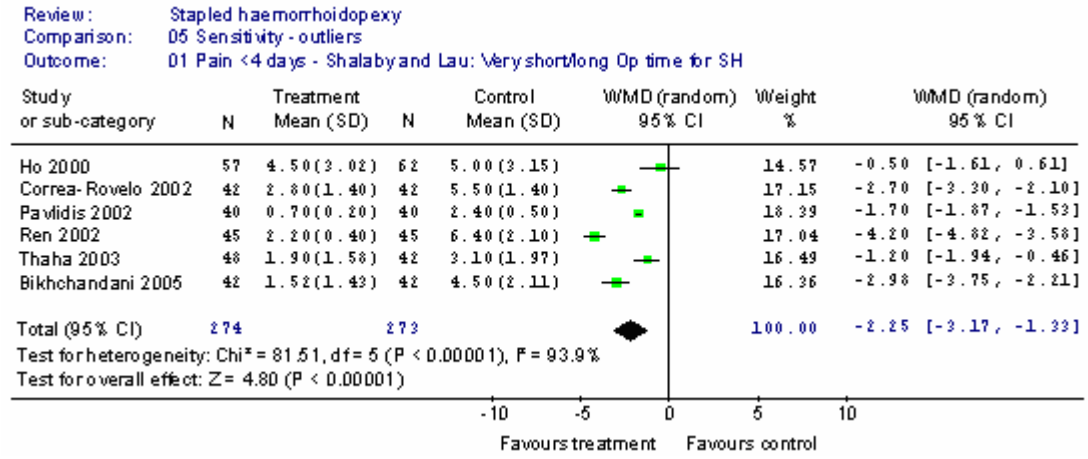


Figure 10.2: The mean post-operative VAS pain score when the underpowered trial by Lau (2004) was excluded from the analysis



To further the investigation into the heterogeneity observed for this outcome, the length of operating time was considered. Operating time seems to have an impact on the post-operative pain experience after SH. Therefore this may explain some of the heterogeneity seen between studies in the meta-analysis of pain scores in the early post-operative period. When the two studies that had the shortest (Shalaby 2001)[93] and longest (Lau 2004)[91] operating time for SH were removed from the analysis, there was little impact on the result (Figure 10.3).

Figure 10.3: The mean post-operative VAS pain score when the studies with the shortest (Shalaby 2001)[93] and longest (Lau 2004)[91] operating time for SH were excluded from the analysis



Pain during the short-term

The number of patients reporting pain between 6 weeks and 12 months varied across studies (Figure 10.4). The trial conducted by Cheetham (2003)[77] reported a significantly greater number of patients complaining of discomfort after SH, and recruitment was suspended. The authors stated that the incorporation of muscle into the resected tissue may have resulted in an increased incidence of pain and urgency after SH, but differences in surgical practice and the presence of concomitant anal pathology, may also have contributed.[56, 77] When this study was removed from the analysis the pooled OR reduced, further favouring SH; this did not reach statistical significance (Figure 10.5). However, there was no longer any significant heterogeneity between studies.

Figure 10.4: The number of patients experiencing pain at short-term follow-up when all studies were included in the analysis.

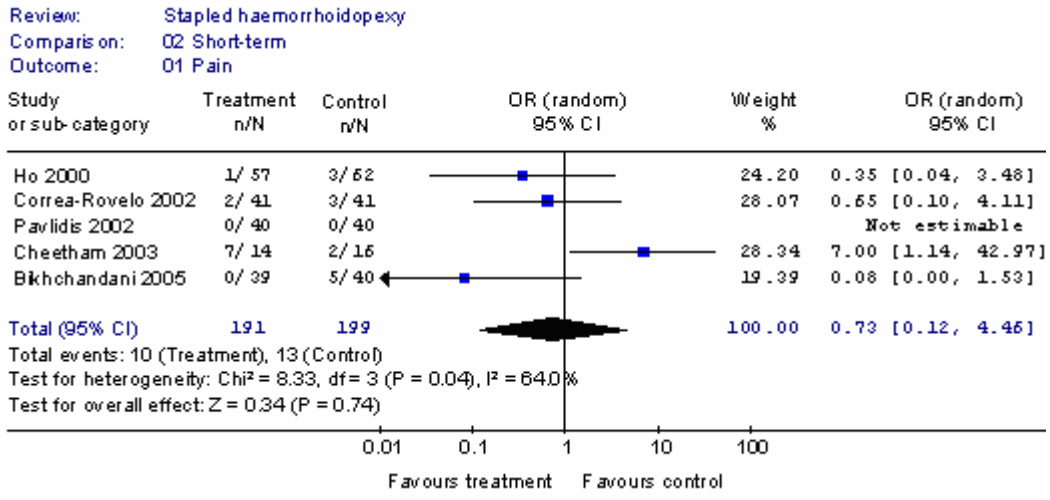
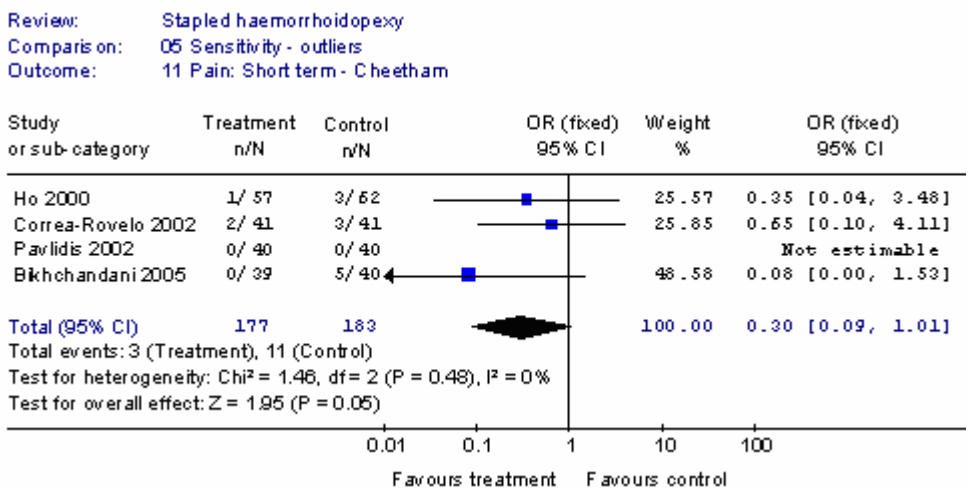


Figure 10.5: The number of patients experiencing pain at short-term follow-up when the study by Cheetham (2003) was excluded from the analysis



Bleeding during early post-operatively

Visual inspection of the forest plot (Figure 10.6) showed that the trial by Ren (2002),[75] published in Chinese, had a much higher rate of bleeding with SH than any other study. In fact, the OR (148.2) was higher than any upper 95% CI value for any

of the other studies (range 0.71 to 123.08). When extracting bleeding, we were interested in the patients that bled post-operatively. It is possible that the number of peri-opertive bleeding episodes during requiring haemostatic sutures were included the outcome. This would bring the numbers in line with the other studies included in the review. When this study was removed from the analysis (Figure 10.7), there was no longer any significant heterogeneity between studies (Chi^2 p=0.24; I^2=19.2%). In addition, there was shift in the direction of effect, with the OR now 0.86 (95% CI: 0.46, 1.61; p=0.63), and clearly no significant difference between SH and CH.

Figure 10.6: The number of patients experiencing bleeding in the early post-operative period when all studies were included in the analysis

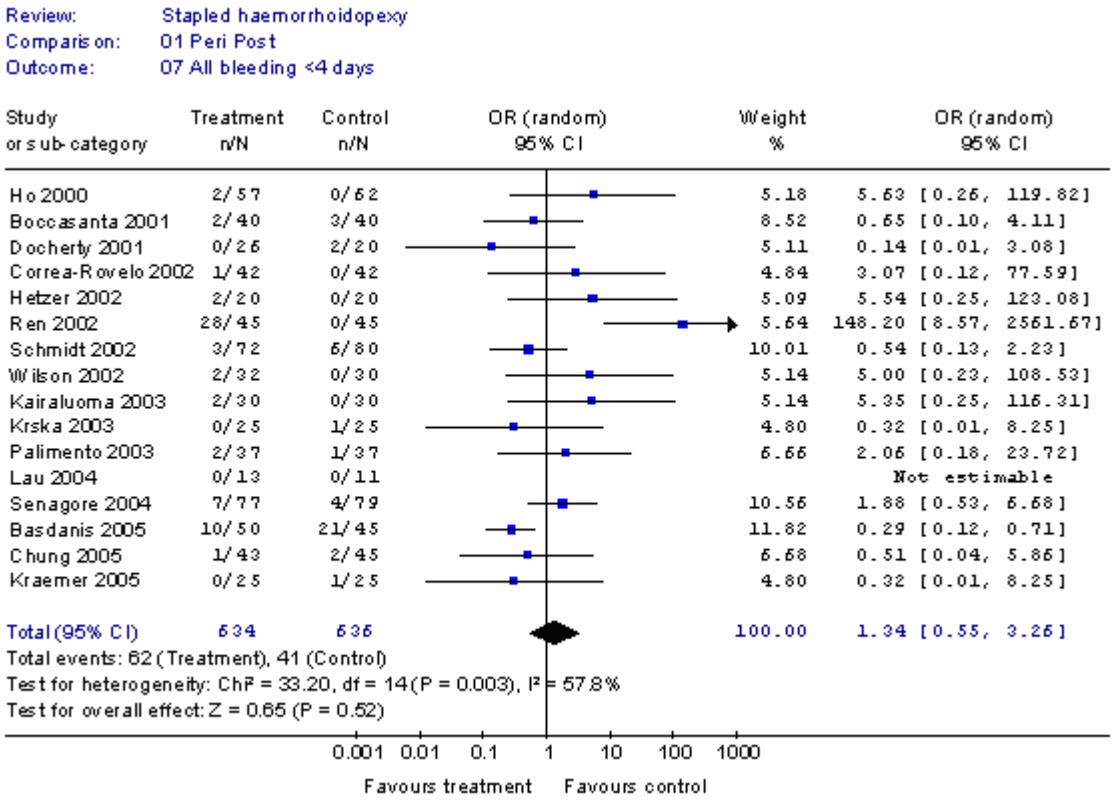
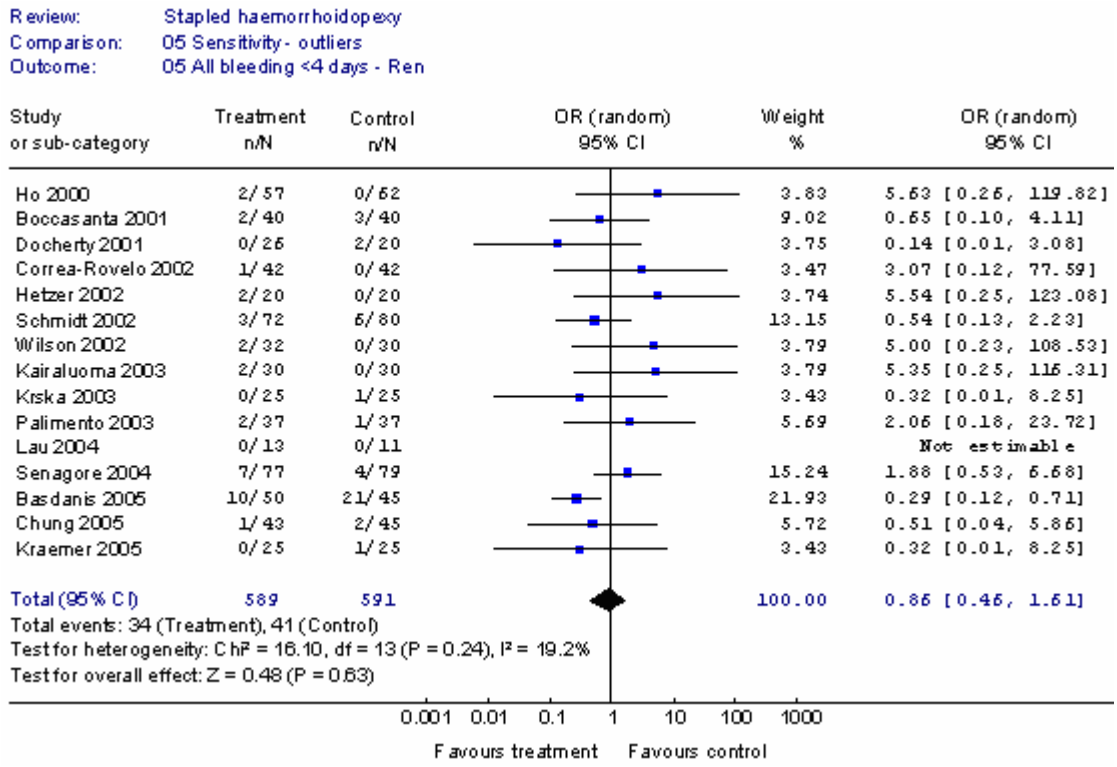


Figure 10.7: The number of patients experiencing bleeding in the early post-operative period when the trial by Ren (2002), which may have included peri-operative bleeding in the result, is excluded from the analysis



Residual prolapse

The pooled estimate showed a statistically significant difference between SH and CH in favour of CH (Figure 10.8). However, The trial by Kairaluoma (2003)[80] reported an uncharacteristically high rate of residual prolapse after SH compared to the other studies. The authors attributed some of these failures to technical difficulties during the SH procedure. They highlighted their concerns over technical issues such as misplacement of the pursestring suture and the control over the amount of rectal mucosa being excised. This high rate of residual prolapse in this study may therefore be an indication of the inexperience of the surgeons conducting the SH procedures. When this study was removed from the analysis, the difference between SH and CH no longer reached statistical significance (Figure 10.9).

Figure 10.8: The number of patients with residual prolapse when all studies were included in the analysis

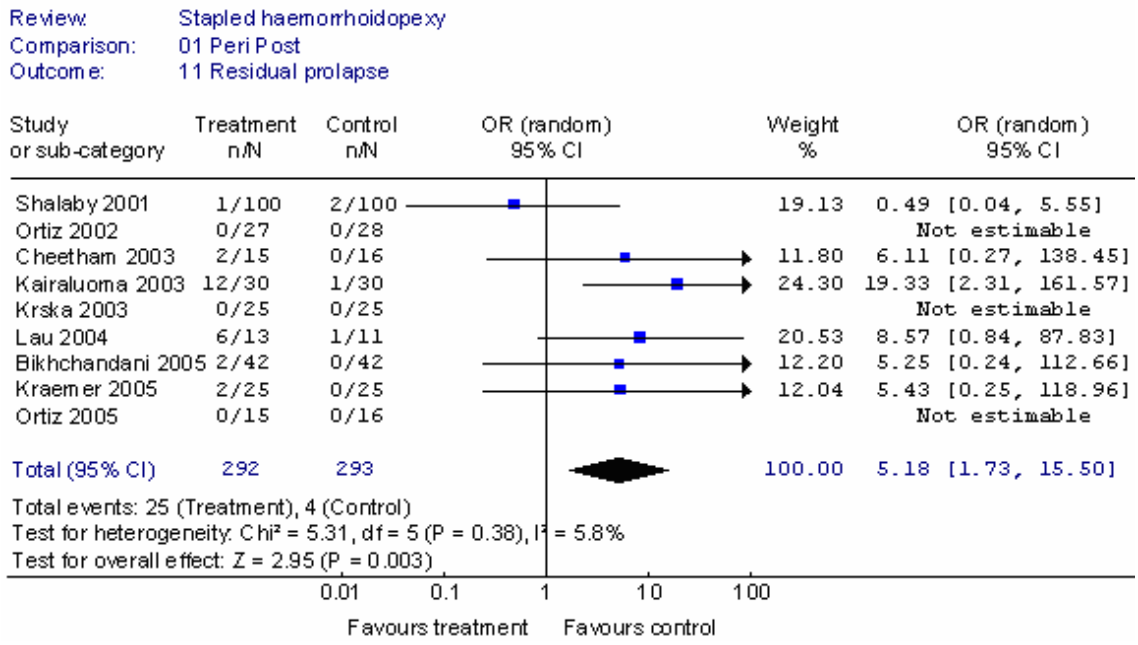
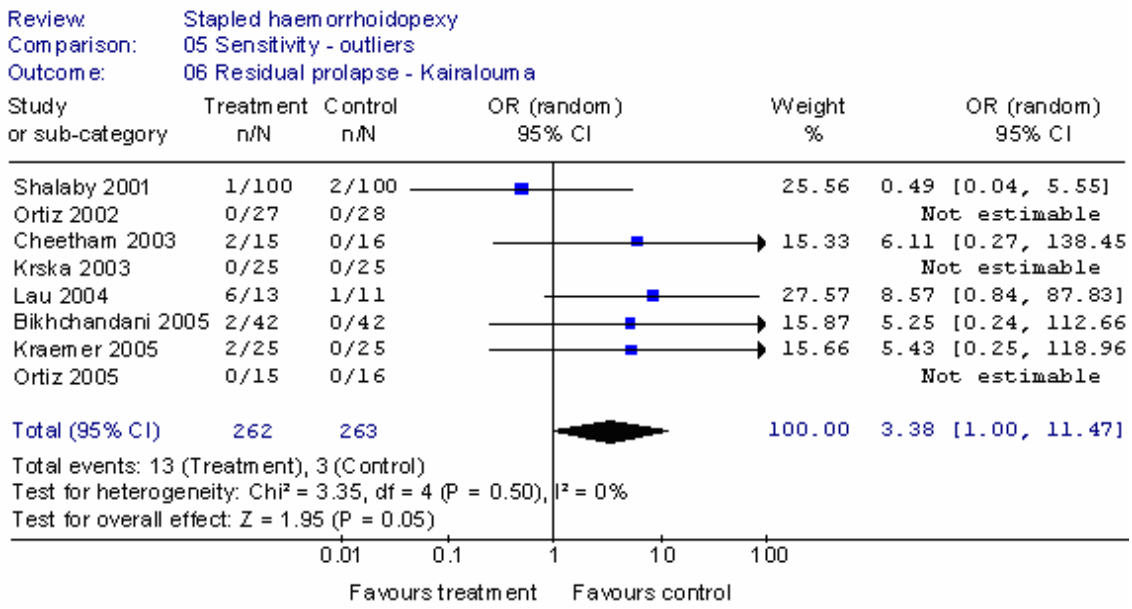


Figure 10.9: The number of patients with residual prolapse when the Kairaluoma trial (2003) that reported technical difficulties was excluded from the analysis



Prolapse at 12 months

The trial by Ortiz (2005)[86] recruited only patients with grade IV haemorrhoids, and reported a particularly high rate of prolapse following SH; this seemed to be responsible for the heterogeneity between the studies for this outcome (Figure 10.10). When this study was removed from the analysis, there was no longer any significant heterogeneity between studies (Figure 10.11).

Figure 10.10: The number of patients with prolapse at 12 months, when all studies were included in the analysis

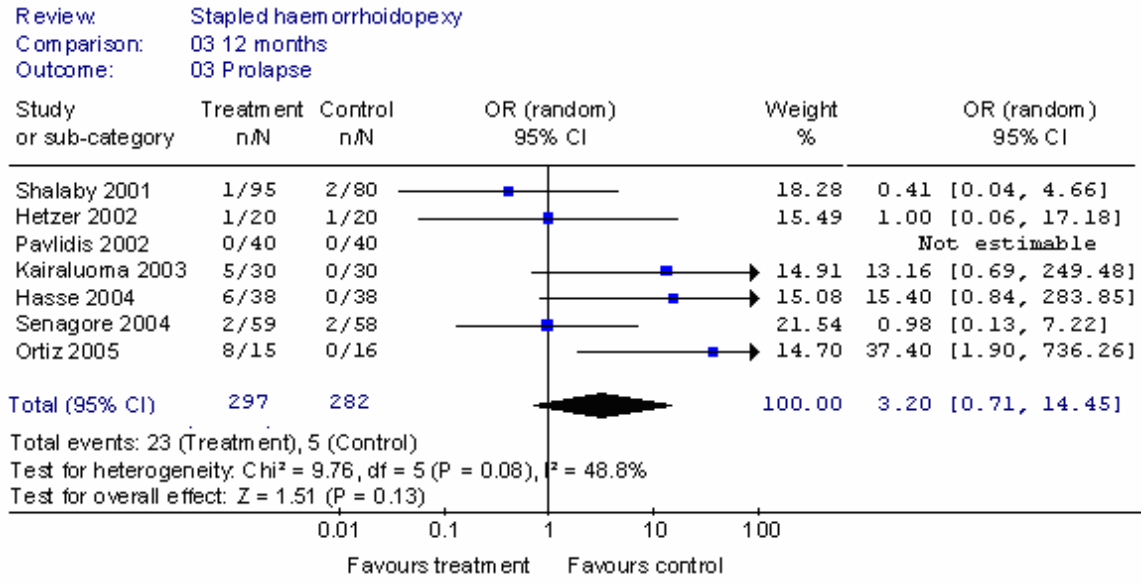
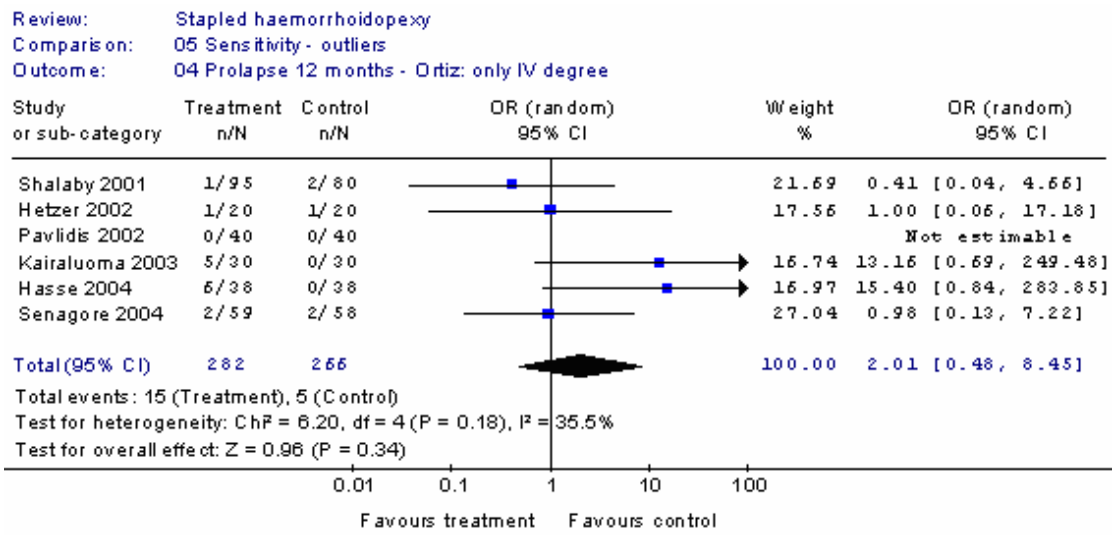


Figure 10.11: The number of patients with prolapse at 12 months when the trial by Ortiz (2005) that included only patients with IV degree haemorrhoids was excluded from the analysis



In Section 5.2.2.6, we undertook an analysis of studies that reported prolapse at 12 months or longer post-surgery. Although there was no statistically significant heterogeneity between the studies in this analysis (Figure 10.12), we investigated the effect of the trial by Ortiz (2005)[86] by excluding it from this analysis (Figure 10.13). It can be seen that there remains a highly significant effect in favour of CH, with only a slight reduction in I^2.

Figure10.12: The number of patients with prolapse at 12 months and over, when all studies were included in the analysis

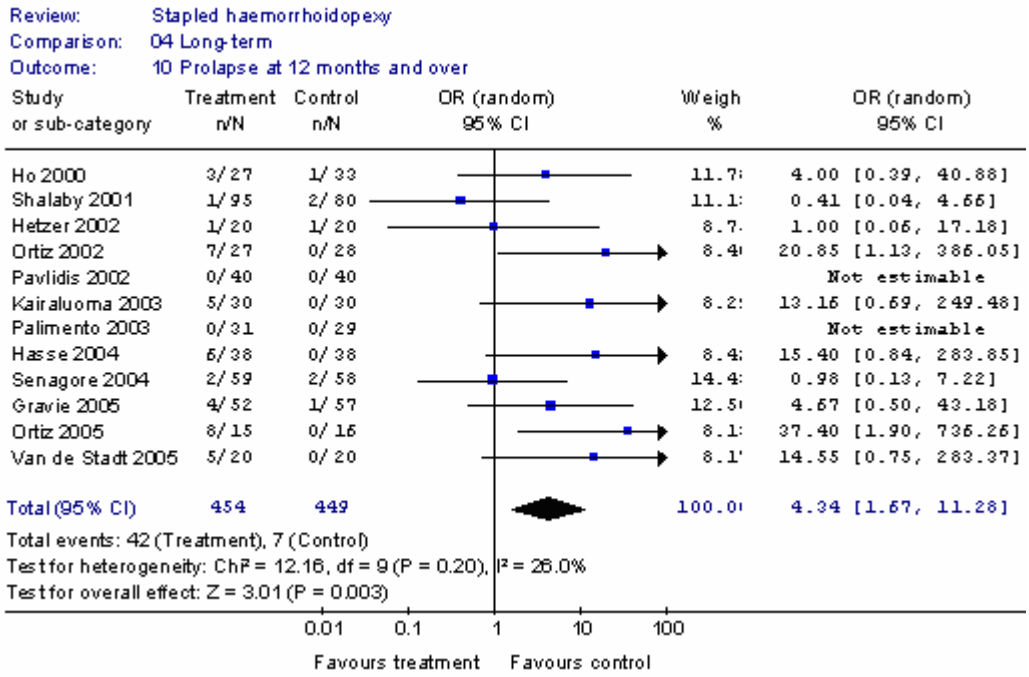
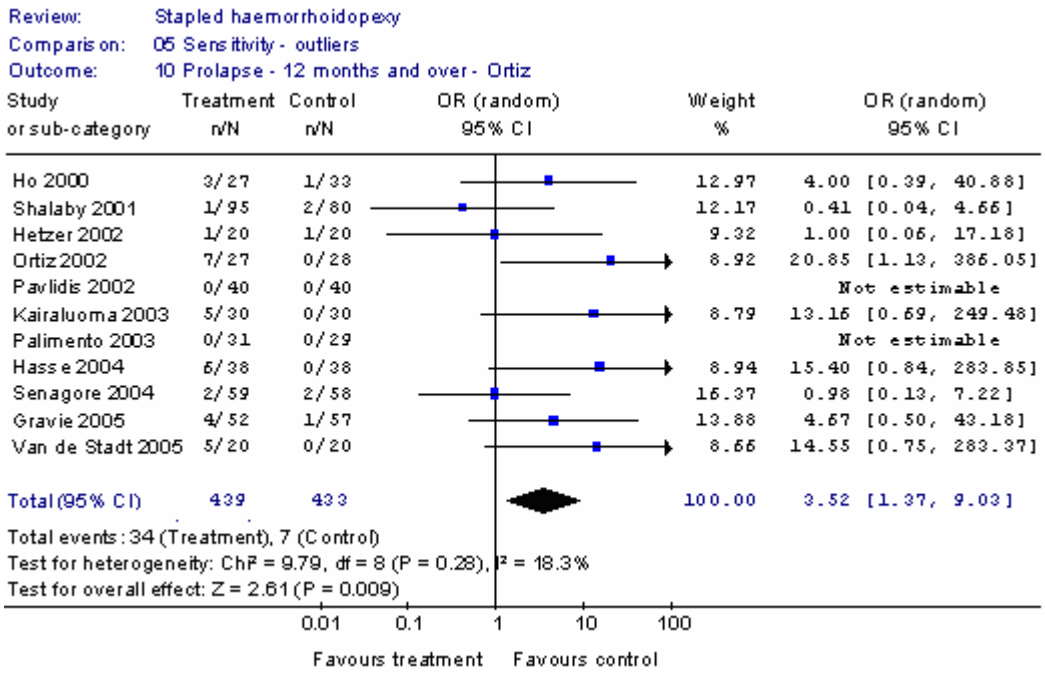
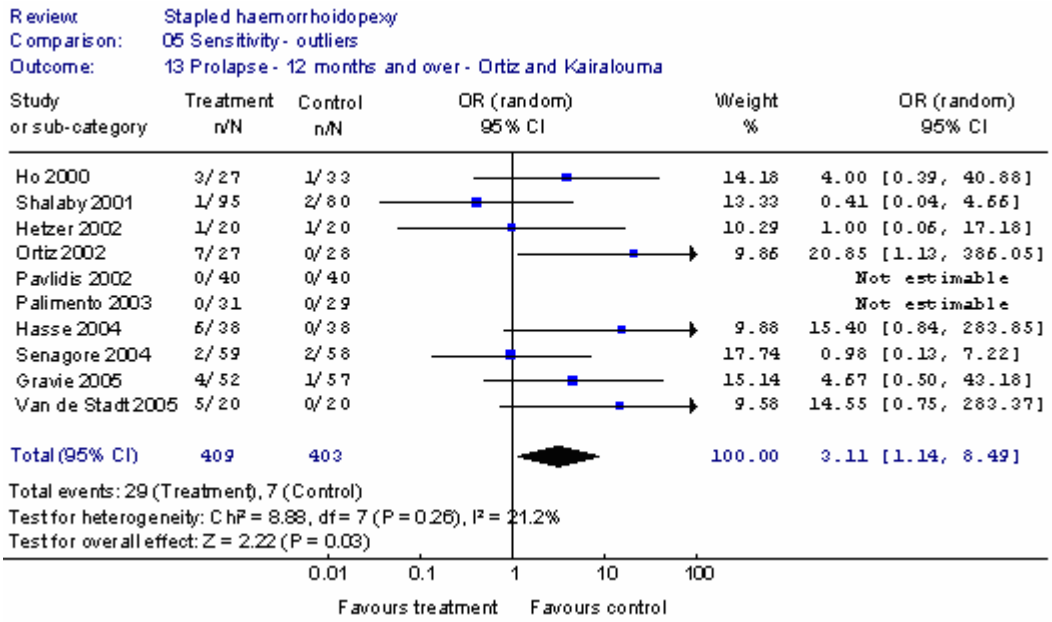


Figure 10.13: The number of patients with prolapse at 12 months and over, when the trial by Ortiz (2005) was excluded from the analysis



When Kairaluoma (2003)[80] was also excluded from the analysis due to the technical difficulties experienced, there was still a statistically significantly higher rate of prolapse after SH than CH (Figure 10.14)

Figure 10.14: The number of patients with prolapse at 12 months and over, when the trials by Ortiz (2005) and Kairaluoma (2003) were excluded from the analysis



Symptoms uncontrolled

There was no evidence from the individual trials that the number of patients reported as having haemorrhoidal symptoms was consistently greater after either SH or CH, however, there was statistically significant heterogeneity observed between studies for each of the meta-analyses. The study by Kairaluoma (2003)[80] that experienced technical difficulties was included in the analysis of data from <3 months (Figure 10.15) and 12 months (Figure 10.17). When this study was excluded from the analyses, there was no longer any statistical heterogeneity at <3 months (Figure 10.16; Chi^2 p=0.66, I^2=0%), and a moderate degree of heterogeneity at 12 months

(Figure 10.18; Chi^2 p=0.11, I^2=59.9%). Neither of these sensitivity analyses showed a statistically significant difference between SH and CH in the control of symptoms (<3 months: OR 0.85, 95% CI: 0.48, 1.53, p=0.59; 12 months: OR 1.05, 95% CI: 0.52, 2.11, p=0.89).

Figure 10.15: The number of patients with uncontrolled symptoms up to 3 months post-surgery, when all trials were included in the analysis

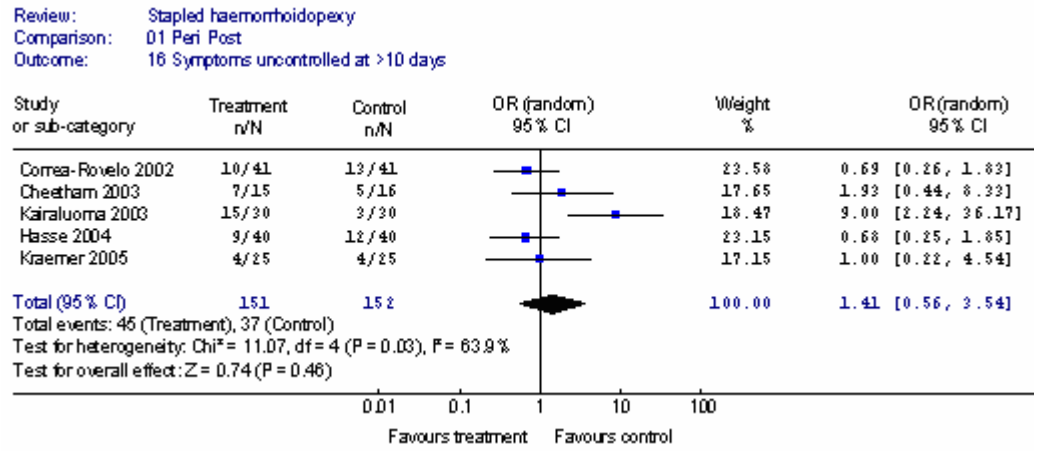


Figure 10.16: The number of patients with uncontrolled symptoms up to 3 months post-surgery, when the trial by Ortiz (2005) and Kairaluoma (2003) were excluded from the analysis

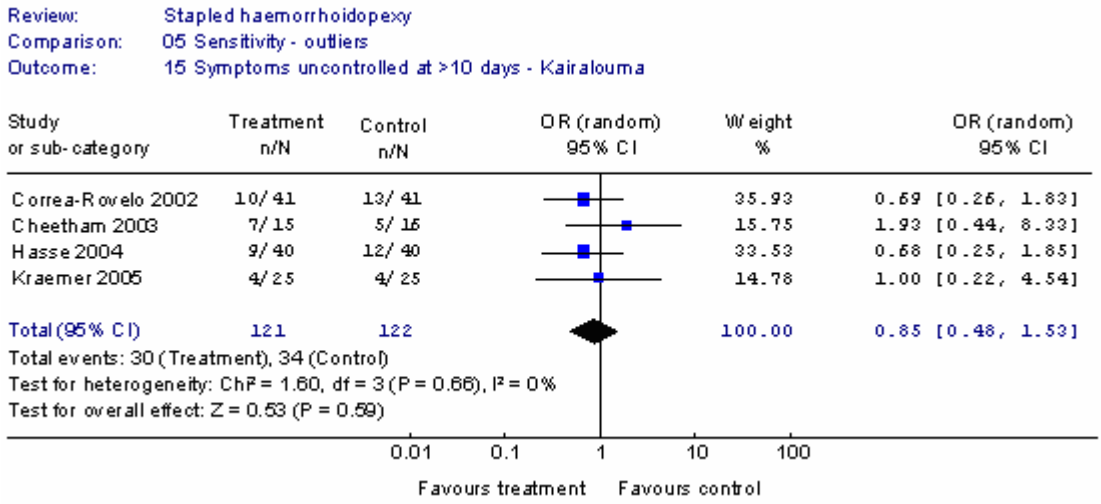


Figure 10.17: The number of patients with uncontrolled symptoms at 12 months post-surgery, when all trials were included in the analysis

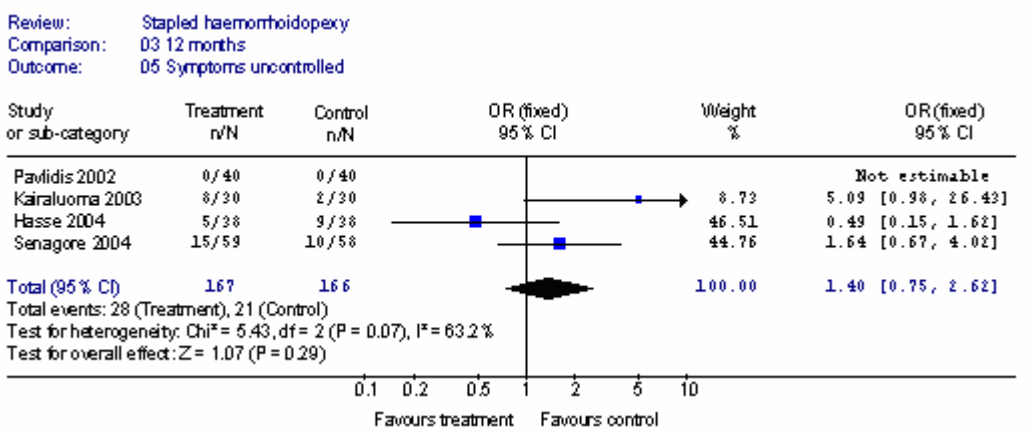
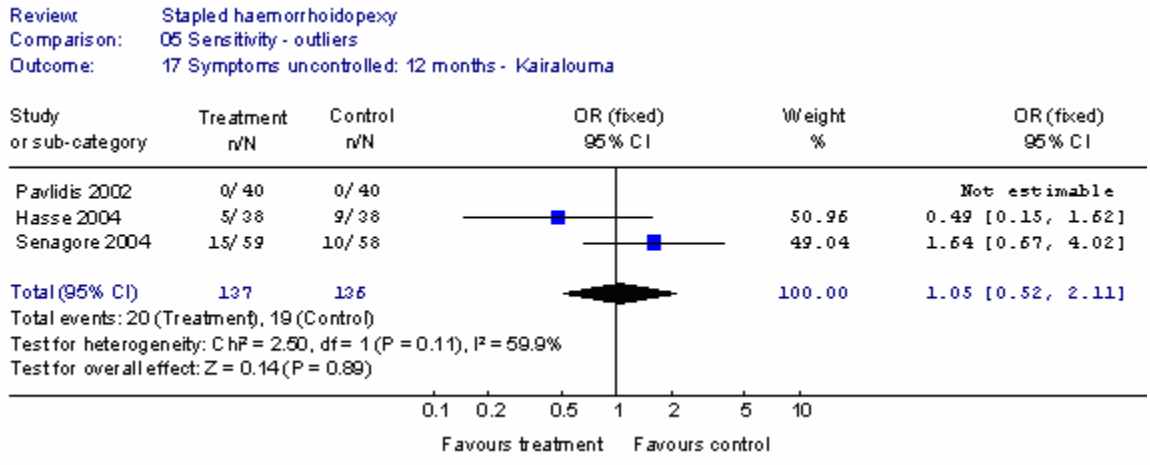


Figure 10.18: The number of patients with uncontrolled symptoms at 12 months post-surgery, when the trial by Kairaluoma (2003) was excluded from the analysis



Urinary retention

Nineteen studies reported urinary retention post-operatively; the pooled estimate revealed no statistically significant differences between the two groups (Figure 10.19). The trial by Wilson (2002)[43] reported a much higher incidence of urinary retention after SH (31%) compared to CH, and to other studies. When this study was removed from the analysis, the OR decreased further, favouring SH, but not statistically significantly so (Figure 10.20).

Figure 10.19: The number of patients with urinary retention post-operatively, when all studies were included in the analysis

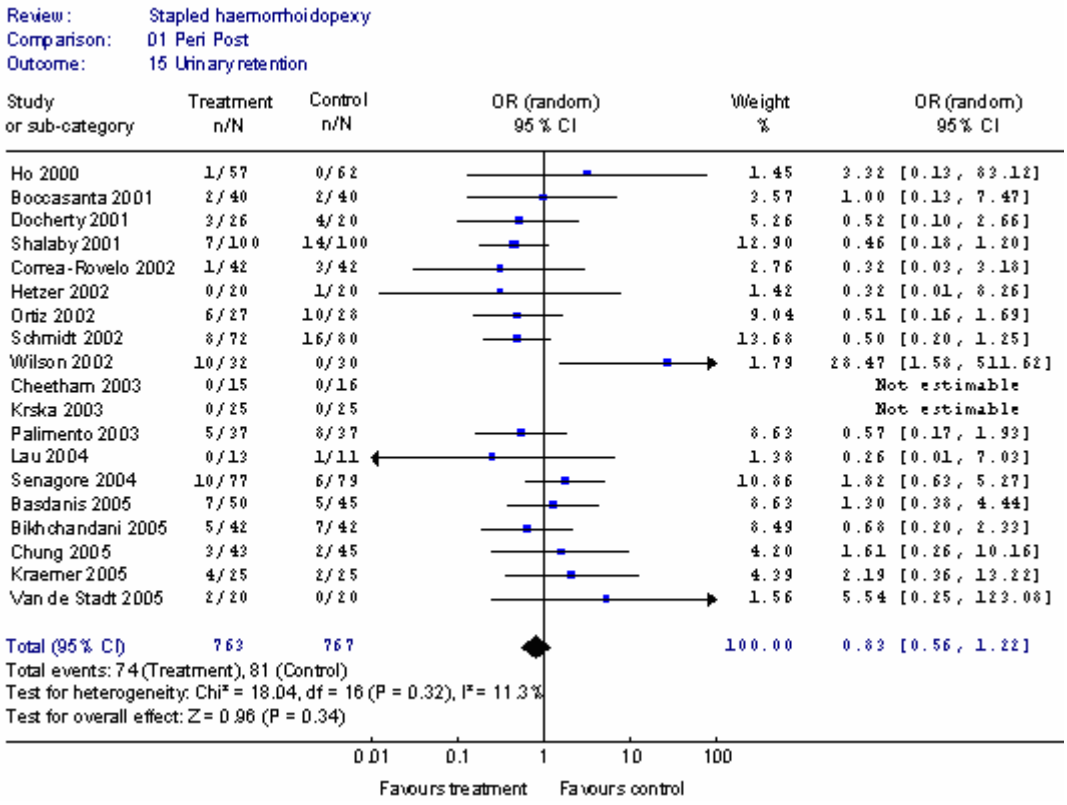
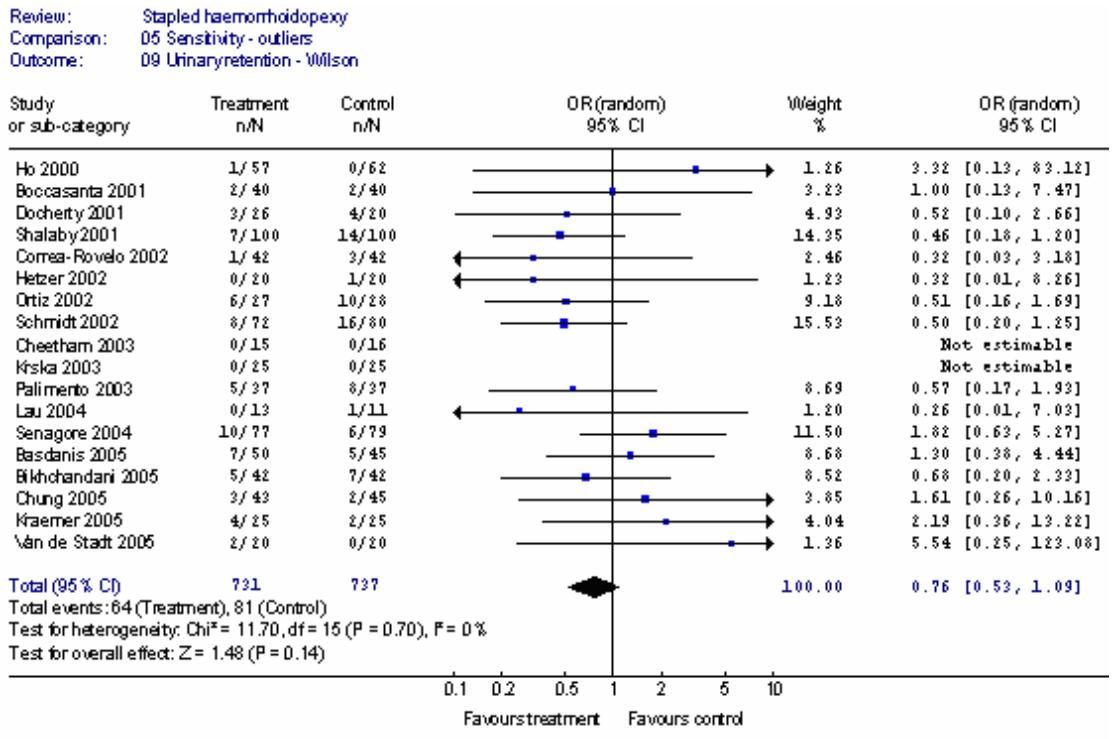


Figure 10.20: The number of patients with urinary retention post-operatively, when the trial by Wilson (2002) was excluded from the analysis



Total number of reinterventions

Two studies reported much greater rate of reintervention after SH compared to CH at 1 year which seem to account for the heterogeneity observed (Figure 10.21). One was the trial by Kairaluoma (2003)[80] that reported an uncharacteristically high incidence of prolapse after SH, which encountered technical difficulties during SH. The other was conducted by Ortiz (2005)[86] and included only patients with IV degree haemorrhoids. When these trials were removed from the analysis, there was no significant difference between SH and CH, and there was no longer any significant heterogeneity between the studies (Figure 10.22).

Figure 10.21: The total number of patients requiring reintervention at 12 months

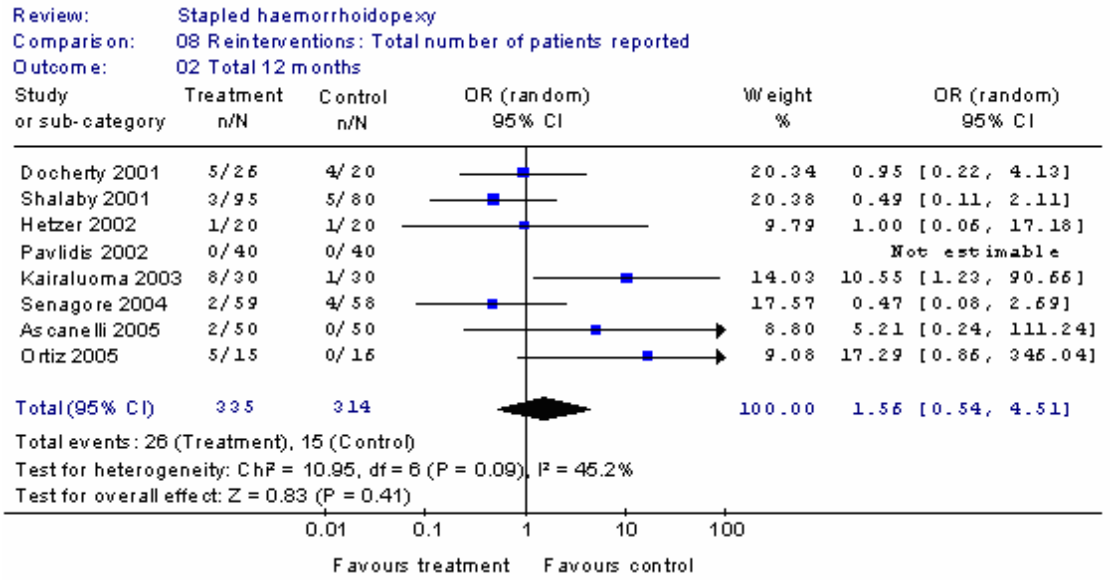
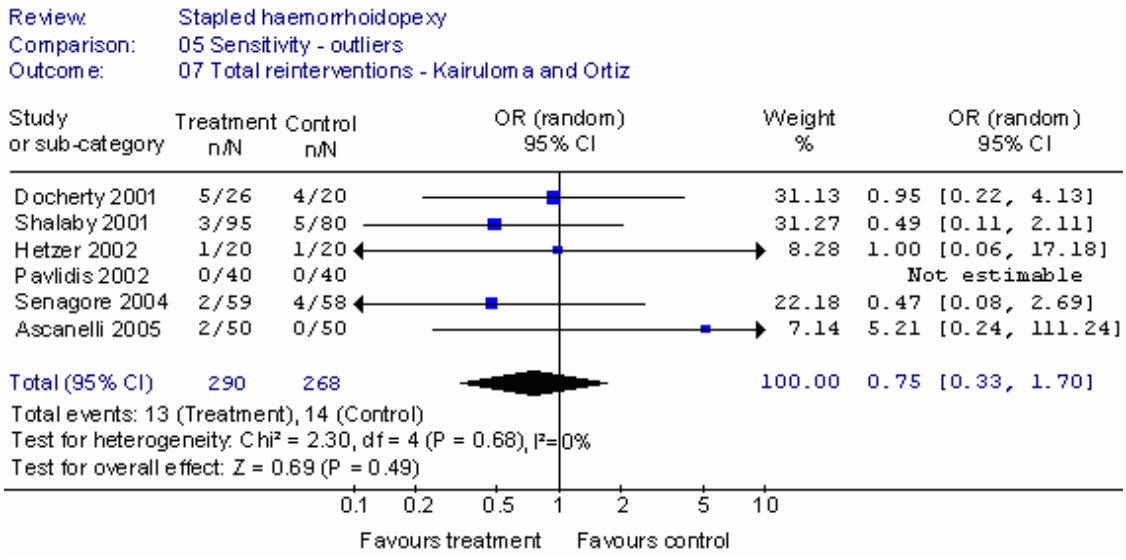


Figure 10.22: The total number of patients requiring reintervention at 12 months with the trials by Kairaluoma (2003) and Ortiz (2005) excluded from the analysis



Reintervention: For prolapse

Six studies reported the number of reinterventions for prolapse; the pooled OR demonstrated a significantly higher incidence after SH than CH (Figure 10.23). When the studies by Ortiz (2005)[86] and Kairaluoma (2003)[80] were removed from the analysis (Figure 10.24) there was still a statistically significantly higher rate of reintervention for prolapse after SH than CH (OR 4.99; 95% CI: 1.05, 23.60, p=0.04).

Figure 10.23: The number of patients requiring reintervention for prolapse at 12 months and over with all trials included in the analysis

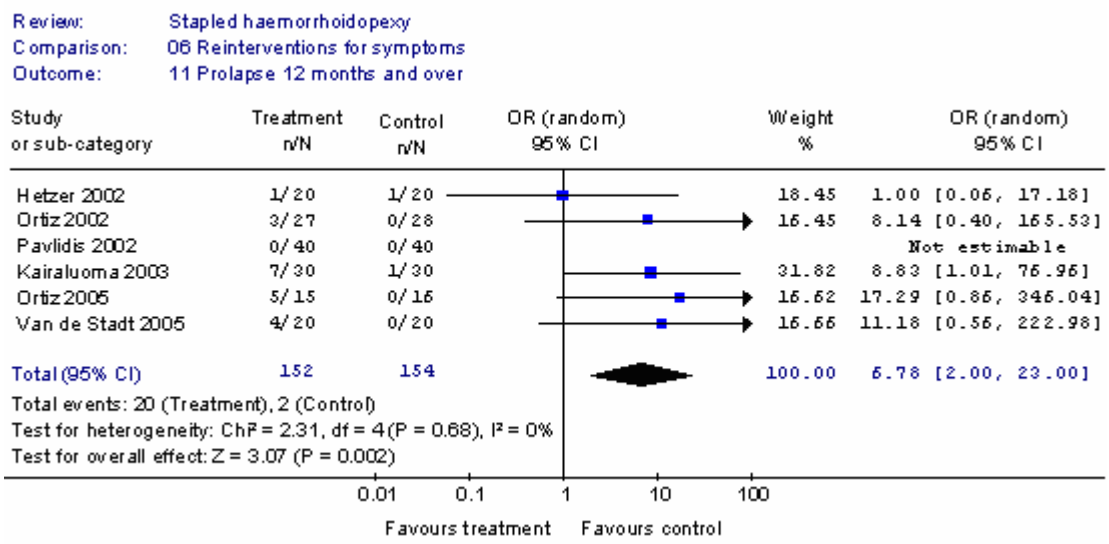
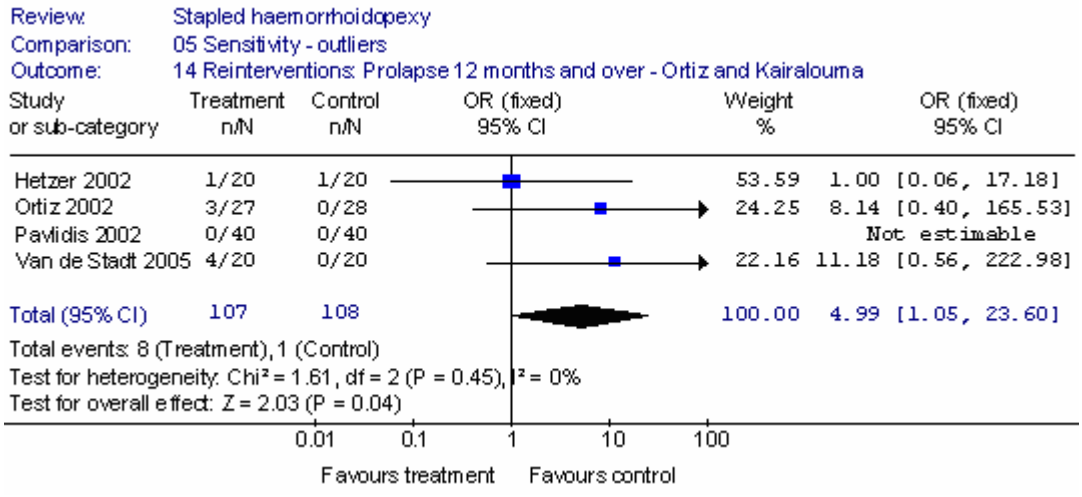


Figure 10.24: The number of patients requiring reintervention for prolapse at 12 months and over with the trials by Kairaluoma (2003) and Ortiz (2005) excluded from the analysis



Reintervention: Conventional haemorrhoidectomy

The need to undertake a CH was significantly higher after SH than CH year or later post-operatively (Figure 10.25). However, as with the previous analysis, this analysis included the trials by Kairaluoma (2003)[80] and Ortiz (2005).[86] When these studies are removed from the analysis, the difference no longer reaches statistical significance (Figure 10.26).

Figure 10.25: The number of patients requiring CH at 12 months or later post-surgery

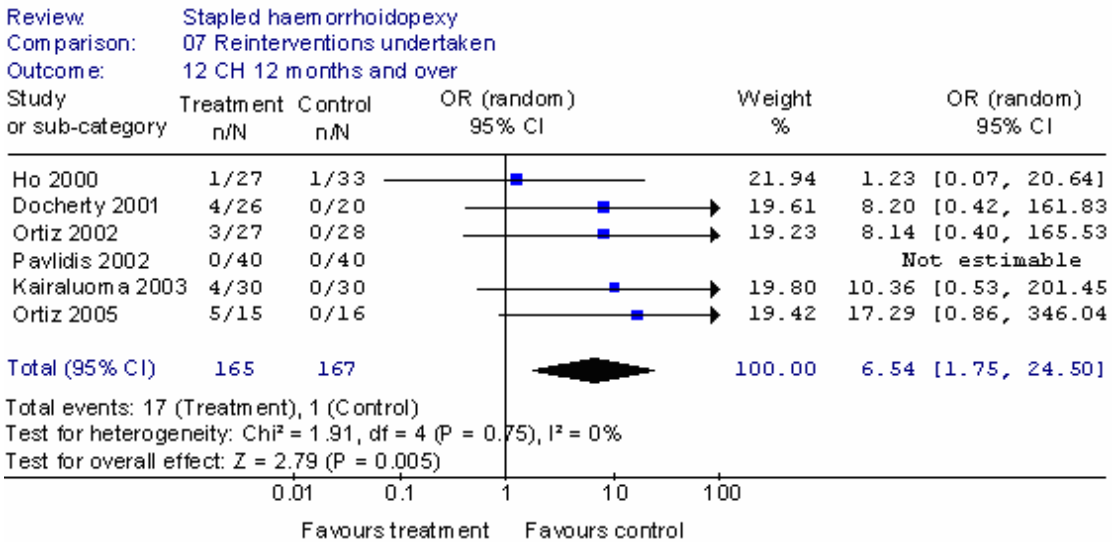
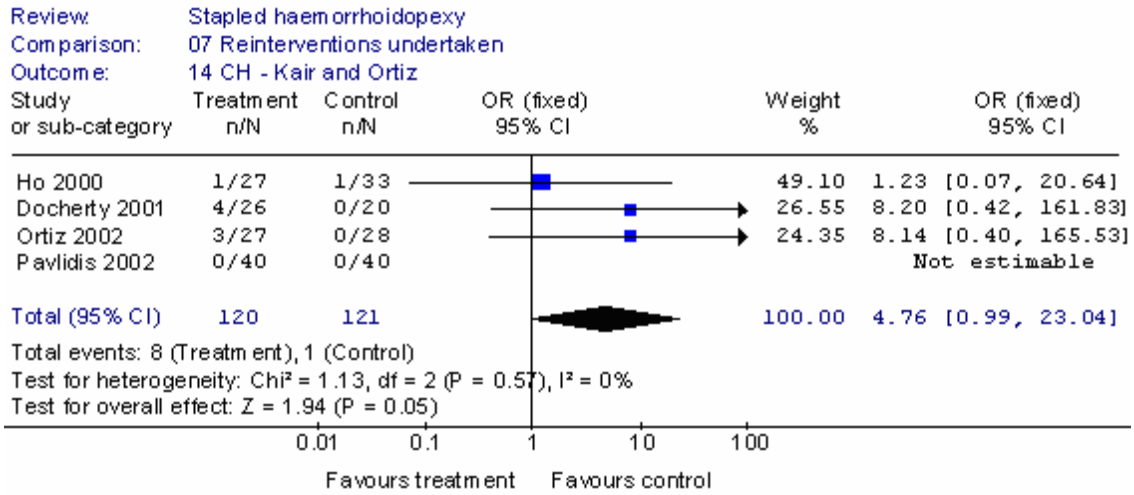


Figure 10.26: The number of patients requiring CH at 12 months or later post-surgery with the trials by Kairaluoma (2003) and Ortiz (2005) excluded from the analysis



Operating time

To investigate the relationship between operating time and the type of anaesthetic used or degree of haemorrhoids, studies were ordered with respect to operating time for SH and CH separately (Table 10.5). As can be seen from Table 10.5, there is no clear relationship between the mean operating time and either the type of anaesthetic used or the degree of haemorrhoids of the patients recruited into the trials. This outcome may be confounded by the method of measuring operating time (onset of anaesthesia; time in the operating theatre; time from incision to closure)

Table 10.5: Trials ordered from the shortest to longest operating time and the anaesthesia used (GA: General; RA: regional; C: combination) and degree of haemorrhoids of patients recruited into the trials

SH				CH			
Study	**Mean operating time**	**Anaesthetic**	**Disease severity**	**Study**	**Mean operating time**	**Anaesthetic**	**Disease severity**
Shalaby (2001) [93]	9	GA	II-IV	Ho (2000) [61]	11.4	GA	II+III
Correa-Rovelo (2002)[94]	11.9	C	III+IV	Ren (2002) [75]	17.6	GA	III+IV
Ren (2002) [75]	12.3	GA	III+IV	Chung (2005)[90]	18.5	C	III
Hasse (2004)[73]	16.3	GA	III	Shalaby (2001) [93]	19.7	GA	II-IV
Chung (2005)[90]	17	C	III	Kairaluoma (2003)[80]	22.46	GA	III
Ho (2000) [61]	17.6	GA	II+III	Van de Stadt (2005) [78]	25.7	C	II+III
Ortiz (2002)[87]	19	RA	III+IV	Kraemer (2005) [28]	26	C	III+IV
Kraemer (2005) [28]	21	C	III+IV	Lau (2004) [91]	29.8	GA	II-IV
Schmidt (2002) [72]	21.65	C	III+IV	Ortiz (2002)[87]	33.5	RA	III+IV
Kairaluoma (2003)[80]	21.86	GA	III	Ascanelli (2005)[74]	35	C	II+III
Ascanelli (2005)[74]	22	C	II+III	Pavlidis (2002) [83]	35	RA	II-IV
Van de Stadt (2005) [78]	22.2	C	II+III	Senagore (2004) [89]	35	NR	III
Pavlidis (2002) [83]	23	RA	II-IV	Ortiz (2005)[86]	39	RA	IV
Ortiz (2005)[86]	24	RA	IV	Bikhchandani (2005) [92]	45.21	RA	III+IV
Bikhchandani (2005) [92]	24.28	RA	III+IV	Krska (2003) [79]	46	RA	III
Boccasanta (2001) [85]	25	C	IV	Correa-Rovelo (2002)[94]	46.4	RA	III+IV
Krska (2003) [79]	28	RA	III	Hasse (2004)[73]	49	GA	III
Senagore (2004) [89]	31	NR	III	Boccasanta (2001) [85]	50	C	IV
Lau (2004) [91]	35.4	GA	II-IV	Schmidt (2002) [72]	52.98	C	III+IV

Number of days hospital stay

Two studies favoured SH far more than the other studies (Figure 10.27). The trial by Hasse (2004)[73] was restricted to patients with III degree haemorrhoids, and the trail by Ren (2002)[75] recruited 76% of patients with III degree haemorrhoids, with the remainder with IV degree haemorrhoids. Another study (Pavlidis 2002[83]) had a similar high proportion of patients with III degree haemorrhoids (69%), but this study had a more representative population with patients with both II and IV degree haemorrhoids recruited. When the studies by Hasse (2004) and Ren (2002) were removed from the analysis, there was little effect on the result and there was still significant heterogeneity between studies (Figure 10.28).

To investigate the relationship between the degree of haemorrhoids and length of hospital stay further, studies were ordered with respect to the duration of hospital stay for SH and CH separately (Table 10.6). It can be seen from Table 10.6 that there is a general trend for trials recruiting patients with II degree haemorrhoids to report shorter hospital stays, particularly after CH.

Figure 10.27: The mean number of days hospital stay with all studies included in the analysis

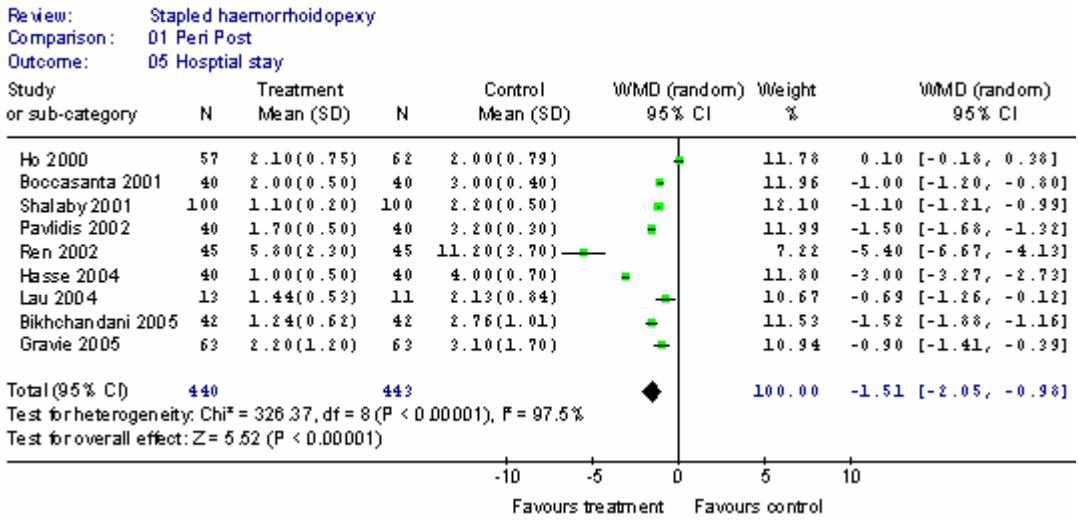


Figure 10.28 The mean number of days hospital stay with the two studies removed that reported uncharacteristically long duration of hospital stay after CH excluded

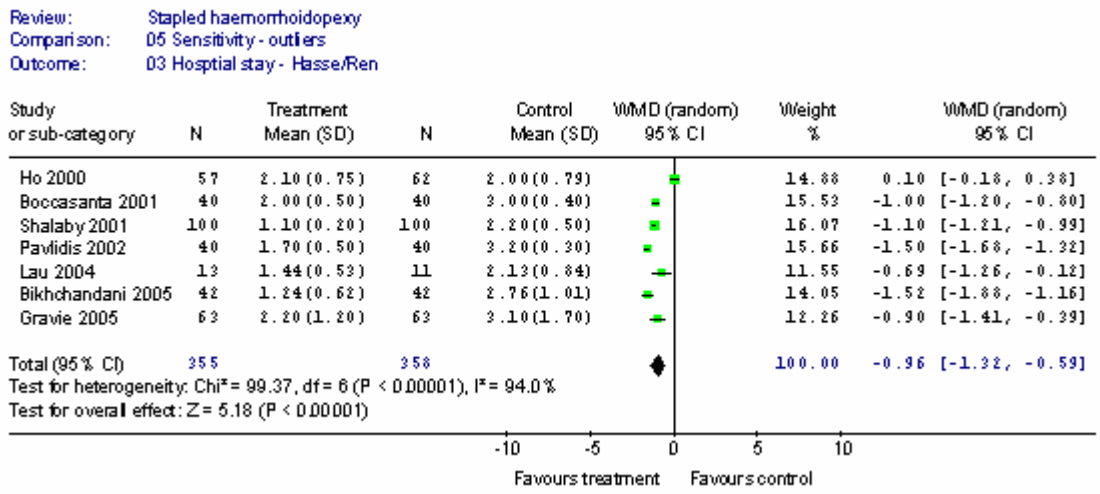


Table 10.6: Trials ordered from the shortest to longest reported duration of hospital stay and the degree of haemorrhoids of patients recruited into the trials

	SH			CH	
Study	**Mean days hospital stay SH**	**Degree of haemorrhoids**	**Study**	**Mean days hospital stay CH**	**Degree of haemorrhoids**
Ascanelli (2005)[74]	0.75	II+III	Ascanelli (2005)[74]	0.92	II+III
Hasse (2004)[73]	1	III	Ho (2000) [61]	2	II+III
Shalaby (2001) [93]	1.1	II-IV	Basdanis (2005) [82]	2.1	III+IV
Bikhchandani (2005) [92]	1.24	III+IV	Hetzer (2002) [88]	2.1	II+III
Lau (2004) [91]	1.44	II-IV	Lau (2004) [91]	2.13	II-IV
Van de Stadt (2005) [78]	1.5	II+III	Shalaby (2001) [93]	2.2	II-IV
Basdanis (2005) [82]	1.6	III+IV	Van de Stadt (2005) [78]	2.25	II+III
Pavlidis (2002) [83]	1.7	II-IV	Bikhchandani (2005) [92]	2.76	III+IV
Boccasanta (2001) [85]	2	IV	Boccasanta (2001) [85]	3	IV
Ho (2000) [61]	2.1	II+III	Gravie (2005)[81]	3.1	NR
Gravie (2005)[81]	2.2	NR	Pavlidis (2002) [83]	3.2	II-IV
Hetzer (2002) [88]	2.4	II+III	Hasse (2004)[73]	4	III
Schmidt (2002) [72]	3.04	III+IV	Kraemer (2005) [28]	5	III+IV
Krska (2003) [79]	3.5	III	Schmidt (2002) [72]	6.14	III+IV
Kraemer (2005) [28]	4	III+IV	Krska (2003) [79]	6.2	III
Ren (2002) [75]	5.8	III+IV	Ren (2002) [75]	11.2	III+IV

Time to normal activity

The study with the largest number of participants (Shalaby 2001[93]), reported a far greater period of time before a return to normal activity after CH than any other study (Figure 10.29). This was the only study to report including patients with II to IV degree haemorrhoids in this analysis, however, they were unclear as to the proportion of patients that had different degree of haemorrhoidal disease prior to surgery. They reported that 38.5% had IV degree, 31% III degree and 11.5% with II degree haemorrhoids. A further 18.5% were described as having prolapse. One patient was not classified at all. Despite this, the distribution of these classifications between the SH and CH groups was comparable. The authors provided no explanation for this extended period of convalescence, and it cannot be explained by any of the factors we investigated. When this study was removed from the analysis, there was little effect on the overall result or the observed heterogeneity (Figure 10.30).

Figure 10.29 The mean number of days to normal activity

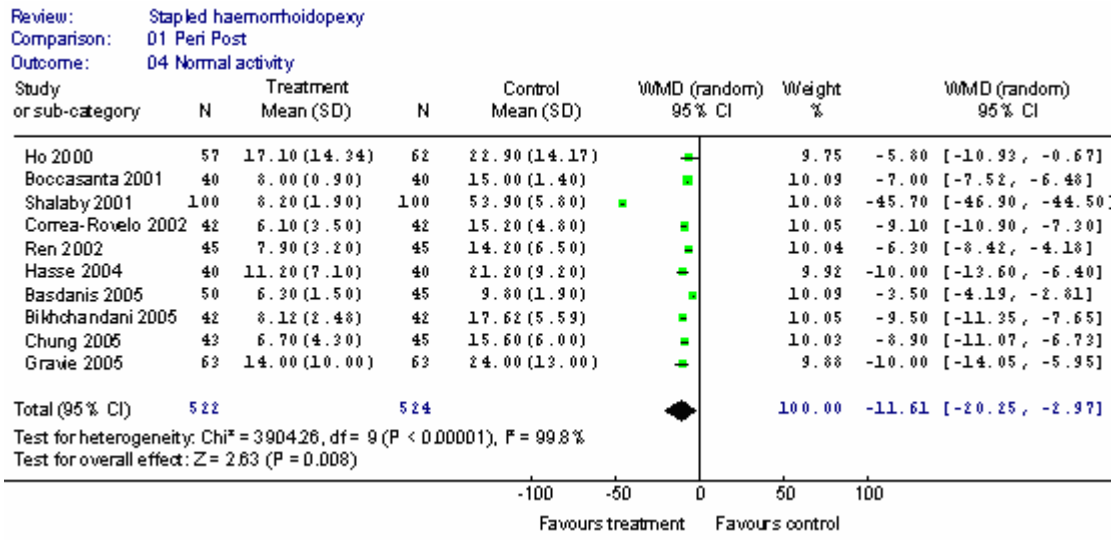
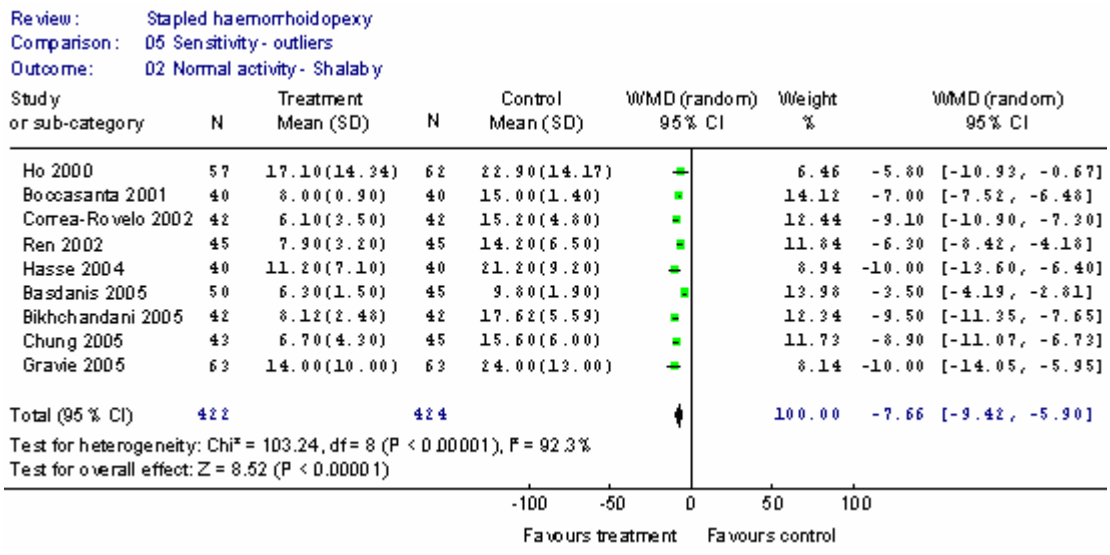


Figure 10.30 The mean number of days to normal activity with the trial by Shalaby (2001) reporting an uncharacteristically long convalescence time after CH excluded



10.8 Results of a literature search to identify data to inform estimates of resource use and costs

Farinetti and Saviano [65] undertook a cost analysis from the perspective of the health care provider. The study is written in Italian. The authors compared the full hospital costs of 35 patients who underwent SH with 35 patients who underwent CH. To assess the costs associated with each procedure they conducted a matched-control study in a single hospital in Italy. They assigned patients to one of the two procedures, attempting to match them by socio-demographic characteristics.

Data were collected on the resource use for the pre-admission outpatient examination which the patients underwent, as well as the resource use associated with surgery and post-operative care. Outpatient appointment costs were based on national hospital trust costs. A micro-costing study was undertaken to calculate the cost of surgery. Costs of surgery included the cost of pre-medication, anaesthesia, surgery consumables and equipment and the cost of the time spent on the operation by the surgical team. The overhead costs associated with surgery were omitted since the authors believed them to be similar across procedures. Unit costs of inpatient stays were obtained from a regional database. All costs were expressed in Italian Lire and the price year was not reported but was assumed to be 1998, that is the year that the paper was first submitted for publication in the journal. Alongside Italian Lire, costs are presented in British Pounds (http://www.oanda.com/convert/classic conversion rate: 1 Italian Lira = 0.0003427 British Pound, 15/06/98). Table 10.29 reports relevant costs.

Table 10.29: The cost of SH compared to CH Farinetti and Saviano [65]

Service/resource use	SH		CH	
	Italian Lire	British Pounds	Italian Lire	British Pounds
Pre-operative care	100,900	35	100,900	35
Surgical operation	896,992	307	289,177	99
Inpatient stay	600,900	206	1,200,00	411
Total costs	1,596,892	547	1,590,077	545

The cost of pre-operative care: the admission outpatient appointment, pre-medication and anaesthesia, were identical across surgical procedures. The cost of SH consumables and equipment were higher than for CH due to the cost of the staple gun. The cost of the surgery team was lower in the SH arm compared to the CH arm since the operation time was longer for CH. Following SH, patients were discharged from hospital after 16 hours whereas following CH patients were discharged after 42 hours. The total costs of either type of surgery were estimated as approximately Lire 1,600,000 or £550.

The authors concluded that although the staple gun added to the cost of the SH procedure (Lire 683,000 or £234), this was offset due to the higher costs associated with longer surgery time and longer hospital stay for CH. In addition, the authors suggested that patients undergoing SH typically had a speedier return to work; on average after 4 to 5 days following surgery as compared to 4 to 5 weeks for those undergoing CH. However, these costs were not calculated.

In spite of the detail in which the costs were presented, this study is of limited use to inform the cost-effectiveness of SH compared to CH. The study was set in Italy and resource use and unit costs associated with SH and CH may differ in the UK. In addition no outcomes were presented and therefore the effectiveness of both types of surgery is unclear. However, given that the study suggests that cost differences for SH compared to CH are minimal, it supports the need to consider outcomes to inform decisions based on cost-effectiveness.

Based on the NICE reference case, the aim was to include costs from the perspective of the NHS and Personal Social Services. The published literature was searched to obtain this data. A number of trials that were identified in the clinical effectiveness review (Chapter 5) included cost data.[43, 61, 73, 75, 85] Of these, only one (Wilson 2002[43]) was set in the UK. This study compared the costs and effectiveness of SH in 32 patients and CH in 30 patients. The data were collected from a single hospital. The authors estimated costs of operating time usage ($1.40 per minute), and the hourly cost of the hospital stay ($34) - that is about £1 and £23 respectively, assuming the price year was 2001, the date on which the work was originally presented at a conference. The operation costs and hospital stay costs for SH were $504 and $806

respectively, giving a total of around $1,310. In UK sterling that is, £347 and £555, totalling £902. The operation costs and hospital stay costs for CH were $252 and $1,546 respectively, giving a total of around $1,798. In UK sterling that is, £173 and £1,064, totalling £1,237. The methodology used to calculate costs was not specified clearly and this lack of transparency undermines the use of the costs. Costs were reported in US dollars and it is not know which financial year the costs related to.

In addition, to the RCTs, a review [158] and a cohort study were found, both of which included cost data.[159]. The review (The National Horizon Scanning Centre Briefing [158]) was conducted by the University of Birmingham (January 2001) in which the use of SH for the treatment of haemorrhoids was reviewed. The unit cost of a stapling device was £256. The unit cost of CH, excluding operating theatre costs was thought be around £1 for the sutures. The cost an inpatient stay was estimated at around £300 per day, and £9000 for an average 3 day stay. The authors suggest that if SH performed as a day case procedure, cost-savings may be generated in terms of inpatient costs. The authors also noted that surgeons are recommended to give antibiotics prophylactically prior to SH, thus adding an extra cost. No price date was provided. The Briefing did not identify any evidence on the cost-effectiveness of using SH to treat third and fourth degree haemorrhoids. The cohort study was dated [159] and relates to the Spanish setting so was of limited use.

10.9 Abstract relevant to calculation of utilities

Abstract submitted to International Society of Pharmacoeconomics and Outcomes Research Conference 12th Annual International Meeting, May 19-23 2007[111]

SF-36 And EQ-5D: A Simple And Original Solution To The Complexities Of Conversion

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Objectives: SF-36 suffers from a fatal design flaw common to many profile measures in being unable to represent health status as a single aggregate measure – a required attribute of any instrument used to measure benefits in cost-effectiveness analysis of healthcare. Over the past decade significant effort has been made to remedy this shortcoming in SF-36 by converting it into a utility-weighted index such as EQ-5D using regression models of varying complexity. These methods require access to micro-level data. Where SF-36 data are reported in summary form such transformation models are no longer feasible. This paper reports on a novel solution to the problem of conversion.

Methods: This distance between two SF-36 profiles S_i and S_j can be computed as the root mean square of the 8 pairs of subscale scores given by $\left[\sum \left(S_{ik} - S_{jk}\right)^2\right]^{0.5}$ for k=1,8. The root mean square (RMS8) represents the average distance between the profiles across all dimensions. This metric is a general measure that can be used to identify the most closely matching SF-36 profiles.

Results: The Health Survey for England is a national population survey in which both EQ-5D and SF-36 were completed by some 16,000 adults. For a given target vector of SF-36 scores the 20 most closely matching individuals were selected on the basis of the RMS8 distance function. The mean observed EQ-5D index for this subset was computed, together with its variance. As expected, the correlation between observed and derived EQ-5D index values was high. However, values estimated for SF-36 profiles from other surveys indicate the robustness of the methodology. Estimated values in survey that lack comparative EQ-5D data appear entirely consistent with indicators of disease severity.

Conclusion: EQ-5D index values can be derived easily from SF-36 profiles.

10.10 Methods of the statistical analysis to determine the probabilities of health states

A statistical analysis was conducted to determine the probabilities of each of the health states at one year. Sixteen RCTs provided sufficient data to be included in the statistical model. The included RCTs and the data are shown in Table 10.30. The reasons for exclusion of RCTs are listed in Table 10.31.

Table 10.7: Data from the studies included in the statistical model

Study	n	None	Complications		Symptoms			Treat group	Mean Follow-up (Years)
			Non-serious	Serious	Mild	Moderate	Severe		
Basdanis *et al* 2005[82]	50	47	0	0	3	0	0	SH	0.5
	40	40	0	0	0	0	0	CH	
Correa-Rovello 2002[94]	41	29	1	0	11	0	0	SH	0.5
	41	34	1	0	6	0	0	CH	
Cheetham *et al* 2003[77]	14	8	0	0	6	0	0	SH	0.7
	16	12	0	0	4	0	0	CH	
Boccasanta *et al* 2002[85]	40	38	2	0	0	0	0	SH	0.9
	40	35	3	0	2	0	0	CH	
Ortiz *et al* 2005[86]	15	3	0	2	5	0	5	SH	1.0
	16	11	0	3	2	0	0	CH	
Kairaluoma *et al* 2003[80]	30	18	1	3	1	4	3	SH	1.0
	30	28	0	1	0	1	0	CH	
Hetzer *et al* 2002[88]	20	19	0	0	0	1	0	SH	1.0
	20	19	0	0	0	1	0	CH	
Shalaby *et al* 2001[93]	95	92	2	0	0	0	1	SH	1.0
	80	73	5	0	0	0	2	CH	
Ascanelli *et al* 2005[74]	50	45	0	3	0	2	0	SH	1.0
	50	48	1	1	0	0	0	CH	
Sengaore *et al* 2004[89]	59	45	0	3	9	2	0	SH	1.0
	58	44	1	6	4	0	3	CH	
Pavlidis *et al* 2002[83]	40	39	0	1	0	0	0	SH	1.0
	40	39	0	1	0	0	0	CH	
Ortiz *et al* 2002[87]	27	16	0	2	6	0	3	SH	1.3
	28	23	0	4	1	0	0	CH	
Palimento *et al* 2003[84]	37	24	0	0	13	0	0	SH	1.5
	37	25	0	0	12	0	0	CH	
Ho *et al* 2000[61]	27	23	0	0	3	0	1	SH	1.5
	33	31	0	0	0	1	1	CH	
Gravie *et al* 2005[81]	52	48	0	0	4	0	0	SH	2.0
	57	56	0	0	1	0	0	CH	
Van de Stadt *et al* 2005[78]	20	8	0	0	8	0	4	SH	3.8
	20	10	2	0	8	0	0	CH	
Total	1223	1030 (84%)	19 (2%)	30 (2%)	109 (9%)	12 (<1%)	23 (2%)		

n: number randomised

Note: there were very few mild complications and therefore mild and moderate complications have been combined as "non-serious complications" in this table

Note: The definitions of mild, moderate and severe symptom, and serious complications, are given in Figure 6.3

Table 10.8: Reasons for exclusion of some RCTs or data from the statistical model of complications, symptoms and reinterventions during the follow-up period

Reason for exclusion from statistical model	Number of studies excluded	References
Did not report interventions	2	Ren (2002)[75] Chung (2005)[90]
Did not report symptoms	1	Docherty (2001)[76]
Data not reported in a useable format – discrepancy between individual symptoms and total symptoms	1	Hasse (2004)[73]
Long term follow-up of RCT reported as full manuscript or reported at multiple time points	Included time point nearest to 1 year	Ooi (2002)[69] Palimento (2003)[84] Senagore (2004)[89] Pavlidis (2002)[83]

A two-step model was used. In the first step, outcomes were classified into three categories: (i) no adverse outcome, (ii) complications of surgery, and (iii) symptoms associated with haemorrhoids. These sets were considered heterogeneous, since complications and symptoms can arise from distinct processes. Complications are a technical failure of surgery, which represents the safety of the technology, whereas control of symptoms represents the effectiveness of the technology. Therefore the model calculated separate probabilities of incidence of complications and symptoms, and separate parameters to estimate the relative effect of treatment. Random effects at the first step takes into account the effect of unobservable characteristics being study and category-specific. For complications, this might include variations in the skill of the surgical teams between studies. For symptoms, there might be variations in patient characteristics or lifestyles making recurrence in particular studies more or less likely than average.

At the second step, the symptoms of haemorrhoids were categorised as mild, moderate or severe, conditional on a symptom having occurred. Within this higher level, these categories were considered homogenous, that is, there is a natural ordering of severity of the symptom. A treatment effect can be estimated at the second step from the data, that is, a difference between SH and CH in the mix of severities, given a patient has a recurrence of symptom, although a priori this might not be expected.

Similarly, at the second step, the complications of surgery were classified as mild, moderate and serious. There were very few mild complications observed in the data, and therefore the categories of mild and moderate complications were combined and the model was only estimated for two categories: serious and non-serious complications.

The statistical analysis used a multi-categorical response model. The multivariate response variable $\mathbf{y_{ij}}$ is a vector of the number of participants in arm **j** of study **i** reporting one of 6 possible values;

1=no adverse outcome

2=mild or moderate complications

3=serious complications

4=mild symptoms

5=moderate symptoms

6=severe symptoms

In a trial arm of size n_{ij}, y_{ij} is multinomially distributed

$$y_{ij} \sim M(n_{ij}, p_{ij})$$

where

$$y_{ij} = (y_{1ij},..,y_{6ij}),\ p_{ij} = \left(p_{1ij},...,p_{6ij}\right)$$

$$p_{rij} = P(Y_{ij} = r \mid x_{ij})$$

In the first step, a multinomial logit model was used to estimate the probability that patients had no adverse outcomes, complications, or a symptom. The offset term, **$\log(follow_{ij})$,** adjusted the probability of observing outcome **r** for the average length of follow-up in the study, with the coefficient constrained to be 1. A random effect takes into account the effect of unobservable characteristics being study and category-specific.

$$p_{rij} = \exp(z_{rij}) / \left(1 + \exp(z_{1ij}) + \exp(z_{2ij})\right)$$

with

$$z_{rij} = \log(follow_{ij}) + \alpha_{ri} + \beta_r * T_{ij}, r = 1,2$$

$$\alpha_{ri} \sim N(\alpha_r, \sigma_r^2)$$

alpha$_1$ can be interpreted as the mean log-odds of having complications with respect to the log-odds of having no adverse outcomes, and **alpha$_2$** is the mean log-odds of having symptoms with respect to the log-odds of having no adverse outcomes, for patients who have **CH. beta$_1$** is the relative risk (log-odds ratio) of complications for patients who have SH, and **beta$_2$** the relative risk of symptoms for patients who have SH. Using a Bayesian perspective, **alpha$_r$ and beta$_r$ (r=1,2)** take uninformative independent normal priors. **sigma_sq$_r$ (r=1,2)** is the between-study variance for category r and **sigma$_r$** take uninformative independent uniform priors.

At the second step, the probability that patients have mild, medium or severe symptoms, conditioned on having some kind of symptom, is estimated by a cumulative threshold model. The underlying and unobserved latent variable (severity of symptom) **U** is on an underlying continuous scale from –**Inf to +Inf.** The latent variable **U** is determined by the explanatory variables in a linear form;

$$U_{ij} = -(\gamma_0 + \gamma_1 * T_{ij}) + e_{ij}$$

It is unlikely that a treatment effect for the severity of the symptom would persist, conditional on a symptom having occurred, and this would only be included in the final model if the coefficient **gamma$_1$** were statistically significant at the 5% level. To reduce the computational burden in the model, all parameters were considered constants at the second step, that is, there is no study- and category-specific random effect.

Y and **U** are connected by;

$$Y = r \mid Y \geq 4 \Leftrightarrow \Theta_{r-1} < \mathrm{U} \leq \Theta_r, r = 4,5,6$$

where

$$-\infty = \Theta_3 < \Theta_4 < \Theta_5 < \Theta_6 = \infty$$

The error term **e$_{ij}$** was assumed to take a logistic distribution function F**(e) =1/(1+exp(-e))** . The second step of the statistical model was;

$$P(Y_{ij} \leq r \mid Y_{ij} \geq 4, x_{ij}) = F(\Theta_r + \gamma_1 * T_{ij}), r = 4,5,6$$

The threshold **theta$_4$** is the log-odds of observing mild symptoms (with no treatment effect), if symptoms occur. The threshold **theta$_5$** is the log-odds of observing mild or moderate symptoms (with no treatment effect), given symptoms occur. For identifiability the intercept term **gamma$_0$** was dropped. To avoid problems with estimation that may occur if the thresholds are very similar, the thresholds **theta$_4$** and **theta$_5$** were re-parameterised by;

$$a_1 = \Theta_4$$
$$a_2 = \log(\Theta_5 - \Theta_4)$$

The parameters **a$_1$, a$_2$** and **gamma$_1$** were given independent uninformative normal priors. A similar conditional logistic model was used to classify complications as serious or non-serious, given complications occur.

Winbugs code used to estimate the statistical model of the probabilities of complications and recurrent symptoms

```
Statistical model
#shtest15_7
model {
#offset
offset<-1
for (i in 1:NData) {
        #follow is mean length of follow-up in trial i in years
        lnF[i]<-log(Follow[i])
        #two step model
        #first step - probability patient has no symptoms
        #create linear predictor
        #Reference: Page 309 Fahrmeir and Tutz
        z[i,1]<-offset*lnF[i]+(alpha1[study[i]]+beta[1]*T[i])
        z[i,2]<-offset*lnF[i]+(alpha2[study[i]]+beta[2]*T[i])

        #None=R1, Complications = R2+R3, symptoms = R4+R5+R6
        #Assuming errors follow a logistic  distribution
        #gets the proportional odds multinomial model
        #first step probabilities
        #complications
        steps[i,1]<-exp(z[i,1])/(1+exp(z[i,1])+exp(z[i,2]))
        #symptoms
        steps[i,2]<-exp(z[i,2])/(1+exp(z[i,1])+exp(z[i,2]))
        #no problems
```

```
steps[i,3]<-1-steps[i,1]-steps[i,2]

#second step
#cumulative probability patient has either no reintervention, outpatient or surgery
#given syptoms
#assume logistic distribution for errors

logit(Q[i,1])<--(a[1])

logit(Q[i,2])<- -(a[2] )
logit(Q[i,3])<- -(a[2]+exp(a[3]))

p[i,1]<-steps[i,3]

#probability of moderate complications
p[i,2]<-steps[i,1]*Q[i,1]
#probability of severe complications
p[i,3]<- steps[i,1]*(1-Q[i,1])

# probability of mild symptoms
p[i,4]<-steps[i,2]*(1-Q[i,2])
#probability of moderate symptoms
p[i,5]<-steps[i,2]*(Q[i,2]-Q[i,3])
#probability of severe symptoms
p[i,6]<-steps[i,2]*Q[i,3]

#multinomial likelihood of observing data
R[i,1:6]~dmulti(p[i,],N[i])
}
#priors
# study effects
for(k in 1:NStudy) {
        alpha1[k]~dnorm(mu[1],Tau[1])
        alpha2[k]~dnorm(mu[2],Tau[2])
        }
#mean log-odds of observing no symptoms
mu[1]~dnorm(0,0.0001)
mu[2]~dnorm(0,0.0001)

#mean probabilities for no symptoms given treatment 1=CH and 2=SH
#at 1 year
#logistic distribution for step 1
#remember mu is already "negative"
pi[1]<- exp(mu[1])/(1+exp(mu[1])+exp(mu[2]))
pi[2]<- exp(mu[2])/(1+exp(mu[1])+exp(mu[2]))
pi[3]<- exp(mu[1]+beta[1])/(1+exp(mu[1]+beta[1])+exp(mu[2]+beta[2]))
pi[4]<- exp(mu[2]+beta[2])/(1+exp(mu[1]+beta[1])+exp(mu[2]+beta[2]))

#probabilities of interventions given complications
#logistic distribution for step 2
```

```
        pi[5]<-1- 1/(1+exp(a[1]))
        pi[6]<-1- pi[5]
        #given symptoms
        pi[7]<-1- 1/(1+exp(a[2]))
        pi[8]<-1/(1+exp(a[2]+exp(a[3])))
        pi[9]<-1- pi[7]-pi[8]

        #between-study variance of observing no symptoms
        Tau[1]<-1/(sd[1]*sd[1])
        sd[1]~dunif(0,10)
        Tau[2]<-1/(sd[2]*sd[2])
        sd[2]~dunif(0,10)
        #population common treatment effects

        beta[1]~dnorm(0, 0.0001)
        beta[2]~dnorm(0, 0.0001)
        #thresholds
        #mild vs moderate symptom
        a[1] ~dnorm(0, 0.0001)
        #moderate vs severe
        a[2] ~dnorm(0, 0.0001)
        #mod vs severe complication
        a[3] ~dnorm(0, 0.0001)
}
#inits
list(
alpha1=c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0),
alpha2=c(0,0,0,0,0, 0,0,0,0,0, 0,0,0,0,0, 0),
        beta=c(0,0),
        a=c(0,0,0), mu=c(0,0), sd=c(1,1))
#data
list(NStudy=16,NData=32)
study[] N[] R[,1] R[,2] R[,3] R[,4] R[,5] R[,6] T[] Follow[]
1 50 47 0 0 3 0 0 1 0.50
1 40 40 0 0 0 0 0 0 0.50
2 41 29 1 0 11 0 0 1 0.50
2 41 34 1 0 6 0 0 0 0.50
3 14 8 0 0 6 0 0 1 0.67
3 16 12 0 0 4 0 0 0 0.67
4 40 38 2 0 0 0 0 1 0.92
4 40 35 3 0 2 0 0 0 0.92
5 15 3 0 2 5 0 5 1 1.00
5 16 11 0 3 2 0 0 0 1.00
6 30 18 1 3 1 4 3 1 1.00
6 30 28 0 1 0 1 0 0 1.00
7 20 19 0 0 0 1 0 1 1.00
7 20 19 0 0 0 1 0 0 1.00
8 95 92 2 0 0 0 1 1 1.00
8 80 73 5 0 0 0 2 0 1.00
9 50 45 0 3 0 2 0 1 1.00
```

9 50 48 1 1 0 0 0 0 1.00
10 59 45 0 3 9 2 0 1 1.00
10 58 44 1 6 4 0 3 0 1.00
11 40 39 0 1 0 0 0 1 1.00
11 40 39 0 1 0 0 0 0 1.00
12 27 16 0 2 6 0 3 1 1.33
12 28 23 0 4 1 0 0 0 1.33
13 37 24 0 0 13 0 0 1 1.50
13 37 25 0 0 12 0 0 0 1.50
14 27 23 0 0 3 0 1 1 1.50
14 33 31 0 0 0 1 1 0 1.50
15 52 48 0 0 4 0 0 1 2.00
15 57 56 0 0 1 0 0 0 2.00
16 20 8 0 0 8 0 4 1 3.83
16 20 10 2 0 8 0 0 0 3.83
END

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