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Surgical interventions for the management of chronic pelvic pain in women (Review)

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[Intervention Review]

Surgical interventions for the management of chronic pelvic pain in women

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ABSTRACT

Background

Chronic pelvic pain (CPP) is a common gynaecological condition accounting for 20% of all gynaecological referrals. There are wide ranges of causes with overlapping symptomatology, therefore the management of the condition is a formidable challenge for clinicians. The aetiology of CPP is heterogeneous and in many cases, no clear diagnosis can be reached. It is in this scenario that the label of chronic pelvic pain syndrome (CPPS) can be applied. We defined women with CPPS as having a minimum duration of pain of at least 6 months, including with a diagnosis of pelvic congestion syndrome, but excluding pain caused by a condition such as endometriosis. Many surgical interventions have been tried in isolation or in conjunction with non-surgical interventions in the management with variable results. Surgical interventions are invasive and carry operative risks. Surgical interventions must be evaluated for their effectiveness prior to their prevalent use in the management of women with CPPS.

Objectives

To review the effectiveness and safety of surgical interventions in the management of women with CPPS.

Search methods

We searched the Cochrane Gynaecology and Fertility Group (CGF) Specialised Register of Controlled Trials, CENTRAL, MEDLINE, Embase and PsycINFO, on 23 April 2021 for any randomised controlled trials (RCT) for surgical interventions in women with CPPS. We also searched the citation lists of relevant publications, two trial registries, relevant journals, abstracts, conference proceedings and several key grey literature sources.

Selection criteria

RCTs with women who had CPPS. The review authors were prepared to consider studies of any surgical intervention used for the management of CPPS. Outcome measures were pain rating scales, adverse events, psychological outcomes, quality of life (QoL) measures and requirement for analgesia.

Data collection and analysis

Two review authors independently evaluated studies for inclusion and extracted data using the forms designed according to Cochrane guidelines. For each included trial, we collected information regarding the method of randomisation, allocation concealment, blinding,

data reporting and analyses. We reported pooled results as mean difference (MDs) or odds ratios (OR) and 95% confidence interval (CI) by the Mantel-Haenszel method. If similar outcomes were reported on different scales, we calculated the standardised mean difference (SMD). We applied GRADE criteria to judge the overall certainty of the evidence.

Main results

Four studies met our inclusion criteria involving 216 women with CPP and no identifiable cause.

Adhesiolysis compared to no surgery or diagnostic laparoscopy

We are uncertain of the effect of adhesiolysis on pelvic pain scores postoperatively at three months (MD −7.3, 95% CI −29.9 to 15.3; 1 study, 43 participants; low-certainty evidence), six months (MD −14.3, 95% CI −35.9 to 7.3; 1 study, 43 participants; low-certainty evidence) and 12 months postsurgery (MD 0.00, 95% CI −4.60 to 4.60; 1 study, 43 participants; very low-certainty evidence).

Adhesiolysis may improve both the emotional wellbeing (MD 24.90, 95% CI 7.92 to 41.88; 1 study, 43 participants; low-certainty evidence) and social support (MD 23.90, 95% CI −1.77 to 49.57; 1 study, 43 participants; low-certainty evidence) components of the Endometriosis Health Profile-30, and both the emotional component (MD 32.30, 95% CI 13.16 to 51.44; 1 study, 43 participants; low-certainty evidence) and the physical component of the 12-item Short Form (MD 22.90, 95% CI 10.97 to 34.83; 1 study, 43 participants; low-certainty evidence) when compared to diagnostic laparoscopy.

We are uncertain of the safety of adhesiolysis compared to comparator groups due to low-certainty evidence and lack of structured adverse event reporting.

No studies reported on psychological outcomes or requirements for analgesia.

Laparoscopic uterosacral ligament ablation or resection compared to diagnostic laparoscopy/other treatment

We are uncertain of the effect of laparoscopic uterosacral ligament/nerve ablation (LUNA) or resection compared to other treatments postoperatively at three months (OR 1.26, 95% CI 0.40 to 3.93; 1 study, 51 participants; low-certainty evidence) and six months (MD −2.10, 95% CI −4.38 to 0.18; 1 study, 74 participants; very low-certainty evidence). At 12 months post-surgery, we are uncertain of the effect of LUNA on the rate of successful treatment compared to diagnostic laparoscopy. One study of 56 participants found no difference in the effect of LUNA on non-cyclical pain (P = 0.854) or dyspareunia (P = 0.41); however, there was a difference favouring LUNA on dysmenorrhea (P = 0.045) and dyschezia (P = 0.05). We are also uncertain of the effect of LUNA compared to vaginal uterosacral ligament resection on pelvic pain at 12 months (MD 2.00, 95% CI 0.47 to 3.53; 1 study, 74 participants; very low-certainty evidence).

We are uncertain of the safety of LUNA or resection compared to comparator groups due to the lack of structured adverse event reporting.

Women undergoing LUNA may require more analgesia postoperatively than those undergoing other treatments (P < 0.001; 1 study, 74 participants).

No studies reported psychological outcomes or QoL.

Authors' conclusions

We are uncertain about the benefit of adhesiolysis or LUNA in management of pain in women with CPPS based on the current literature. There may be a QoL benefit to adhesiolysis in improving both emotional wellbeing and social support, as measured by the validated QoL tools. It was not possible to synthesis evidence on adverse events as these were only reported narratively in some studies, in which none were observed. With the inadequate objective assessment of adverse events, especially long-term adverse events, associated with adhesiolysis or LUNA for CPPS, there is currently little to support these interventions for CPPS.

PLAIN LANGUAGE SUMMARY

Surgical management of chronic pelvic pain in women

Why we did this Cochrane Review

We wanted to find out whether there are any effective and safe surgical treatments for women with chronic pelvic pain. We wanted to understand how effective these surgical treatments are compared to alternative treatments or no treatment at all.

Background

Chronic pelvic pain in women is a common and debilitating condition. Definitions vary, but generally it is defined as pelvic pain for a period of six months or greater. There are many causes of chronic pelvic pain, but these can sometimes be difficult to identify. Regardless of identifying any or the specific cause, treatment is aimed at reducing symptoms. Occasionally, a diagnostic surgery with insertion of laparoscope is completed (inserting a telescope into the belly to visualise pelvic structures). When identifiable causes of chronic pelvic pain are present, such as endometriosis (tissue similar to the lining of the womb that starts to grow in other places) or adenomyosis (tissue

similar to the lining of the womb is found deep in the muscle of the womb), there may be different treatment strategies necessary than when there are no obvious problems. When no disease is identified at the time of a diagnostic surgery despite chronic pelvic pain, we may consider various surgical procedures to treat the chronic pelvic pain, including removing scar tissue originating from infection or previous operation (called adhesiolysis), or cauterising (heat treatment) or excising (removing) the nerves carrying the pain sensation from pelvis to brain (called uterosacral ligament ablation/resection). Despite it being unclear how effective these surgical treatments are, they are being offered and done.

What we found

We found four randomised controlled trials (a type of study that gives the most reliable evidence about the effects of treatment) involving 216 women with chronic pelvic pain and no identifiable cause. The main outcome measures were pain scores after surgery and quality of life. The evidence is current to 23 April 2021.

Key results

Adhesiolysis versus no surgery/diagnostic laparoscopy

We are uncertain of the effect of adhesiolysis compared with diagnostic laparoscopy on pain scores at three, six and 12 months after surgery. Pain was measured using a visual analogue score (VAS), which is a widely used rating scale where the person ranks pain from 0 (no pain) to 100 (worst pain). Adhesiolysis may improve health-related quality of life at six months after surgery when compared to diagnostic laparoscopy.

Laparoscopic uterosacral ligament ablation versus other treatment

We are uncertain of the effect of laparoscopic uterosacral ligament ablation (LUNA) versus diagnostic laparoscopy or vaginal uterosacral ligament resection, on pain scores measured by VAS at three, six and 12 months. Women undergoing LUNA may require more pain relief after surgery than those undergoing alternative treatments.

No studies in either comparison reported on psychological outcomes.

Certainty of evidence

The certainty of the evidence ranged from very low to low. Limitations included poor reporting of study methods and imprecision (too few events, too few included studies) for some comparisons.

Summary of findings 1. Summary of findings table - Adhesiolysis compared to no surgery or diagnostic laparoscopy

Adhesiolysis compared to no surgery or diagnostic laparoscopy

Patient or population: health problem or population
Setting: Clinic/Hospital
Intervention: Adhesiolysis
Comparison: Control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Control	Risk with Adhesiolysis				
Effectiveness of treatment assessed with: 100mm Visual analogue scale (VAS) follow-up: 3 months	The mean effectiveness of treatment was **27.3**	MD **7.3 lower** (29.87 lower to 15.27 higher)	-	43 (1 RCT)	⊕⊕⊖⊖ Low[a]	Due to the wide CIs, we are uncertain of the effect of adhesiolysis on pelvic pain scores at 3 months postsurgery.
Effectiveness of treatment assessed with: 100mm Visual analogue scale (VAS) follow-up: 6 months	The mean effectiveness of treatment was **27.3**	MD **14.3 lower** (35.91 lower to 7.31 higher)	-	43 (1 RCT)	⊕⊕⊖⊖ Low[a]	Due to the wide CIs, we are uncertain of the effect of adhesiolysis on pelvic pain scores at 6 months postsurgery.
Effectiveness of treatment assessed with: 100mm Visual analogue scale (VAS) follow-up: 12 months	The mean effectiveness of treatment was **24**	MD **0** (4.6 lower to 4.6 higher)	-	43 (1 RCT)	⊕⊖⊖⊖ Very low[a,b]	We are uncertain of the effect of adhesiolysis on pelvic pain scores at 12 months postsurgery.
Adverse events	Authors reported there were no complications related to surgery			43 (1 RCT)	⊕⊕⊖⊖ Low[a]	Due to both the low certainty of the study and the lack of structured adverse event reporting we are uncertain of the safety of adhesiolysis compared to comparator groups.
Psychological outcomes - not reported	-	-	-	-	-	No studies reported on this outcome.
Quality of life assessed with: 12-item Short Form (SF-12) Physical (high-	The mean quality of life was	MD **22.9 change from baseline higher**	-	43 (1 RCT)	⊕⊕⊖⊖ Low[a]	Adhesiolysis may improve physical health-related quality of life at 6 months postsurgery.

er scores indicate improved quality of life) follow-up: 6 months	**6.3** change from baseline	(10.97 higher to 34.83 higher)				
Quality of life assessed with: 12-item Short Form (SF-12) Emotional (higher scores indicate improved quality of life) follow-up: 6 months	The mean quality of life was **-3.7** change from baseline	MD **32.3 change from baseline higher** (13.16 higher to 51.44 higher)	-	43 (1 RCT)	⊕⊕⊖⊖ Low[a]	Adhesiolysis may improve emotional health-related quality of life at 6 months postsurgery.
Requirement for analgesia - not reported	-	-	-	-	-	No studies reported this outcome.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_427465143401005369.

[a] Downgraded two levels due to very serious imprecision due to small study size (43 participants).
[b] Downgraded one level due to serious risk of bias due to unclear selection bias.

Summary of findings 2. Summary of findings table - LUNA (laparoscopic uterosacral ligament nerve ablation) compared to diagnostic laparoscopy/other treatments

LUNA (laparoscopic uterosacral ligament nerve ablation) compared to diagnostic laparoscopy/other treatments

Patient or population: health problem or population
Setting: Clinic/Hospital
Intervention: LUNA (laparoscopic uterosacral nerve ablation)
Comparison: Control

Outcomes	Anticipated absolute effects* (95% CI)	Relative effect (95% CI)	№ of participants	Certainty of the evidence	Comments

	Risk with Control	Risk with LUNA (laparoscopic uterosacral nerve ablation)		(studies)	(GRADE)	
Effectiveness of treatment assessed with: Participants with at least a 50% reduction from the baseline visual analogue scale pelvic pain score. follow-up: 3 months	469 per 1000	**526 per 1000** (261 to 776)	**OR 1.26** (0.40 to 3.93)	51 (1 RCT)	⊕⊕⊖⊖ Low[a]	Due to the wide CIs we are uncertain about the effect of ablation or resection compared to other treatments on pelvic pain 3 months postsurgery.
Effectiveness of treatment assessed with: 100 mm visual analogue scale (VAS) follow-up: 6 months	The mean effectiveness of treatment was **40.6**	MD **2.1 lower** (4.38 lower to 0.18 higher)	-	74 (1 RCT)	⊕⊖⊖⊖ Very low[b,c]	We are uncertain about the effect of LUNA on pelvic pain scores at 6 months postsurgery.
Effectiveness of treatment assessed with: 100 mm visual analogue scale (VAS) follow-up: 12 months	The mean effectiveness of treatment was **48.5**	MD **2 higher** (0.47 higher to 3.53 higher)	-	74 (1 RCT)	⊕⊖⊖⊖ Very low[b,c]	We are uncertain about the effect of LUNA on pelvic pain scores at 12 months postsurgery.
Adverse events	2 studies reported on this narratively. Both studies reported no intraoperative or postoperative events.			121 (2 RCTs)	-	Due to the narrative nature of the reporting, we are uncertain of the safety of ablation or resection compared to other treatments.
Psychological outcomes - not reported	-	-	-	-	-	No studies reported this outcome.
Quality of life - not reported	-	-	-	-	-	No studies reported this outcome.
Requirement for analgesia	1 study reported women in the LUNA group required significantly (P < 0.001) more analgesia (measured by number of vials of tramadol used during hospital stay) with a median of 7 (range 5–9) vials vs to women undergoing VUSR who used a median of 4 (range 2–5) vials.			74 (1 RCT)	-	Women undergoing LUNA may require more analgesia postoperatively than women undergoing other treatments.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

See interactive version of this table: https://gdt.gradepro.org/presentations/#/isof/isof_question_revman_web_424428033590495750.

[a] Downgraded two levels due to very serious imprecision: one very small study (51 participants).
[b] Downgraded one level due to risk of bias: the single included trial was at a high risk of bias for performance and detection bias due to the lack of sham incisions.
[c] Downgraded two levels due to very serious imprecision: one small study (74 participants).

BACKGROUND

Description of the condition

Chronic pelvic pain (CPP) is a common condition experienced by women. Definitions of CPP may vary, but a minimum duration of six months is considered necessary to define the pain as chronic (ACOG 2004; RCOG 2012; Jarrell 2018). Accordingly, the prevalence rates vary with the definition used to describe the condition, country and social-economic factors. The prevalence around the world ranges from 5.7% to 26.6% (Ahangari 2014). The reported annual prevalence in primary care in the UK in women aged 15 to 73 years is 38/1000 women, almost comparable to chronic back pain (41/1000) in men and women (Zondervan 2001). There are a number of possible aetiological factors in the genesis of CPP, including changes to the central and peripheral nervous system, endometriosis, adenomyosis, adhesions, irritable bowel syndrome, interstitial cystitis, musculoskeletal sources and nerve entrapment (RCOG 2012); therefore, the condition is a challenge to diagnose and treat. It is important to note that not every woman who exhibits one or more aetiological factors of CPP actually exhibits CPP. The aetiology of CPP is heterogeneous and, in many cases, there is no clear diagnosis. It is in this scenario that the label of chronic pelvic pain syndrome (CPPS) can be applied (Baranowski 2012). Historically, CPP was the indication for 40% of diagnostic laparoscopies (Howard 1993), and an estimated 12% of hysterectomies in the US (Reiter 1990). In 2016, CPP was an indication for hysterectomy in 39.2% of women in one large study of 12,118 hysterectomies (Mowers 2016). It remains a common indication for diagnostic laparoscopy today (Mirowska-Allen 2019). Though our understanding of CPP and our ability to better diagnose some common aetiologies of CPP has advanced, surgical intervention for CPP is still utilised for diagnosis and treatment. In addition, various pharmacological and non-pharmacological interventions have been tried in isolation or in conjunction with each other in the management of CPP (Stones 2005).

Description of the intervention

Current and past surgical interventions commonly employed for management of CPP are diverse, as would be expected based on the variety of aetiological factors. Possible interventions include diagnostic laparoscopy, excision or ablation (or both) of endometriosis, conscious pain-mapping laparoscopy, microlaparoscopy, adhesiolysis (surgical removal of adhesions), uterosacral nerve ablation (UNA) (laparoscopic or open surgery to disrupt the nerve plexus), presacral neurectomy, pelvic vein ligation (interventional radiology or surgical), total or subtotal hysterectomy, oophorectomy and ventrosuspension. Though clinical and non-invasive imaging diagnoses are constantly improving, laparoscopy remains a cornerstone in establishing (or confirming) a diagnosis and treatment of identifiable pathology, but also providing reassurance to women in its absence. Occasionally, other surgical approaches (laparotomy or vaginal surgery) may be performed to achieve diagnoses or administer treatment, or both.

How the intervention might work

Broadly, surgical intervention may be targeted at the primary aetiological factor of the CPP or be used diagnostically, to guide surgical intervention, which is often implemented at the same time as the diagnostic procedure. The mechanism of the intervention depends on the aetiology. In the case of this systematic review and meta-analysis, we will focus on the interventions that are targeted at CPPS. Therefore, any surgical interventions that may target confirmed infection or other obvious local pathology will not be considered.

Adhesions are commonly seen in women with CPP but the value of adhesiolysis in the treatment of CPP is still controversial (Cheong 2006). Adhesions may originate from an organic source (e.g. pelvic inflammatory disease (PID), diverticulitis or endometriosis) in a virgin abdomen or occur in an individual who has undergone surgery (i.e. iatrogenic adhesions). Adhesions have been shown to carry nerve fibres (Tulandi 1998), and hence may be a possible mechanical cause for pelvic pain. Adhesiolysis is aimed at releasing this mechanical restriction and therefore disrupt the perpetuation of pain. Adhesiolysis can be performed during laparoscopy or at laparotomy. It is also possible that adhesions may not be the source of CPP in the context of other pathology (deep endometriosis beneath areas of adhesions, changes in the central and peripheral nervous system following an episode of treated PID). These potential pathologies may have the potential to be recognised, while others may only be diagnosed after excluding all other possibilities.

CPP can occur as a result of an altered physical, psychological or functional state; it is likely that interaction of the neurophysiological and psychological processes is complex and dynamic (Vercellini 2009). In many cases, even when pathology is removed, there may be ongoing generation of pain in the absence of stimulus, implying there have been changes to the central nervous system (CNS) (Brawn 2014). Pain from the uterus, cervix and proximal tubes passes through nerve fibres that join at the base of the uterosacral ligaments (USL) to form the Lee-Frankenhauser plexus. From here they exit to join the superior and inferior hypogastric plexus. The ovaries derive their nerve supply from the ovarian plexus that originate from the renal and aortic nerve plexuses and travel in proximity to the ovarian artery and veins. In addition, these fibres also network with the presacral neural network. Visceral pain originates in the intraperitoneal organs and is transmitted through the sympathetic fibres of the autonomic nervous system. In the spinal cord, there is diffuse dispersal of the pain stimuli and hence patients may perceive the sensation across several dermatomes. Sometimes, this is poorly localised and can provoke associated autonomic manifestations (Vercellini 2009).

Many surgical interventions are designed to disrupt the nerve plexus that may be involved with the perpetuation of the perception of pain. These operations include UNA, uterosacral ligament resection (USR), or presacral neurectomy (PSN). These procedures can be performed via laparoscopic route (laparoscopic uterosacral nerve ablation (LUNA), laparoscopic uterosacral ligament resection (LUSR), PSN), vaginal route (vaginal uterosacral ligament resection (VUSR)) and laparotomy (UNA, USR, PSN), and one or both of the USLs are removed/ablated (Johnson 2004; Palomba 2006; Daniels 2009). Resection of the USL usually involves the surgical removal of a small segment of the ligament usually about 1 cm in length, although there is variation in the surgical practice (Latthe 2004). The ablation of the USL can be performed using laser (Gürgan 1992), mono or bipolar diathermy to ablate approximately 1 cm to 2 cm distally to the attachment of the ligament to the cervix (Latthe 2004). Resection allows for the histological examination of the tissue to ensure the

presence of nerve fibre but not when the ablative technique is being used. UNA aims to transect the USLs to sever the sensory pathways entering the Lee-Frankenhauser plexus. Theoretically, this would only disrupt the uterine and cervical nerve pain fibres and only benefit women with pelvic pain originating from these structures. Conversely, PSN divides the hypogastric nerve plexus at the level of sacrum and potentially may be a more effective technique. However, neither procedure interrupts the sympathetic and parasympathetic nerve fibres arising in the S2-S4 nerves, as they travel through the uterovaginal vascular plexus and pelvic sidewalls.

Besides these anatomically oriented concepts, some have explored the pelvic vascular system. The female pelvis has extensive anastomosis and collateral vascular circulation with different visceral components including the uterus, bladder and bowel. The pelvic veins are thin-walled and poorly supported with relatively few venous valves. These features predispose women to pelvic congestion syndrome, which is defined as CPP resulting from 'incompetent' pelvic veins (Jurga-Karwacka 2019). 'Incompetent' veins are described by dysfunctional dilation of ovarian and para-uterine veins, slow blood flow (congestion), retrograde flow and reflux (Champaneria 2016). However, the diagnostic criteria for pelvic congestion have not been clearly defined or validated (Amin 2021), and thus the literature in this field remains inconsistent and difficult to interpret. Stopping the flow through an incompetent vein is thought to be an effective treatment strategy (Champaneria 2016). Surgical pelvic vein ligation is occasionally performed in women with pelvic congestion syndrome (Gargiulo 2003). An alternative, and now more commonly used, tool to surgical ligation is an interventional radiological procedure called ovarian vein embolisation (Maleux 2000). While there is evidence for the release of potentially pain-producing agents from venous endothelium and perivascular nerve terminals (Stones 2000), the role of pelvic venous congestion in the pathogenesis remains unclear.

More radical, though more common, procedures such as hysterectomy or oophorectomy (or both) are also considered in women with CPP of unclear aetiology (Jarrell 2018). In the past, CPP has been listed as the main indication for 10% to 12% of hysterectomies in the US (Lee 1984; Hillis 1995). Recently, CPP was noted as an indication for hysterectomy in almost 40% of the patients (Mowers 2016). The implications on family planning and menopause are significant, so there may be hesitancy in utilising these procedures. In women with CPP of unclear aetiology, these procedures may be implemented in an attempt to 'do something'. In some cases, unrecognised pathology such as adenomyosis, pelvic congestion syndrome or chronic PID may be inadvertently treated resulting in improvement. However, posthysterectomy CPP is possible and reported in up to 22% of women (Stovall 1990). Hence, the management of women with CPP in the absence of identifiable pathology is still a significant challenge.

Notwithstanding the above anatomical considerations and clinical applications, there are fundamental neurophysiological barriers to the likely success of nerve-cutting procedures for the relief of chronic pain in general and pelvic pain in particular. The pathophysiology of establishing a chronic pain state includes changes in the CNS including expression of pain mediators, physical sprouting of afferents, and complex reorganisation of central pain processing (Brawn 2014). As-Sanie and colleagues found structural grey matter alterations in the brains of women with CPP, which has also been identified in patients with other types of chronic pain (As-Sanie 2012). Anatomical, mechanical and neurophysiological factors contributing to CPP also need to be placed in a context with psychological propensities such as fear avoidance, catastrophising and depression, which all influence pain experience and render the impact of surgical interventions more difficult to discern (Stones 2007; ACOG 2020).

Why it is important to do this review

Gynaecologists use various surgical procedures for the treatment of CPP, including in the absence of obvious infectious or other pathology (CPPS). For many of these surgical procedures, there is no current consensus for best practice. For example, the most recent 2020 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin on CPP makes no mention of hysterectomy, despite its frequent use (ACOG 2020). Therefore, it is important to perform a systematic review and meta-analysis on this area to inform practitioners of the value of the various surgical interventions in the management of women with CPPS.

OBJECTIVES

To review the effectiveness and safety of surgical interventions in the management of women with CPPS.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs).

Types of participants

Women with CPPS (minimum pain duration six months) including those with a diagnosis of pelvic congestion syndrome, but excluding those with pain known to be caused by:

- endometriosis;
- adenomyosis;
- primary dysmenorrhoea (period pain), a recurrent painful condition exclusively related to menstruation;
- pain due to active chronic PID, that is chronic low-grade sepsis in devitalised tubal tissue with acute exacerbations that has been incompletely treated by antibiotics;
- irritable bowel syndrome;
- interstitial cystitis/bladder pain syndrome;
- urethral syndrome.

However, if a study population was overall ineligible but included an eligible subgroup of participants, we considered data pertaining to this subgroup.

Types of interventions

Any study that undertook any surgical intervention for management of CPPS, including but not limited to:

- diagnostic laparoscopy;
- conscious pain-mapping laparoscopy;
- microlaparoscopy;
- abdomino-pelvic adhesiolysis (by any method);

- LUNA/open uterine nerve ablation;
- USL resection;
- laparoscopic/open PSN;
- hysterectomy;
- oophorectomy/salpingo-oophorectomy;
- pelvic vein ligation (surgical);
- ventrosuspension.

Types of outcome measures

Primary outcomes

- Effectiveness of treatment: pain: measured by validated pain scales, for example, visual analogue pain scale (VAS) scores, the McGill Pain Questionnaire (MPQ), a pain improvement rating scale, general pain experience and a gynaecological pain questionnaire. If studies used multiple pain measures, we preferred VAS, followed by the MPQ and then any other validated pain scale. Most studies were expected to have assessed these outcomes at three, six and beyond six months to exclude placebo effect. Outcomes that were reported out of this three, six, 12 months period were combined with the nearest quarter if appropriate. Where trials expressed their outcomes as recommended by Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT), which are benchmarked in terms of pain intensity, physical function, emotional functioning and global rating of improvement (Dworkin 2008), these were to be analysed accordingly.
- Adverse events (e.g. intraoperative and postoperative surgical complications).

Secondary outcomes

- Psychological outcomes indicated by scores such as depression scores (Hamilton Depression Rating Scale (HAM-D) score, Hospital Anxiety Depression Scale, which would be given priority if any other scales were presented) and mood scores.
- Quality of life (QoL): indicated by, for example, the Medical Outcomes Study Short Form 36 (SF-36), the Social Adjustment Survey (SAS-WR), the Sickness Impact Profile (SIP), a general health questionnaire (GHQ), the revised Sabbatsberg Sexual Rating Scale (rSSRS) and EuroQOL-5D (EQ-5D). If multiple scales were used, we gave the SF-36 priority, followed by SAS-WR and then any other validated QoL questionnaire.
- Requirement for analgesia.

Search methods for identification of studies

We searched for published and unpublished RCTs from each database's inception to April 2021 with no language restriction and in consultation with the Cochrane Gynaecology and Fertility Group (CFG) Information Specialist.

Electronic searches

We searched the following electronic databases:

- The Cochrane Gynaecology and Fertility Specialised Register of Controlled Trials, ProCite platform, searched 23 April 2021 (Appendix 1);
- CENTRAL, via the Cochrane Register of Studies Online (CRSO), Web platform, searched 23 April 2021 (Appendix 2);
- MEDLINE, Ovid platform, searched from 1946 to 23 April 2021 (Appendix 3);
- Embase, Ovid platform, searched from 1980 to 23 April 2021 (Appendix 4);
- PsycINFO, Ovid platform, searched from 1806 to 23 April 2021 (Appendix 5).

Searching other resources

We handsearched reference lists of relevant trials and systematic reviews retrieved by the search and contact experts in the field to obtain any additional trials. We searched two trial registries and handsearched relevant journals and conference abstracts that are not covered in the CGF register, in liaison with the Information Specialist.

Data collection and analysis

Selection of studies

Two review authors (TG and AC) conducted an initial screen of titles and abstracts retrieved by the search and retrieved the full texts of all potentially eligible studies. Two review authors (TG and AC) independently examined these full-text articles for compliance with the inclusion criteria and selected eligible studies. We corresponded with study investigators as required, to clarify study eligibility. We resolved disagreements by discussion. We documented the selection process with a PRISMA flow chart.

Data extraction and management

Two review authors (TG and AC) independently extracted data from eligible studies using a data extraction form designed and pilot-tested by the authors. We resolved disagreements by discussion. Data extracted included study characteristics and outcome data. We corresponded with study investigators for further information: where results data required for inclusion in the meta-analysis were not present either in the text or able to be extracted from graphs/figures; and to clarify methods (e.g blinding, randomization) if needed to determine risk of bias accurately.

Assessment of risk of bias in included studies

Two review authors (ML and MA) independently assessed the included studies for risk of bias using the Cochrane risk of bias assessment tool (Higgins 2011) to assess: selection (random sequence generation and allocation concealment); performance (blinding of participants and personnel); detection (blinding of outcome assessors); attrition (incomplete outcome data); reporting (selective reporting) and other bias. Judgements were assigned as recommended in the *Cochrane Handbook of Systematic Reviews of Interventions* Section 8.5 (Higgins 2011). We resolved disagreements by discussion.

Measures of treatment effect

For dichotomous data, we used the numbers of events in the control and intervention groups of each study to calculate Mantel-Haenszel odds ratios (ORs) or (where events are very rare) Peto ORs. For continuous data, if all studies report exactly the same outcomes, we calculated mean difference (MDs) between treatment groups. If similar outcomes were reported on different scales, we calculated the standardised mean difference (SMD). We reversed the direction of effect of individual studies, if required, to ensure consistency across trials. We treated ordinal data (e.g. QoL

scores) as continuous data. We presented 95% confidence intervals (CI) for all outcomes. Where data to calculate ORs or MDs were not available, we utilised the most detailed numerical data available that would facilitate similar analyses of included studies (e.g. test statistics, P values). We assessed whether the estimates calculated in the review for individual studies were compatible in each case with the estimates reported in the study publications.

Unit of analysis issues

The primary analysis was per woman randomised. We planned to briefly summarised data that did not allow valid analysis in an additional table and not a meta-analysis. We sought statistical advice regarding the analysis of cross-over trials, to facilitate the appropriate inclusion of cross-over data in meta-analyses.

Dealing with missing data

We analysed the data on an intention-to-treat basis as far as possible (i.e. including all randomised participants in analysis, in the groups to which they were randomised). We attempted to obtain missing data from the original trialists. In the event of unobtainable data, we planned imputation for the primary outcomes, and only where data were dichotomous.

If studies reported sufficient detail to calculate MDs, but there was no information on associated standard deviations (SD), we assumed the outcome to have an SD equal to the highest SD from other studies within the same analysis.

Assessment of heterogeneity

We considered whether the clinical and methodological characteristics of the included studies were sufficiently similar for meta-analysis to provide a clinically meaningful summary. We assessed statistical heterogeneity using the I^2 statistic. An I^2 statistic greater than 50% was taken to indicate substantial heterogeneity (Higgins 2011).

Assessment of reporting biases

In view of the difficulty of detecting and correcting for publication bias and other reporting biases, we aimed to minimise their potential impact by ensuring a comprehensive search for eligible studies and by being alert for duplication of data. If there were 10 or more studies in an analysis, we used a funnel plot to explore the possibility of small-study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies).

Data synthesis

If the studies were sufficiently similar, we combined the data. We assumed that the underlying effect size was the same for all the trials in the analysis and therefore used a fixed-effect model to obtain an overall summary in the following comparisons.

- Adhesiolysis versus no surgery/diagnostic laparoscopy, subgrouped by severity of adhesions.
- Surgery including the ablation or resection of USL versus diagnostic laparoscopy/other treatment.
- Surgery including pelvic vein ligation versus diagnostic laparoscopy.
- Surgery including pelvic vein ligation versus placebo/sham procedures.

We performed statistical analysis using Review Manager Web (Review Manager Web).

Subgroup analysis and investigation of heterogeneity

If there was significant heterogeneity and the data were available, we conducted subgroup analyses to determine the separate evidence within the following subgroups:

- severity and extent of adhesions;
- variation in methodology of surgery on USLs (e.g. unilateral versus bilateral ablation/resection of USLs);
- open versus laparoscopic interventions;
- surgical versus interventional radiological interventions.

Sensitivity analysis

We planned sensitivity analyses for the primary outcomes to determine whether the conclusions were robust to arbitrary decisions made regarding the eligibility and analysis. These analyses were to consider whether the review conclusions would have differed if:

- eligibility had been restricted to studies at low risk of bias, defined as studies at low risk of selection bias;
- a random-effects model had been adopted.

Summary of findings and assessment of the certainty of the evidence

We generated summary of findings tables using GRADEpro GDT software (GRADEpro GDT). These tables evaluate the overall certainty of the body of evidence for the main review outcomes: pain (effectiveness), adverse events, psychological outcomes, QoL and requirement for analgesia using GRADE criteria.

We justified, documented and incorporated judgements about evidence certainty (high, moderate, low or very low) into reporting of results for each of these outcomes.

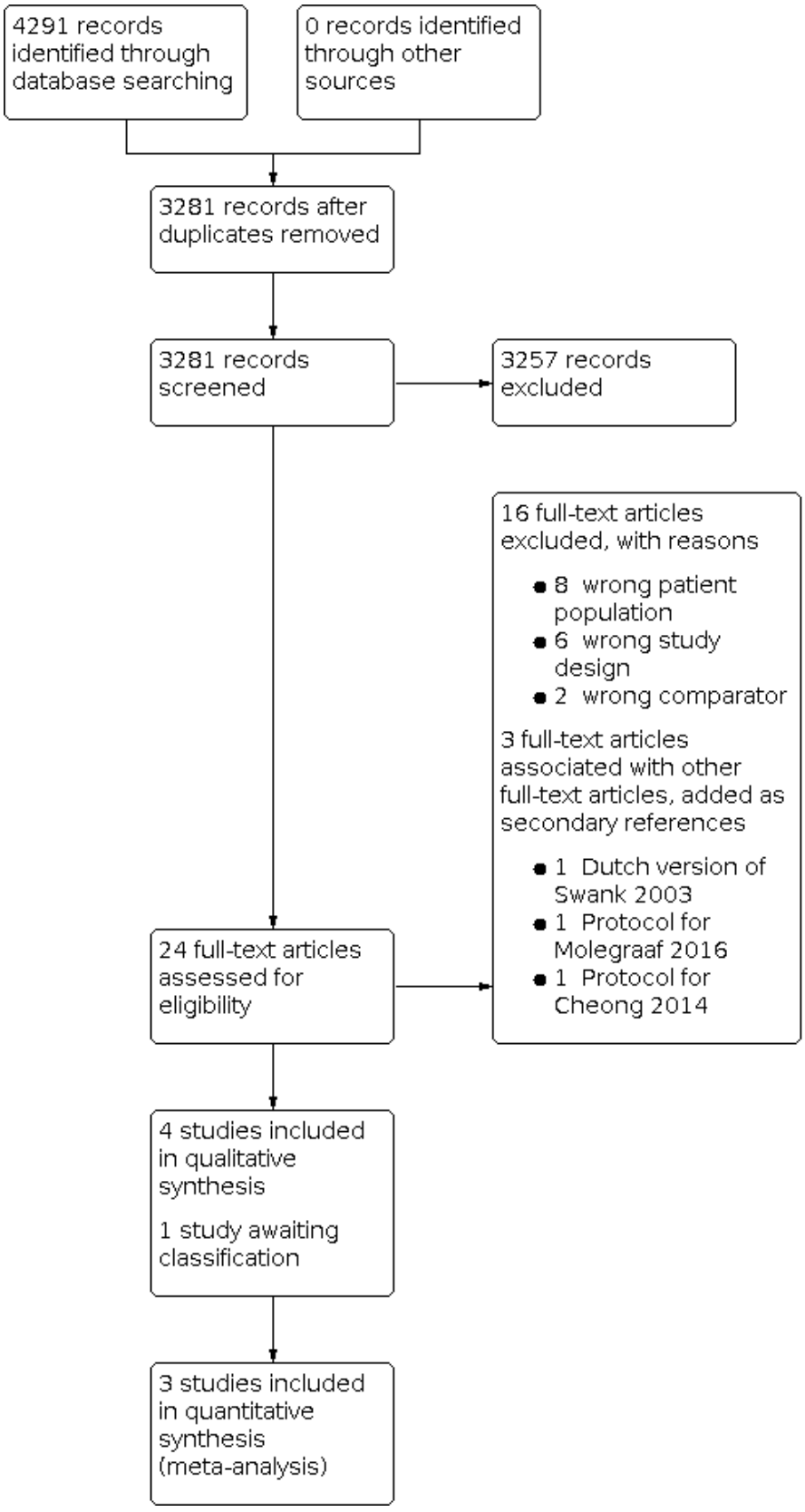
RESULTS

Description of studies

Results of the search

The search revealed 24 studies that were potentially eligible and were retrieved in full text. Four studies met our inclusion criteria. One study was awaiting classification (Daniels 2009). Sixteen studies were excluded. Two study protocols were identified and added as secondary references to primary study references for included studies (Cheong 2014; Molegraaf 2016). One translation of an excluded study was identified and added as a secondary reference to the primary study reference (Swank 2003). The selection process has been documented with a PRISMA flow chart (Figure 1). See the Characteristics of included studies and Characteristics of excluded studies tables.

Figure 1.



Included studies

Study design and setting

We included four RCTs (Peters 1992; Johnson 2004; Palomba 2006; Cheong 2014). All studies had a parallel design. One was undertaken in the Netherlands (Peters 1992), one in Italy (Palomba 2006), one in New Zealand (Johnson 2004), and one in the UK (Cheong 2014).

Participants

The trials enrolled 216 participants (overall: intervention 102, control 114; Cheong 2014: 43; Johnson 2004: 56; Palomba 2006: 74; Peters 1992: 43). All studies used power calculations to estimate the sample size (Peters 1992: intervention 21, control 22; Cheong 2014: intervention 23, control 20; Johnson 2004: intervention 22, control 34; Palomba 2006: intervention 36, control 38).

The age distribution of the participants in this review ranged from 21 to 60 years. All studies only recruited women. Palomba 2006 recruited postmenopausal women, while all other authors included either reproductive-aged women or a combination of reproductive-aged and postmenopausal women. Most participants were multiparous. Only Palomba 2006 reported the body mass index (BMI) of the participants, which was comparable in both the intervention and control groups. In Palomba 2006, the mean BMI in the intervention group was 27.2 (SD 2.1) and in the control group was 28.2 (SD 2.3). Most participants in both groups had symptoms for more than one year. In Cheong 2014 and Johnson 2004, more than half of the participants in the intervention and control group had some prior abdominal/pelvic operative procedure before the index operation, whereas Palomba 2006 and Peters 1992 did not specify the number and type of previous surgeries the participants had prior to the index operation. All trials rigorously excluded the presence of any significant medical and gynaecological conditions. Only Johnson 2004 did not exclude women with a mental health disorder; participants in Palomba 2006 underwent formal psychiatric and psychological assessment. In Cheong 2014, the intervention group had a statistically significantly higher baseline adhesion assessment score compared to the control group.

Interventions

All participants in the four included trials were randomised at the time of surgery.

- One study examined laparoscopic adhesiolysis versus diagnostic laparoscopy without adhesiolysis (Cheong 2014).
- One study compared adhesiolysis via laparotomy versus diagnostic laparoscopy without adhesiolysis (Peters 1992).
- Two studies compared LUNA versus an alternative (diagnostic laparoscopy (Johnson 2004) or VUSR (Palomba 2006)).

No studies evaluated the following possible interventions: conscious pain-mapping laparoscopy, microlaparoscopy, conscious pain-mapping laparoscopy, PSN, hysterectomy, oophorectomy, salpingo-oophorectomy, pelvic vein ligation or ventrosuspension. No studies involved a comparison of surgical versus interventional radiological interventions.

Outcome measures

- Three studies reported the difference in post-treatment VAS scores at three, six and 12 months (Peters 1992; Palomba 2006; Cheong 2014). One study reported the reduction of pain outcomes using the VAS score (significant reduction in pain defined as at least 50% reduction from baseline VAS pelvic pain) at six months (Johnson 2004). One study also reported the number of participants 'cured' ('cured' was defined as complete relief of those with CPP not requiring further medical treatment) (Palomba 2006).
- One study reported QoL using a variety of questionnaire-based QoL outcome measures (SF-12, EQ-5D (measured on scale of −0.59 to 1 based on responses to five questions about QoL) and EQ-VAS measured on 0 to 100 scale, modified Endometriosis Health Profile (EHP)-30) (Cheong 2014). Although the modified EHP-30 scoring system has not yet been validated for measuring CPP (only for endometriosis), the data were included due to the paucity of studies reporting on this outcome, and as no other scale was used in the one study reporting QoL.
- One study compared the costs of the intervention and alternative (Palomba 2006).

No subgroup analyses were performed since each would only have a single study comprising the data.

Excluded studies

We excluded 16 studies (Peters 1991; Saravelos 1995; Ouhilal 1999; Ventolini 1999; Aaltomaa 2001; Moon 2001; Garcia Leon 2003; Swank 2003; Fernandez 2004; Palomba 2005; Keltz 2006; El-Din Shawki 2011; Andersen 2015; Molegraaf 2016; Muzamil Ahmed 2019; Bautrant 2020); see Characteristics of excluded studies table).

Keltz 2006 conducted a double-blind RCT of right-sided paracolic adhesiolysis in management of CPP. They identified and recruited 25 women for each group. The intervention group was compared with women who underwent diagnostic laparoscopy, but no paracolic adhesiolysis. The study included women who complained of CPP (duration of symptoms prior to recruitment not specified) in the absence of any other identifiable cause. Randomisation was at the time of laparoscopy. Follow-up was four to eight weeks after the procedure. There were no missing data in terms of withdrawal after recruitment or loss to follow-up. The trial reported significant reduction in site-specific pain, but reported no difference in pain scores between the two groups. The trial was excluded as there were no details of duration of symptoms prior to recruitment, randomisation method and allocation concealment, and the postoperative duration of follow-up was only up to eight weeks, which was an inappropriate study outcome.

Swank 2003, Daniels 2009, and El-Din Shawki 2011 conducted RCTs assessing the efficacy of LUNA in the treatment of unexplained CPP. However, as all three studies included women with mild endometriosis (American Fertility Society score less than 5), these studies could not be included unless additional data were obtained, pertaining to only women without pathology identified at laparoscopy. Despite our best efforts, we were unable to obtain the data required in order to include these studies.

Studies awaiting classification

One study is awaiting classification (Daniels 2009).

Ongoing studies

We found no ongoing studies.

Risk of bias in included studies

See Figure 2 for risk of bias graph and Figure 3 for risk of bias summary.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

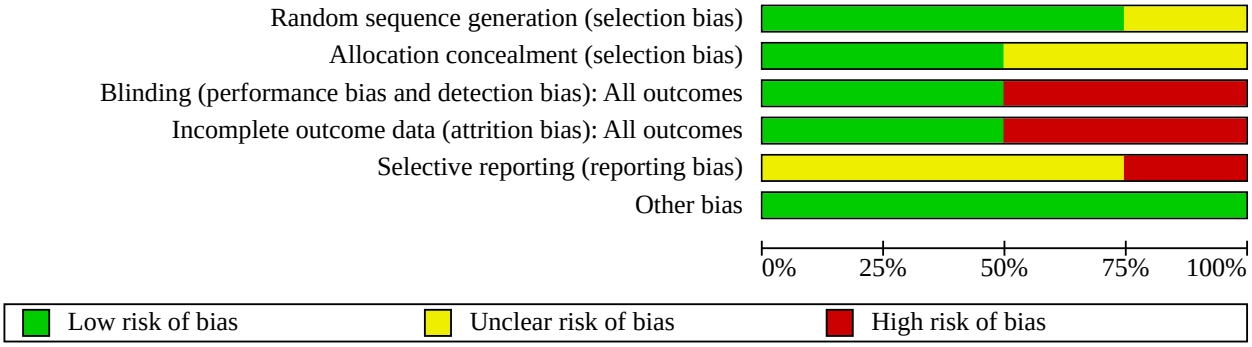
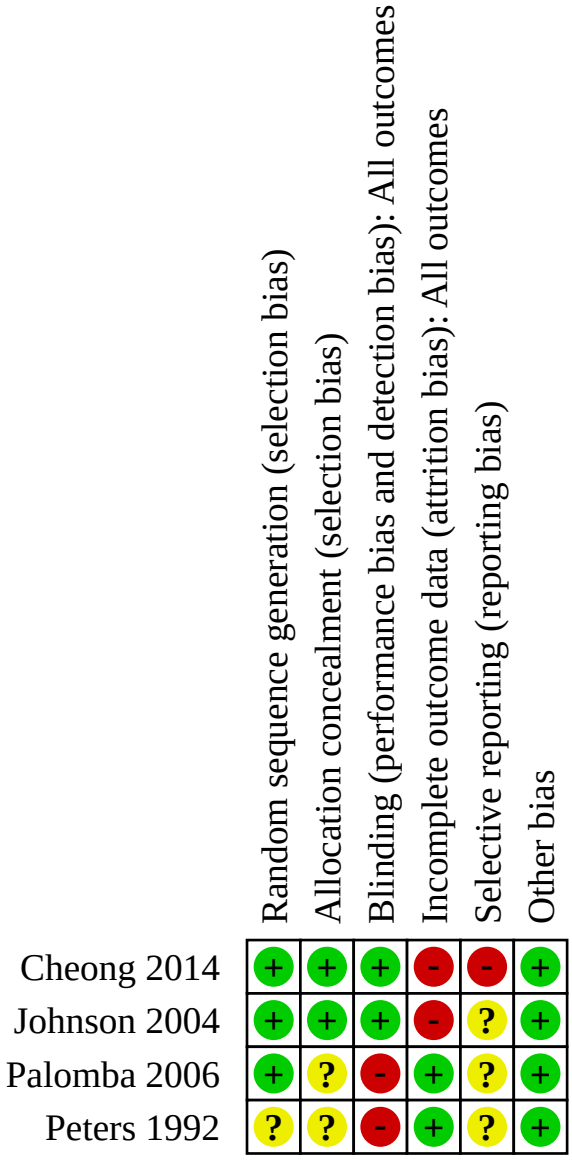


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Sequence generation

Three studies were at low risk of selection bias related to sequence generation, as they used computer randomisation (Johnson 2004; Palomba 2006; Cheong 2014). One study was at an unclear risk of selection bias due to an unclear method of randomisation (Peters 1992).

Allocation concealment

Two studies described methods of allocation concealment and were at low risk of bias in this regard (Cheong 2014; Johnson 2004); two studies were at unclear risk of allocation bias due to unclear method of allocation (Palomba 2006; Peters 1992). In all cases, it appears allocation was concealed to the point of surgery.

Blinding

Two studies were at low risk of performance and detection bias as both the participants and the assessors (research nurses) of the trial were blinded (Johnson 2004; Cheong 2014).

Two studies were at high risk of performance bias as the participants were not blinded by sham or placebo procedures (Peters 1992; Palomba 2006).

As these are surgical trials, the surgeons were not blinded but the research nurses assessing the outcomes were blinded to the intervention that the participants received. We did not consider the lack of blinding of surgeons to cause bias because we did not expect their performance to differ due to the trial context.

Incomplete outcome data

Two studies had attrition rate greater than 10% and were, therefore, at high risk of attrition bias (Johnson 2004; Cheong 2014).

Selective reporting

One study was at high risk of selective reporting bias (Cheong 2014), as the trial was prospectively registered and the outcomes reported in the manuscript differ from the protocol. Specifically, one stated primary outcome, medication usage, was not reported. Moreover, different QoL validated tools were used than planned (SF-12 and EHP-30 used when only SF-36 was planned). Three studies were at unclear risk of bias due to the fact there was no trial protocol published and were not registered in a trial registry (Johnson 2004; Palomba 2006; Peters 1992).

Other potential sources of bias

There were no risks of other bias identified.

Effects of interventions

See: **Summary of findings 1** Summary of findings table - Adhesiolysis compared to no surgery or diagnostic laparoscopy; **Summary of findings 2** Summary of findings table - LUNA (laparoscopic uterosacral ligament nerve ablation) compared to diagnostic laparoscopy/other treatments

1 Adhesiolysis versus no surgery/diagnostic laparoscopy

Primary outcomes

See Summary of findings 1.

1.1 Effectiveness of treatment at three months

One study reported effectiveness of treatment at three months (Cheong 2014). Due to wide CIs, we are uncertain of the effect of adhesiolysis versus diagnostic laparoscopy on pain scores measured by VAS at three months after surgery (MD −7.30, 95% CI −29.87 to 15.27; 43 participants; low-certainty evidence; Analysis 1.1).

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

1.2 Effectiveness of treatment at six months

One study reported effectiveness of treatment at six months (Cheong 2014). Due to wide CIs, we are uncertain of the effect of adhesiolysis versus diagnostic laparoscopy on pain scores measured by VAS at six months after surgery (MD −14.30, 95% CI −35.91 to 7.31; 43 participants; low-certainty evidence; Analysis 1.2).

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

1.3 Effectiveness of treatment at 12 months

One study reported effectiveness of treatment at 12 months (Peters 1992). We are uncertain whether adhesiolysis improves pain scores at 12 months postsurgery (MD 0, 95% CI −4.60 to 4.60; 43 participants; very low-certainty evidence; Analysis 1.3).

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

1.4 Adverse events

One study assessed adverse events (Cheong 2014). There was no detailed adverse event reporting postsurgery so a meta-analysis was not possible. The authors stated there were "no complications of adverse effects associated with surgery".

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

Secondary outcomes

1.5 Psychological outcomes

No studies reported psychological outcomes.

1.6 Quality of life

One study reported QoL at six months postsurgery (Cheong 2014). Adhesiolysis may improve both emotional wellbeing and social support components of the EHP-30 when compared to diagnostic laparoscopy (emotional wellbeing: MD 24.90, 95% CI 7.92 to 41.88; social support; MD 23.90, 95% CI −1.77 to 49.57; 43 participants; both low-certainty evidence; Analysis 1.4). Adhesiolysis may improve both the emotional component and physical component of the SF-12 when compared to diagnostic laparoscopy (emotional: MD 32.30, 95% CI 13.16 to 51.44; physical: MD 22.90, 95% CI 10.97 to 34.83; 43 participants; both low-certainty evidence; Analysis 1.4).

1.7 Requirement for analgesia

No studies reported requirement for analgesia.

2 Laparoscopic uterosacral ligament ablation versus diagnostic laparoscopy/other treatment

Primary outcomes

2.1 Effectiveness of treatment at three months

One study reported effectiveness of treatment at three months (Johnson 2004). Due to the wide CIs, we are uncertain about the effect of ablation or resection compared to other treatments on pelvic pain at three months after surgery (OR 1.26, 95% CI 0.40 to 3.93; 51 participants; low-certainty evidence; Analysis 2.1).

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

2.2 Effectiveness of treatment at six months

One study reported effectiveness of treatment at six months (Palomba 2006). We are uncertain about the effect of ablation or resection compared to other treatments on pelvic pain at six months after surgery (MD −2.10, 95% CI −4.38 to 0.18; 74 participants; very low-certainty evidence; Analysis 2.2).

Sensitivity analysis: due to only one study being included in this outcome, none of the preplanned sensitivity analyses could be performed.

2.3 Effectiveness of treatment at 12 months

Two studies reported effectiveness of treatment at 12 months (Johnson 2004; Palomba 2006). Data were not suitable for combination in the meta-analysis due to the non-parametric data from Johnson 2004 requiring reporting as a dichotomous outcome, and this study is, therefore, reported narratively.

Johnson 2004 reported that at 12 months, when using an intention-to-treat analysis, those in the group receiving LUNA showed no difference in the rate of successful treatment for non-cyclical pain (P = 0.854) or dyspareunia (P = 0.41) compared to those who did not receive LUNA. There was a difference in the rate of successful treatment for those receiving LUNA for dysmenorrhea (P = 0.045) and dyschezia (P = 0.05). Success was defined as a 50% or greater reduction in VAS from baseline.

We are uncertain about the effect of ablation or resection compared to other treatments on pelvic pain at 12 months after surgery (MD 2.00, 95% CI 0.47 to 3.53; 1 RCT, 74 participants; very low-certainty evidence; Analysis 2.3).

Sensitivity analysis: due to only one study being included in the meta-analysis of this outcome, none of the preplanned sensitivity analyses could be performed.

2.4 Adverse events

Two studies reported adverse events narratively (Johnson 2004; Palomba 2006). Both studies reported no intraoperative or postoperative complications in either group.

Sensitivity analysis: due to the narrative outcome, a random-effects model could not be used.

Secondary outcomes

2.5 Psychological outcomes

No studies reported psychological outcomes.

2.6 Quality of life

No studies reported QoL.

2.7 Requirement for analgesia

One study reported requirement for analgesia, but the data were not suitable for meta-analysis and are reported narratively (Palomba 2006). Participants in the LUNA group required significantly more analgesia (measured by the number of vials of tramadol used during hospital stay) with a median of seven (range five to nine) vials compared to participants undergoing VUSR who used a median of four (range two to five) vials (P < 0.001).

3 Surgery including pelvic vein ligation versus diagnostic laparoscopy

No studies compared surgery including pelvic vein ligation versus diagnostic laparoscopy.

4 Surgery including pelvic vein ligation versus placebo/sham procedures

No studies compared surgery including pelvic vein ligation versus placebo/sham procedures.

DISCUSSION

Summary of main results

This systematic review included four RCTs, involving 216 participants and evaluating two primary interventions. The included trials evaluated adhesiolysis and LUNA for the management of CPPS.

We are uncertain about the benefit of adhesiolysis or LUNA in the management of pain in women with CPPS based on the current literature.

Only one study reported the secondary outcome of QoL (Cheong 2014). There may be a benefit to adhesiolysis (compared to diagnostic laparoscopy) in improving both emotional wellbeing and social support, as measured by the EHP-30, and in the emotional and physical components of the SF-12. The benefit of adhesiolysis should be interpreted with caution given that EHP-30 is not a validated scale for measuring CPP, but for pain that is related to endometriosis. There was a demonstrated difference in the baseline adhesion score whereby women who underwent adhesiolysis had statistically more severe adhesions than controls. However, as there was an adequate randomisation and concealment process, this random imbalance will have been accounted for in the 95% CI. The study was terminated early due to protracted recruitment and cessation of study funding.

Pain is one element of a person's interpretation of their QoL. If other elements of QoL (e.g. bloating, bowel symptoms, fatigue) were improved with adhesiolysis despite a lack of improvement in pain, this may explain why there is a benefit in the QoL metric. It is not possible to attribute this effect to the placebo effect, which is appreciated in the literature on surgery for endometriosis (Abbott 2004), as the Cheong 2014 study was placebo-controlled and included abdominal wall incisions.

There was substantial clinical heterogeneity among the studies included in this review. For example, with respect to adhesiolysis, Cheong 2014 performed laparoscopic adhesiolysis, while Peters 1992 examined the role of adhesiolysis via laparotomy. The control group in Cheong 2014 underwent diagnostic laparoscopy without adhesiolysis, but the Peters 1992 control group did not have a sham surgery, resulting in an inability to blind participants to their group allocation. We are left uncertain whether adhesiolysis is helpful, harmful or does nothing.

There was also variation in surgical techniques for USL transection employed by the studies included in this review. For example, with respect to LUNA, the point of transection of the ligament from the attachment to the uterus, whether the ligament was completely or partially transected and the laterality of the surgery differed with the trials. The technique used in Johnson 2004

involved application of electrocautery 0.5 cm from the ligamentous insertion to the cervix until the tissue was blanched, followed by complete transection using scissors and concluded by finally applying electrocautery to the base. Palomba 2006 coagulated about 2 cm from the ligamentous insertion to the cervix until the tissue was blanched, followed by excision of a small piece of tissue for the pathological confirmation using scissors and concluded by applying electrocautery to the base.

Overall completeness and applicability of evidence

In view of a low number of studies evaluating this specific population and significant clinical heterogeneity in the included studies, the evidence must be interpreted with caution. All included trials were performed in high-income countries, so generalisability to low- or middle-income countries is an important consideration.

A further conundrum faced by researchers in the evaluation of CPPS is in selecting effective outcome assessment tools. The IMMPACT recommendations have highlighted significant issues with utilising the current pain assessment tools in the evaluation of CPPS and have recommended studies in this area to use at least two or more recognised pain assessment tools to be able to identify clinically significant changes in outcome (Dworkin 2008). Similarly, instruments used to measure health-related QoL issues need to have both clinical face validity (address issues that are of importance to patients and reflect their experiences and concerns) and adequate psychometric properties. Due to the absence of instruments that are disease-specific to CPPS (in the absence of clear pathological aetiologies of CPP), there is concern that QoL data produced do not adequately address clinical face validity relating to this area of research (Neelakantan 2004). Our meta-analysis can only utilise outcome measures provided by the studies.

Finally, CPPS is often multifactorial. Although we excluded studies that were designed to assess other sources of pain (e.g. irritable bowel syndrome, interstitial cystitis/bladder pain syndrome), these studies did not systematically assess whether these were present.

Quality of the evidence

The available data were extracted from four small trials including 216 women. Unfortunately, there were too few studies for most planned comparisons. A meta-analysis could only be performed for the outcome of pain at 12 months following LUNA versus diagnostic laparoscopy.

Using GRADE methods of assessment, the certainty of the evidence for effectiveness outcomes was low or very low for all comparisons. The reason for downgrading the certainty of evidence included risk of bias (e.g. unclear method of randomisation and blinding), indirectness (e.g. the outcome was reported by the number in each treatment group where the pain was reported as 'improved'), and imprecision due to small study size. As a result, we are uncertain of the effectiveness of the interventions compared. Therefore, further research is likely to have a significant impact on our confidence in the estimate of effect and may change the estimate. Evidence on QoL was of low certainty due to imprecision from a small sample size. Evidence on adverse events was also of low certainty due to unclear and unstructured methods of adverse events reporting.

Potential biases in the review process

Numerous steps were taken during the process of this review to prevent bias. First, the CGF developed and ran the search with no limitations in language or date. Second, two review authors independently performed screening and extraction. Any conflicts that could not be resolved by the two review authors were discussed with a third review author. Despite efforts to minimise bias, there were multiple outcomes assessed using evidence from a small number of trials, with a small sample size, which may have introduced bias and resulted in difficulties extrapolating clinically relevant conclusions. Furthermore, three studies were excluded despite including relevant populations as it was not possible to distinguish between ineligible populations (e.g. trials including men and women); thus introducing the potential of publication bias.

Agreements and disagreements with other studies or reviews

The findings of this review agree with the authors' conclusions in the now withdrawn 2005 Cochrane systematic review and meta-analysis (Stones 2005). No subgroup analysis based on the degree of severity of adhesions was performed in this version of the review. We excluded Swank 2003, though it was included in the previous review (Stones 2005). This study was determined to be ineligible due to its inclusion of men and people with chronic abdominal (not necessarily pelvic) pain.

AUTHORS' CONCLUSIONS

Implications for practice

In order to label a woman with chronic pelvic pain syndrome (CPPS), laparoscopy remains necessary as a diagnostic tool in order to exclude several common entities of chronic pelvic pain (CPP) (e.g. endometriosis, chronic pelvic inflammatory disease). A diagnosis of CPPS also relies on thorough assessment for non-gynaecological pathology such as inflammatory bowel disease or bladder pain syndrome. Assuming that the clinical assessment has been thorough to rule out entities that do not require laparoscopy to diagnose them, laparoscopy may be the next step. If laparoscopy is used as a diagnostic tool and CPPS is the result (after excluding conditions that still rely on laparoscopy to diagnose them), this review provides guidance.

The currently available information suggests no evidence of benefit for use of adhesiolysis or laparoscopic uterosacral ligament/nerve ablation (LUNA) in management of pain in women with CPPS. There may be a quality of life (QoL) benefit to adhesiolysis in improving both the emotional wellbeing and social support, as measured by the Endometriosis Health Profile-30, and in the emotional and physical components of the 12-item Short Form. It was not possible to synthesis evidence on adverse events as these were only narratively reported in some studies, in which there were none. It is important to note that chronic postsurgical pain is an entity that was poorly understood when most of these studies were performed and was not incorporated into the outcome variables assessed (Macrae 2008). Chronic postsurgical pain is an entity of pain distinct from the indication of surgery that arises postoperatively and can be considered a long-term adverse outcome. Without an adequate assessment of the long-term adverse outcomes associated with

adhesiolysis or LUNA for CPPS, there is currently little to support the intervention of surgery for CPPS.

Finally, it is also important to note that these studies are likely underpowered to determine if there is a difference in adverse events. Surgical complications are important though rare, and so these studies are too small to determine the impact of the interventions on them as well as long-term adverse events.

Implications for research

This review reveals that very few of the routinely employed surgical interventions have been rigorously evaluated for the management of CPPS. As only single studies have been reported for some of these interventions, this limits the available evidence upon which clinical practice can be based. Given the prevalence and the economic impact on healthcare, randomised controlled trials are required to evaluate the other surgical interventions used in the treatment of CPPS and CPP in the context of recognisable conditions. Any future study on surgical intervention for CPP must ensure that all possible aetiologies for CPP are evaluated and measured to best understand their contribution to CPP. The spectrum of disease entities and pathophysiology that leads to CPP is so diverse that it is probably inappropriate to meta-analyse surgical interventions. Studies on hysterectomy with and without oophorectomy are also needed since this is one of the most common procedures performed for women with CPP (Mowers 2016). Studies on interventions (surgical versus radiological) for CPP secondary to pelvic congestion syndrome are also necessary. Even though no high-quality research was available on presacral neurectomy, we must question whether this is an area of future research need or whether it should become a procedure of the past. Last, it is important that studies are large enough to assess for differences in surgical complications and postoperative adverse events, which are necessary considerations for patients when making informed consent decisions.

This review identifies the need to standardise pain and QoL outcome assessment tools for CPP with strong clinical face validity that could be used in clinical trials and practice. Cost-effectiveness studies for the surgical interventions in the management of CPP should be considered.

For future work, perhaps we should also consider the role of brain neuroimaging as an outcome measure (magnetic resonance imaging and functional magnetic resonance imaging) (Passavanti 2017) as monitoring/assessing pain can be challenging (Younger 2009), and the subsequent changes to QoL. Modern monitoring tools (e.g. activity, vitals sensors) could provide a solution but of course, will need to be trialled and tested.

ACKNOWLEDGEMENTS

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REFERENCES

References to studies included in this review

Cheong 2014 *{published data only}*

* Cheong YC, Reading IC, Bailey S, Sadek K, Ledger WL, Li TC.Should women with chronic pelvic pain have adhesiolysis? *BMC Women's Health* 2014;**14**:36.

Randomised controlled trial of laparoscopic adhesiolysis for women with chronic pelvic pain. ISRCTN registry 08/09/2005:https://doi.org/10.1186/ISRCTN43852269.

Johnson 2004 *{published data only}*

Johnson NP, Farquhar CM, Crossley Y, Yu AM, van Peperstraten AM, Sprecher M, et al.A double blind randomised controlled trial of laparoscopic uterine nerve ablation for women with chronic pelvic pain. *BJOG* 2004;**111**:950-9.

Palomba 2006 *{published data only}*

Palomba S, Russo J, Falbo A, Manguso F, Alessandro P, Mattei A, et al.Laparoscopic uterine nerve ablation versus vaginal uterosacral ligament resection in postmenopausal women with intractable midline chronic pelvic pain: a randomised study. *European Journal of Obstetric, Gynecology & Reproductive Biology* 2006;**129**(1):84-91.

Peters 1992 *{published data only}*

* Peters AA, Trimbos-Kemper GC, Admiraal C, Trimbos JB.A randomised clinical trial on the benefit of adhesiolysis in patients with intraperitoneal adhesions and chronic pelvic pain. *British Journal of Obstetrics and Gynaecology* 1992;**99**(1):59-62.

References to studies excluded from this review

Aaltomaa 2001 *{published data only}*

Aaltomaa S, Ala-Opas M.The effect of transurethral needle ablation on symptoms of chronic pelvic pain syndrome – a pilot study. *Scandinavian Journal of Urology and Nephrology* 2001;**35**(2):127-31.

Andersen 2015 *{published data only}*

Andersen LL, Zobbe V, Ottesen B, Gluud C, Tabor A, Gimbel H.Five-year follow up of a randomised controlled trial comparing subtotal with total abdominal hysterectomy. *BJOG* 2015;**122**(6):851-7.

Bautrant 2020 *{published data only}*

Bautrant E, Franke O, Amiel C, Bensousan T, Thiers-Bautrant D, Leveque C.Treatment of acute dysmenorrhoea and pelvic pain syndrome of uterine origin with myometrial botulinum toxin injections under hysteroscopy: a pilot study. *Journal of Gynecology Obstetrics and Human Reproduction* 2020;**50**(4):101972.

El-Din Shawki 2011 *{published data only (unpublished sought but not used)}*

El-Din Shawki H.The efficacy of laparoscopic uterosacral nerve ablation (LUNA) in the treatment of unexplained chronic pelvic pain: a randomized controlled trial. *Gynecological Surgery* 2011;**8**:31-9.

Fernandez 2004 *{published data only}*

Fernandez H.Laparoscopic adhesiolysis in patients with chronic abdominal pain: a blinded randomised controlled multi-centre trial [Adhésiolyse cœlioscopique chez des patientes présentant des douleurs abdominales chroniques: étude multicentrique randomisée contrôlée en aveugle]. *Journal de Gynecologie Obstetrique et Biologie de la Reproduction* 2004;**33**(2):152-3.

Garcia Leon 2003 *{published data only}*

Garcia Leon F, Oviedo Ortega G, Reyes Cuervo H, Ibarrola Buenabad E, von der Meden W.Presacral neurectomy and uterine nerve ablation in chronic pelvic pain. Laparoscopic management. A comparative study [Estudio comparativo entre neurectomía presacra y ablación de uterosacros en el dolor pélvico crónico. Abordaje laparoscópico.]. *Ginecología y Obstetricia de México* 2003;**71**:137-42.

Keltz 2006 *{published data only}*

Keltz MD, Gera PS, Olive DL.Prospective randomised trial of right-sided paracolic adhesiolysis for chronic pelvic pain. *Journal of Society of Laparoscopic Surgeons* 2006;**10**:443-6.

Molegraaf 2016 *{published data only}*

Benefit of laparoscopic adhesiolysis in patients with chronic abdominal pain. clinicaltrials.gov/ct2/show/NCT02839564 (first received 21 July 2016).

* Molegraaf MJ, Torensma B, Lange CP, Lange JF, Jeekel J, Swank DJ.Twelve-year outcomes of laparoscopic adhesiolysis in patients with chronic abdominal pain: a randomized clinical trial. *Surgery* 2016;**161**(2):415-21.

Moon 2001 *{published data only}*

Moon MJ, Kim DK, Yoon KH, Hong JS, Kim YJ, Kim HO, et al.The clinical significance of laparoscopic uterosacral nerve ablation (LUNA) in infertile women with pelvic pain and endometriosis. *Korean Journal of Obstetrics & Gynecology* 2001;**44**(12):2224-8.

Muzamil Ahmed 2019 *{published data only}*

Muzamil Ahmed A, Vikram C, Santhaseelan RG.Comparison of pre-operative & post-operative pain grading after diagnostic laparoscopy in patients presenting with chronic abdominal pain at SBMCH. *Indian Journal of Public Health Research and Development* 2019;**10**(11):4235-6.

Ouhilal 1999 *{published data only}*

Ouhilal S, Sergerie M, Bissonnette F.Laparoscopic section of uterosacral ligaments for pelvic pain. *Fertility & Sterility* 1999;**72**(Suppl 1):S140.

Palomba 2005 *{published data only}*

Palomba S.Laparoscopic uterine nerve ablation improved non-endometriosis-associated dysmenorrhea but not other types of chronic pelvic pain. *Evidence-based Obstetrics and Gynecology* 2005;**7**(2):78-9.

Peters 1991 *{published data only}*

Peters AA, van Dorst E, Jellis B, van Zuuren E, Hermans J, Trimbos JB.A randomized clinical trial to compare two different approaches in women with chronic pelvic pain. *Obstetrics and Gynecology* 1991;**77**(5):740-4.

Saravelos 1995 *{published data only}*

Saravelos H, Li TC, Cooke ID.An analysis of the outcome of microsurgical and laparoscopic adhesiolysis for chronic pelvic pain. *Human Reproduction* 1995;**10**(11):2887-94.

Swank 2003 *{published data only}*

* Swank DJ, Swank-Bordewijk SC, Hop WC, van Erp WF, Janssen IM, Bonjer HJ, et al.Laparoscopic adhesiolysis in patients with chronic abdominal pain: a double blind randomised controlled multi-centre trial. *Lancet* 2003;**361**(9365):1247-51.

Swank DJ, Swank-Bordewijk SC, Hop WC, van Erp WF, Janssen IM, Bonjer HJ, et al.No benefit from adhesiolysis during diagnostic laparoscopy in patients with chronic abdominal pain and adhesions: a double-blind, randomised, multicentre trial [Geen nut van adhesiolyse tijdens diagnostische laparoscopie bij patiënten met chronische buikpijn en adhesies; een dubbelblinde, gerandomiseerde, multicentrische trial]. *Nederlands Tijdschrift voor Geneeskunde* 2004;**148**(1):23-7.

Ventolini 1999 *{published data only}*

Ventolini G, Fremont SL.Laparoscopy with hysteroscopy or with ultrasound in the evaluation of patients with chronic pelvic pain. *Fertility & Sterility* 1999;**72**(Suppl 1):S171.

References to studies awaiting assessment

Daniels 2009 *{published data only (unpublished sought but not used)}*

Daniels J, Gray R, Hills RK, Latthe P, Buckley L, Gupta J, et al.Laparoscopic uterosacral nerve ablation for alleviating chronic pelvic pain: a randomized controlled trial. *JAMA* 2009;**302**:955-61.

Additional references

Abbott 2004

Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R.Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertility & Sterility* 2004;**82**:878-84.

ACOG 2004

American College of Obstetricians and Gynecologists.ACOG Practice Bulletin No. 51. Chronic pelvic pain. *Obstetrics and Gynecology* 2004;**103**(3):589-605.

ACOG 2020

American College of Obstetricians and Gynecologists.ACOG Practice Bulletin No. 218. Chronic pelvic pain. *Obstetrics and Gynecology* 2020;**135**(3):e98-e109.

Ahangari 2014

Ahangari A.Prevalence of chronic pelvic pain among women: an updated review. *Pain Physician* 2014;**17**(2):141-8.

Amin 2021

Amin TN, Wong M, Foo X, Pointer S-L, Goodhart V, Jurkovic D.The effect of pelvic pathology on uterine vein diameters. *Ultrasound Journal* 2021;**13**(1):7.

As-Sanie 2012

As-Sanie S, Harris RE, Napadow V, Kim J, Neshewat G, Kairys A, et al.Changes in regional gray matter volume in women with chronic pelvic pain: a voxel-based morphometry study. *Pain* 2012;**153**(5):1006-14.

Baranowski 2012

Baranowski A, Abrams P, Berger RE, Buffington A, Collett B, Emmanuel A, et al.Classification of Chronic Pain, Second Edition (Revised). Washington (DC): IASP, 2012.

Brawn 2014

Brawn J, Morotti M, Zondervan KT, Becker CM, Vincent K.Central changes associated with chronic pelvic pain and endometriosis. *Human Reproduction Update* 2014;**20**(5):737-47.

Champaneria 2016

Champaneria R, Shah L, Moss J, Gupta JK, Birch J, Middleton LJ, et al.The relationship between pelvic vein incompetence and chronic pelvic pain in women: systematic reviews of diagnosis and treatment effectiveness. *Health Technology Assessment* 2016;**20**(5):1-108.

Cheong 2006

Cheong Y, Stones RW.Chronic pelvic pain: aetiology and therapy. *Best Practice and Research, Clinical Obstetrics and Gynaecology* 2006;**20**(5):695-711.

Daniels 2009

Daniels J, Gray R, Hills RK, Latthe P, Buckley L, Gupta J, et al.Laparoscopic uterosacral nerve ablation for alleviating chronic pelvic pain: a randomised controlled trial. *JAMA* 2009;**302**(9):955-61.

Dworkin 2008

Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al.Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *Journal of Pain* 2008;**9**(2):105-21.

Gargiulo 2003

Gargiulo T, Mais V, Brokaj L, Cossu E, Melis GB.Bilateral laparoscopic transperitoneal ligation of ovarian veins for treatment of pelvic congestion syndrome. *Journal of the American Association of Gynecologic Laparoscopists* 2003;**10**(4):501-4.

GRADEpro GDT [Computer program]

McMaster University (developed by Evidence Prime) GRADEpro GDT.Hamilton (ON): McMaster University (developed by Evidence Prime), accessed December 2020. Available at gradepro.org.

Gürgan 1992

Gürgan T, Urman B, Aksu T, Develioglu O, Zeyneloglu H, Kisnisçi HA.Laparoscopic CO2 laser uterine nerve ablation for treatment of drug resistant primary dysmenorrhoea. *Fertility & Sterility* 1992;**58**(2):422-4.

Higgins 2011

Higgins JP, Green S.Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from training.cochrane.org/handbook/archive/v5.1/.

Hillis 1995

Hillis SD, Marchbanks PA, Peterson HB.The effectiveness of hysterectomy for chronic pelvic pain. *Obstetrics and Gynecology* 1995;**86**(6):941-5.

Howard 1993

Howard FM.The role of laparoscopy in chronic pelvic pain: promise and pitfalls. *Obstetrical & Gynecological Survey* 1993;**48**:357-87.

Jarrell 2018

Jarrell JF, Vilos GA, Allaire C, Burgess S, Fortin C, Gerwin R, et al.No. 164 – Consensus guidelines for the management of chronic pelvic pain. *Journal of Obstetrics and Gynaecology Canada* 2018;**40**(11):e747-87.

Johnson 2004

Johnson NP, Farquhar CM, Crossley Y, Yu AM, van Peperstraten AM, Sprecher M, et al.A double blind randomised controlled trial of laparoscopic uterine nerve ablation for women with chronic pelvic pain. *BJOG* 2004;**111**:950-9.

Jurga-Karwacka 2019

Jurga-Karwacka A, Karwacki GM, Schoetzau A, Zech CJ, Heinzelmann-Schwarz V, Schwab FD.A forgotten disease: pelvic congestion syndrome as a cause of chronic lower abdominal pain. *PloS One* 2019;**14**(4):1-11.

Latthe 2004

Latthe PM, Powell RJ, Daniels J, Hills RK, Gray R, Gupta JK, et al.Variation in practice of laparoscopic uterosacral nerve ablation: a European survey. *Journal of Obstetrics and Gynaecology* 2004;**24**:547-51.

Lee 1984

Lee NC, Dicker RC, Rubin GL, Ory HW.Confirmation of the preoperative diagnoses for hysterectomy. *American Journal of Obstetrics and Gynecology* 1984;**150**(3):283-7.

Macrae 2008

Macrae WA.Chronic post-surgical pain: 10 years on. *British Journal of Anaesthesia* 2008;**101**:77-86.

Maleux 2000

Maleux G, Stockx L, Wilms G, Marchal G.Ovarian vein embolization for the treatment of pelvic congestion syndrome: long-term technical and clinical results. *Journal of Vascular and Interventional Radiology* 2000;**11**(7):859-64.

Mirowska-Allen 2019

Mirowska-Allen KL, Sewell M, Mooney S, Maher P, Ianno DJ, Grover SR.The characteristics of women recommended a laparoscopy for chronic pelvic pain at a tertiary institution. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2019;**59**(1):123-33.

Mowers 2016

Mowers EL, Lim CS, Skinner B, Mahnert N, Kamdar N, Morgan DM, et al.Prevalence of endometriosis during abdominal or laparoscopic hysterectomy for chronic pelvic pain. *Obstetrics and Gynecology* 2016;**127**(6):1045-53.

Neelakantan 2004

Neelakantan D, Omojole F, Clark JT, Gupta JK, Khan KS.Quality of life instruments in studies of chronic pelvic pain: a systematic review. *Journal of Obstetrics and Gynaecology* 2004;**24**(8):851-8.

Passavanti 2017

Passavanti MB, Pota V, Sansone P, Aurilio C, De Nardis L, Pace MC.Chronic pelvic pain: assessment, evaluation, and objectivation. *Pain Research and Treatment* 2017;**2017**:1-15.

RCOG 2012

Royal College of Obstetricians and Gynaecologists.The initial management of chronic pelvic pain: Green-top Guideline No. 41. *Royal College of Obstetricians and Gynaecologists* 2012;**41**:1-16.

Reiter 1990

Reiter RC.A profile of women with chronic pelvic pain. *Clinical Obstetrics and Gynecology* 1990;**33**(1):130-6.

Review Manager Web [Computer program]

The Cochrane Collaboration Review Manager Web (RevMan Web).Version 3.12. The Cochrane Collaboration, 2021. Available at: revman.cochrane.org.

Stones 2000

Stones RW.Sex Gender and Pain. Progress in Pain Research and Management. Seattle (WA): IASP Press, 2000.

Stones 2007

Stones RW.Chapter 25: chronic pelvic pain. In: CockburnJ, PawsonM, editors(s). Psychological Challenges in Obstetrics and Gynecology – the Clinical Management. London (UK): Springer, 2007:291-8.

Stovall 1990

Stovall TG, Ling FW, Crawford DA.Hysterectomy for chronic pelvic pain of presumed uterine etiology. *Obstetrics and Gynecology* 1990;**75**(4):676-9.

Tulandi 1998

Tulandi T, Chen MF, Al-Took S, Watkin K.A study of nerve fibres and histopathology of postsurgical, postinfectious, and endometriosis-related adhesions. *Obstetrics and Gynecology* 1998;**92**(5):766-8.

Vercellini 2009

Vercellini P, Somigliana E, Viganò P, Abbiati A, Barbara G, Fedele L.Chronic pelvic pain in women: etiology, pathogenesis

and diagnostic approach. *Gynecological Endocrinology* 2009;**25**(3):149-58.

Younger 2009

Younger J, McCue R, Mackey S.Pain outcomes: a brief review of instruments and techniques. *Current Pain and Headache Reports* 2009;**13**(1):39-43.

Zondervan 2001

Zondervan KT, Yudkin PL, Vessey MP, Jenkinson CP, Dawes MG, Barlow DH, et al.The community prevalence of chronic pelvic pain in women and associated illness behaviour. *British Journal of General Practice* 2001;**51**:541-7.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cheong 2014

Study characteristics	
Methods	**Country:** UK **Recruiting centres:** 2 hospitals **Design:** double-blind (participants and assessors) randomised control trial **Recruitment dates:** 2008–2012 **Method of randomisation:** computer generated **Analytical approach:** intention to treat **Diagnostic laparoscopy performed:** yes **Follow-up duration:** up to 12 months offered **Follow-up frequency:** 3- and 6-month data reported **Additional investigations and interventions during follow-up:** none stated
Participants	**Total number of participants:** 50 (43 in final analysis) Laparoscopic adhesiolysis group: 26 randomised; 23 included in final analysis Control group: 24 randomised; 20 included in final analysis **Diagnostic criteria:** pelvic pain that was constant/cyclical in nature for ≥ 6 months **Inclusion criteria:** women aged > 18 years with pelvic pain for ≥ 6 months with non-endometriosis-related adhesions detected at laparoscopy **Exclusion criteria:** malignancy; psychiatric disorders for which the woman is taking medication; pathology that required urgent treatment, such as ovarian cyst or pelvic abscess; pregnancy and women taking central nervous system stimulants **Previous treatment for pain:** Laparoscopic adhesiolysis group: 10/23 women had ≥ 1 previous operations for pain (43%) Control group: 7/20 women had ≥ 1 previous operations for pain (35%) **Co-interventions received in the 12-month follow-up duration:** none stated

References to other published versions of this review

Stones 2005

Stones W, Cheong YC, Howard FM, Singh S.Interventions for treating chronic pelvic pain in women. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No: CD000387. [DOI: 10.1002/14651858.CD000387]

* Indicates the major publication for the study

Cheong 2014 *(Continued)*

Interventions	**Intervention group:** laparoscopic adhesiolysis **Control group:** diagnostic laparoscopy with instillation of 1 L Adept
Outcomes	Pain scores 1–100 mm VAS scale from the McGill Pain Questionnaire, QoL questionnaire (modified Endometriosis Health Profile Questionnaire, SF-12)
Notes	Trial stopped after 4 years before reaching sample size of 100, owing to protracted recruitment and cessation of study funding. Women were offered a follow-up at 12 months but no data were obtained as no women elected this choice. Registered prospectively in ISRCTN: 10.1186/ISRCTN43852269.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence with opaque unlabelled envelopes opened after the participant met the intraoperative criteria.
Allocation concealment (selection bias)	Low risk	Concealed opaque envelope opened at the time of surgery.
Blinding (performance bias and detection bias) All outcomes	Low risk	Participant and assessor of trial blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	> 10% attrition.
Selective reporting (reporting bias)	High risk	Protocol published and outcomes not consistent with protocol; different QoL questionnaires used than planned, no reporting of medication usage in final manuscript (stated to be a primary outcome in protocol).
Other bias	Low risk	None.

Johnson 2004

Study characteristics

Methods	**Country:** New Zealand **Recruiting centres:** single centre **Design:** double-blind randomised control trial **Recruitment dates:** 1997–2001 **Method of randomisation:** computer generated **Analytical approach:** intention to treat **Diagnostic laparoscopy performed:** all participants **Follow-up duration:** 12 months postoperatively

Johnson 2004 *(Continued)*

	Follow-up frequency: 24 hours, 3 and 12 months postoperatively **Additional investigations and interventions during follow-up:** none reported **Missing data:** yes (1) **Lost to follow-up:** yes (at 3 months: 3; at 12 months: 17)
Participants	**Number participated:** 137 **Number randomised:** 123 (56 in the no-endometriosis group) **Age:** intervention: 29 (SD 5.83) years; control: 29 (SD 6.49) years **Inclusion criteria:** women aged 18–45 years, chronic pelvic pain of > 6 months' duration, no change in medication 3 months prior to trial recruitment **Exclusion criteria:** previous hysterectomy, pelvic malignancy or known ovarian cysts, pregnancy being contemplated within next 12 months, laparoscopic findings rendering LUNA impossible, uni- or bilateral transection of uterosacral ligaments required to remove endometriosis or pelvic adhesions **Previous treatment for pain** LUNA group: • 12 (55%) previous laparoscopy • 2 (9%) previous laparotomy • 12 (55%) paracetamol • 9 (41%) NSAID • 1 (5%) opiate analgesia • 1 (5%) combined OCP • 2 (10%) progesterone • 5 (23%) other Control group: • 20 (59%) previous laparoscopy • 8 (24%) previous laparotomy • 15 (44%) paracetamol • 21 (62%) NSAID • 2 (6%) opiate analgesia • 0 (0%) combined OCP • 6 (18%) progesterone • 5 (15%) other **Co-interventions received in the 12-month follow-up:** LUNA: 1 hysterectomy; control: 1 Mirena intrauterine coil, 2 OCP and 2 hysterectomies
Interventions	**Intervention group:** LUNA **Control group:** diagnostic laparoscopy but no LUNA. No sham incisions
Outcomes	**Primary outcome:** VAS score (0–10) at 3 and 12 months for each pain domain **Secondary outcomes:** pain on first postoperative day, satisfaction, any further surgery performed within 12 months for continuing pelvic pain, new medical treatment commenced within 12 months and procedure related complications (In this study, pelvic pain was assessed for 4 pain domains of non-menstrual pelvic pain, dysmenorrhoea, deep dyspareunia and dyschezia using VAS 0–10. Improvement was defined as ≥ 50% reduction in VAS and comparison was made between the groups for > 50% reduction in VAS and change in me-

Johnson 2004 *(Continued)*

	dian VAS from baseline at 3 and 12 months. Participants were assessed for satisfaction, further surgical treatment within 12 months and procedure-related complications. Intention-to-treat analysis was done at the end of trial period.)
Notes	LUNA is low-risk procedure that is ineffective for non-menstrual chronic pelvic pain. The numbers were dissimilar in the population with no endometriosis (22 LUNA; 34 no LUNA) owing to unblocking randomisation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number sequences, unknown to the research nurses and surgeons who were executors of the assignment. The numbers were dissimilar in the population with no endometriosis (22 LUNA; 34 no LUNA) owing to unblocked randomisation.
Allocation concealment (selection bias)	Low risk	Opaque sealed envelopes until the interventions were assigned during the laparoscopic procedure.
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blinding of participants and postoperative assessor.
Incomplete outcome data (attrition bias) All outcomes	High risk	> 10% attrition.
Selective reporting (reporting bias)	Unclear risk	No protocol published & no trial registration. Given age of study this is not unusual.
Other bias	Low risk	None.

Palomba 2006

Study characteristics

Methods	**Country:** Italy **Recruiting centres:** 4 university departments of gynaecology centres **Design:** blinded randomised controlled study **Recruitment dates:** 2001–2003 **Method of randomisation:** computer generated **Analytical approach:** intention to treat **Diagnostic laparoscopy performed:** only in the LUNA group as part of the procedure **Follow-up duration:** up to 12 months from surgical intervention **Follow-up frequency:** 6 and 12 months **Additional investigations and interventions during follow-up:** none stated

Palomba 2006 *(Continued)*

	Lost to follow-up: 6 (intervention: 2; control: 4)
Participants	**Number randomised:** 80 **Number included for analysis:** 74 **Age:** LUNA: 55.2 (SD 3.2) years; VUSR: 54.2 (SD 3.7) years **Diagnostic criteria:** severe midline pelvic pain persisting for > 6 months and unresponsive to common medical treatment **Inclusion criteria:** postmenopausal women with severe midline pelvic pain persisting for > 6 months and unresponsive to common medical treatment (i.e. paracetamol, NSAIDs); postmenopausal state was confirmed by an assay of serum FSH and E2 levels (range for postmenopausal age: FSH > 40 U/L, E2 < 20 pg/mL) **Exclusion criteria:** major medical diseases, psychological/psychiatric disorders, neurological alterations of lumbar-sacral tract, previous pelvic surgery, history of severe abdominal or pelvic infections, history of infertility, presence of other gynaecological pathologies, previous or current use of HRT; people unable to complete the daily diary or with a history of alcohol abuse or other drugs; pathology found on gynaecological examination and transvaginal ultrasonographic scan; people affected by psychological syndromes, history of physical/sexual abuse, and psychiatric disorders, as determined by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental – Disorders Fourth Edition **Previous treatment for pain:** none stated **Co-interventions received in the 12-month follow-up duration:** none stated
Interventions	**Intervention group:** LUNA **Control group:** VULR **Duration of follow-up:** 6 and 12 months
Outcomes	**Primary outcome:** cost comparison (in EUR) **Secondary outcomes:** pain score using VAS 0–100 postoperative, at discharge, 6 and 12 months; use of analgesic during hospital stay; procedure-related information: duration of surgery, blood loss, hospital stay and complications; time to return to work or full activity (Pain severity was assessed at baseline, 6 and 12 months using the VAS 0–100. Cure rate is defined as absence of pain or pain not requiring medical treatment at 6 and 12 months after surgery. An arbitrary value of VAS greater than 80 was judged to be significant to recruit participants for the trial.)
Notes	Subgroup analysis – cost comparison of poly-use LUNA instrumentation with VUSR. Not ideal control group for comparing pain outcomes. LUNA is significantly more expensive than VUSR. This was mainly due to mono-use LUNA instrumentation. The mean duration of symptoms prior to intervention was 9.2 (SD 4.6) months compared to 10.7 (SD 3.4) months in control group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence in single blocks; intention-to-treat analysis was performed.

Palomba 2006 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation was maintained until intervention was assigned (i.e. performed as surgeons needed to know randomization group). No specification *how* allocation concealment was maintained.
Blinding (performance bias and detection bias) All outcomes	High risk	Postoperative assessor was blinded. Control group had no sham incisions.
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% attrition.
Selective reporting (reporting bias)	Unclear risk	No protocol published & no trial registration. Given age of study this is not unusual.
Other bias	Low risk	None.

Peters 1992

Study characteristics	
Methods	**Country:** the Netherlands **Recruiting centres:** 1 medical centre **Design:** single-blind randomised controlled trial **Recruitment dates:** 1982–1989 **Method of randomisation:** closed envelope system **Analytical approach:** intention to treat **Diagnostic laparoscopy performed:** yes **Follow-up duration:** 12 months **Follow-up frequency:** 9 and 12 months **Additional investigations and interventions during follow-up:** none reported **Exclusions postrandomisation:** none **Loss to follow-up:** none
Participants	**Number of participants randomised:** 48 **Age:** range: 21–58 years **Diagnostic criteria:** pelvic pain for ≥ 6 months **Inclusion criteria:** pelvic pain for ≥ 6 months; Dutch language proficiency to understand the study questionnaire **Exclusion criteria:** previous malignant disease; suspicion of malignancy at pelvic examination; suspicion of pelvic pathology during pelvic examination contributing to symptoms, mental retardation, psychiatric or psychotherapeutic treatment in 2 years preceding the study and medical treatment for pain at the first visit at the clinic

Peters 1992 *(Continued)*

	Previous treatment for pain: adhesiolysis group: 12 had previous laparotomies; control group: 14 had previous laparotomies **Co-interventions received:** none reported
Interventions	Randomisation after diagnostic laparoscopy **Intervention group:** midline laparotomy and adhesiolysis **Control group:** diagnostic laparoscopy, but no laparotomy and adhesiolysis. No sham incision (low midline laparotomy) were given **Duration of follow-up:** 9–12 months
Outcomes	**Pain:** Dutch version of McGill Pain Score, Delta McGill Pain Score for intraobserver change, subjective improvement **QoL:** interference in daily activities secondary to pain
Notes	Stratification of outcome according to severity of adhesions – benefit if severe (stage IV) adhesions. Median duration of symptoms: intervention: 42 (range 6–350) months; control: 36 (range 8–420) months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No clear details on the method of randomisation.
Allocation concealment (selection bias)	Unclear risk	Allocation: "closed envelope system" until the point of surgery. No clear indication of opaque or numbered envelopes.
Blinding (performance bias and detection bias) All outcomes	High risk	Postoperative assessor was blinded to allocation. Control group had no sham incisions.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition.
Selective reporting (reporting bias)	Unclear risk	No protocol published & no trial registration. Given age of study this is not unusual.
Other bias	Low risk	None.

E2: 17b-estradiol; FSH: follicle-stimulating hormone; HRT: hormone replacement therapy; QoL: quality of life; LUNA: laparoscopic uterosacral nerve ablation; NSAID: non-steroidal anti-inflammatory drug; OCP: oral contraceptive pill; SD: standard deviation; VAS: visual analogue scale; VUSR: vaginal uterosacral ligament resection.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aaltomaa 2001	Wrong patient population.
Andersen 2015	Wrong study comparator.

Study	Reason for exclusion
Bautrant 2020	Wrong study design; open-label, non-comparative study.
El-Din Shawki 2011	Included women with mild endometriosis, which is part of our exclusion criteria. Data sought regarding participants without endometriosis; however, none received from the authors. Decided to exclude this study on the basis of incorrect participants.
Fernandez 2004	Letter to the Editor regarding Swank 2003.
Garcia Leon 2003	Wrong study design; observational.
Keltz 2006	No details of inclusion and exclusion criteria, randomisation process, allocation and allocation concealment. Both intervention and control group had other surgical procedures (e.g. endometriosis ablation/excision, adnexal adhesiolysis) performed at same time as right-sided paracolic adhesiolysis. Participants were followed up for 4–8 weeks following the intervention; therefore, the placebo effect could not be excluded.
Molegraaf 2016	Wrong patient population; 12-year follow-up from Swank 2003 study.
Moon 2001	Wrong patient population; includes women with endometriosis.
Muzamil Ahmed 2019	Wrong patient population.
Ouhilal 1999	Wrong patient population; included women with endometriosis.
Palomba 2005	Commentary on Johnson 2004 paper.
Peters 1991	Wrong comparator.
Saravelos 1995	Wrong study design; not randomised controlled trial.
Swank 2003	Wrong patient population; included male participants and those with chronic abdominal (not necessarily pelvic) pain.
Ventolini 1999	Wrong study design; observational study.

Characteristics of studies awaiting classification *[ordered by study ID]*

Daniels 2009

Methods	Randomised controlled trial
Participants	487 women with chronic pelvic pain lasting > 6 months without or with minimal endometriosis, adhesions or pelvic inflammatory disease.
Interventions	Bilateral LUNA or laparoscopy without LUNA
Outcomes	Primary outcome: pain, assessed by a visual analogue scale. Data concerning the 3 types of pain (non-cyclical pain, dysmenorrhoea and dyspareunia) were analysed separately as was the worst pain level experienced from any of these 3 types of pain. Secondary outcome: health-related quality of life measured using a generic instrument (EuroQoL EQ-5D and EQ-VAS).

Daniels 2009 *(Continued)*

Notes	The results included participants with pelvic inflammatory disease, minimal and mild endometriosis, treated with ablation. Data pertaining to participants without pelvic inflammatory disease and endometriosis were kindly made available by the authors; however, only after finalisation of review, following a greater delay than deemed acceptable in the protocol. Efforts should be made to retrieve and include these data in the review update.

LUNA: laparoscopic uterosacral nerve ablation.

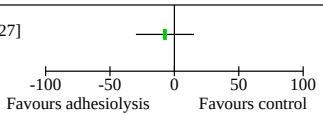
DATA AND ANALYSES

Comparison 1. Adhesiolysis versus no surgery/diagnostic laparoscopy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Effectiveness of treatment (3 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.2 Effectiveness of treatment (6 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.3 Effectiveness of treatment (12 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.4 Quality of life (6 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.4.1 Endometriosis Health Profile (EHP)-30 - Emotional Wellbeing	1	43	Mean Difference (IV, Fixed, 95% CI)	24.90 [7.92, 41.88]
1.4.2 EHP-30 - Social Support	1	43	Mean Difference (IV, Fixed, 95% CI)	23.90 [-1.77, 49.57]
1.4.3 12-item Short Form (SF-12) Physical	1	43	Mean Difference (IV, Fixed, 95% CI)	22.90 [10.97, 34.83]
1.4.4 SF-12 Emotional	1	43	Mean Difference (IV, Fixed, 95% CI)	32.30 [13.16, 51.44]

Analysis 1.1. Comparison 1: Adhesiolysis versus no surgery/diagnostic laparoscopy, Outcome 1: Effectiveness of treatment (3 months)

Study or Subgroup	Adhesiolysis Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Cheong 2014 (1)	20	27.6	23	27.3	44.6	20	-7.30 [-29.87 , 15.27]		+ + + - - +



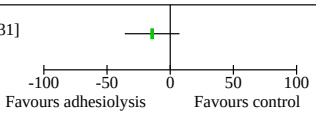
Test for subgroup differences: Not applicable

Footnotes
(1) 100 mm visual analogue scale scores (post-treatment).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.2. Comparison 1: Adhesiolysis versus no surgery/diagnostic laparoscopy, Outcome 2: Effectiveness of treatment (6 months)

Study or Subgroup	Adhesiolysis Mean	SD	Total	No Surgery/Diagnostic lap Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Cheong 2014 (1)	12	18.2	23	26.3	46.3	20	-14.30 [-35.91 , 7.31]		+ + + - - +



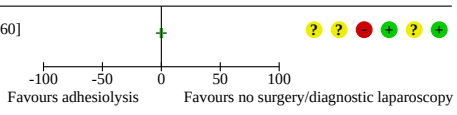
Test for subgroup differences: Not applicable

Footnotes
(1) 100 mm visual analogue scale scores post-treatment.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.3. Comparison 1: Adhesiolysis versus no surgery/diagnostic laparoscopy, Outcome 3: Effectiveness of treatment (12 months)

Study or Subgroup	Adhesiolysis Mean	SD	Total	No surgery/diagnostic laparoscopy Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Peters 1992 (1)	24	7.6	21	24	7.8	22	0.00 [-4.60 , 4.60]		? ? - + ? +

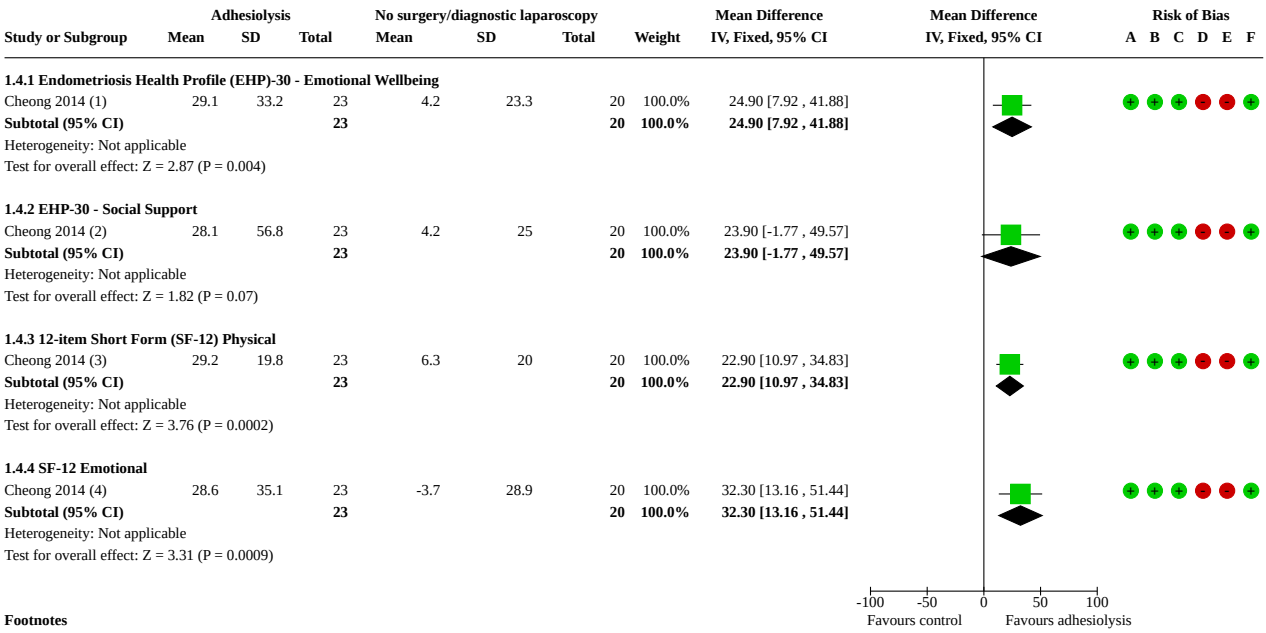


Test for subgroup differences: Not applicable

Footnotes
(1) Visual analogue scale score (post-treatment).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 1.4. Comparison 1: Adhesiolysis versus no surgery/ diagnostic laparoscopy, Outcome 4: Quality of life (6 months)



Footnotes
(1) EHP-30 Emotional Wellbeing Domain – change from baseline.
(2) EHP-30 Social Support Domain – change from baseline.
(3) SF-12 Physical Component – change from baseline.
(4) SF-12 Emotional Component – change from baseline.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

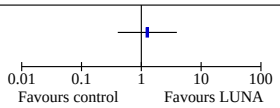
Comparison 2. Surgery including the ablation or resection of uterosacral ligaments versus other treatment (e.g. vaginal uterosacral ligament resection (VUSR)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Effectiveness of treatment (3 months)	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.2 Effectiveness of treatment (6 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.3 Effectiveness of treatment (12 months)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 2.1. Comparison 2: Surgery including the ablation or resection of uterosacral ligaments versus other treatment (e.g. vaginal uterosacral ligament resection (VUSR), Outcome 1: Effectiveness of treatment (3 months)

Study or Subgroup	LUNA (laparoscopic uterosacral nerve ablation) Events	Total	Control Events	Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F
Johnson 2004 (1)	10	19	15	32	1.26 [0.40 , 3.93]		+ + + - ? +

Test for subgroup differences: Not applicable



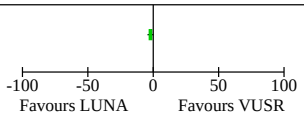
Footnotes
(1) Participants with at least a 50% reduction from the baseline visual analogue scale pelvic pain score.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 2.2. Comparison 2: Surgery including the ablation or resection of uterosacral ligaments versus other treatment (e.g. vaginal uterosacral ligament resection (VUSR), Outcome 2: Effectiveness of treatment (6 months)

Study or Subgroup	LUNA Mean	SD	Total	VUSR Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Palomba 2006 (1)	38.5	5.2	36	40.6	4.8	38	-2.10 [-4.38 , 0.18]		+ ? - + ? +

Test for subgroup differences: Not applicable



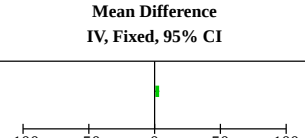
Footnotes
(1) Mean visual analogue scale score 6 months post-treatment.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

Analysis 2.3. Comparison 2: Surgery including the ablation or resection of uterosacral ligaments versus other treatment (e.g. vaginal uterosacral ligament resection (VUSR), Outcome 3: Effectiveness of treatment (12 months)

Study or Subgroup	LUNA Mean	SD	Total	VUSR Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Palomba 2006 (1)	50.5	3.5	36	48.5	3.2	38	2.00 [0.47 , 3.53]		+ ? - + ? +

Test for subgroup differences: Not applicable



Footnotes
(1) Chronic pelvic pain score 12 months post-treatment measured using visual analogue scale.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias)
(D) Incomplete outcome data (attrition bias)
(E) Selective reporting (reporting bias)
(F) Other bias

APPENDICES

Appendix 1. Cochrane Gynaecology and Fertility Group (CGF) specialised register search strategy

ProCite platform

Searched 23 April 2021

Keywords CONTAINS "Pain-abdominal" or "pain-pelvic" or "pelvic pain" or "pelvic venous congestion" or "pelvic tenderness" or "pelvic pressure" or "chronic pelvic pain" or "pelvic congestion" or "pelvic adhesions" or "abdominal pain" or Title CONTAINS "Pain-abdominal" or "pain-pelvic" or "pelvic pain" or "pelvic venous congestion" or "pelvic tenderness" or "pelvic pressure" or "chronic pelvic pain" or "pelvic congestion" or "pelvic adhesions" or "abdominal pain" (603 records)

Appendix 2. CENTRAL via the Cochrane Register of Studies Online (CRSO) search strategy

Web platform

Searched 23 April 2021

#1 MESH DESCRIPTOR Pelvic Pain EXPLODE ALL TREES 1161

#2 (Pelv* adj5 Pain*):TI,AB,KY 2225

#3 (Pelv* adj5 congest*):TI,AB,KY 30

#4 (abdomin* pain*):TI,AB,KY 11807

#5 (abdomin* adj3 congest*):TI,AB,KY 2

#6 (pelvi* condition*):TI,AB,KY 8

#7 (ovar* vein syndrome*):TI,AB,KY 0

#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 14474

#9 MESH DESCRIPTOR Gynecologic Surgical Procedures EXPLODE ALL TREES 4330

#10 (laparoscop* or hysteroscop*):TI,AB,KY 22202

#11 MESH DESCRIPTOR Endometrial Ablation Techniques EXPLODE ALL TREES 38

#12 MESH DESCRIPTOR Minimally Invasive Surgical Procedures EXPLODE ALL TREES 28424

#13 adhesiolys*:TI,AB,KY 211

#14 ((resect* or excis* or surg*) adj5 adhesion*):TI,AB,KY 389

#15 (hysterectom* or salpingooophorectom* or oophorectom* or Ovariectom*):TI,AB,KY 7076

#16 (Endometri* adj3 Ablat*):TI,AB,KY 373

#17 (minilaparoscop* or microlaparoscop*):TI,AB,KY 83

#18 ventrosuspension*:TI,AB,KY 0

#19 (presacral neurectom*):TI,AB,KY 15

#20 PSN:TI,AB,KY 90

#21 (uter* nerve ablation*):TI,AB,KY 25

#22 (LUNA or UNA):TI,AB,KY 767

#23 (ovar* adj2 vein ligation*):TI,AB,KY 1

#24 (ureterolysis or ureterostom*):TI,AB,KY 24

#25 (ovar* adj3 drill*):TI,AB,KY 112

#26 (ovar* adj3 wedge resection*):TI,AB,KY 6

#27 (uter* adj2 ligament*):TI,AB,KY 146

#28 (resect* adj3 uterosacral ligament*):TI,AB,KY 2

#29 #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 52168

#30 #8 AND #29 1359

Appendix 3. MEDLINE search strategy

Ovid platform

Searched from 1946 to 23 April 2021

1 exp Pelvic Pain/ (1739)
2 (Pelv* adj5 Pain*).tw. (3774)
3 (Pelv* adj5 congest*).tw. (155)
4 abdomin* pain*.tw. (19459)
5 (abdomin* adj3 congest*).tw. (26)
6 pelvi* condition*.tw. (15)
7 ovar* vein syndrome*.tw. (6)
8 or/1-7 (23877)
9 exp gynecologic surgical procedures/ (10107)
10 (laparoscop* or hysteroscop*).tw. (42573)
11 endometrial ablation techniques/ or exp ovariectomy/ or exp salpingo-oophorectomy/ or exp minimally invasive surgical procedures/ (96631)
12 adhesiolys*.tw. (586)
13 ((resect* or excis* or surg*) adj5 adhesion*).tw. (794)
14 (hysterectom* or salpingooophorectom* or oophorectom* or Ovariectom*).tw. (14895)
15 (Endometri* adj3 Ablat*).tw. (257)
16 (minilaparoscop* or microlaparoscop*).tw. (51)
17 ventrosuspension*.tw. (2)
18 presacral neurectom*.tw. (19)
19 PSN.tw. (235)
20 uter* nerve ablation*.tw. (11)
21 (LUNA or UNA).tw. (13493)
22 (ovar* adj2 vein ligation*).tw. (2)
23 (ureterolysis or ureterostom*).tw. (231)
24 (ovar* adj3 drill*).tw. (70)
25 (ovar* adj3 wedge resection*).tw. (14)
26 (uter* adj2 ligament*).tw. (431)
27 (resect* adj3 uterosacral ligament*).tw. (7)
28 (USL adj3 resect*).tw. (0)
29 or/9-28 (149630)
30 randomized controlled trial.pt. (84949)
31 controlled clinical trial.pt. (2388)
32 randomized.ab. (176551)
33 randomised.ab. (34897)
34 placebo.tw. (52243)
35 clinical trials as topic.sh. (14562)
36 randomly.ab. (116832)
37 trial.ti. (89150)
38 (crossover or cross-over or cross over).tw. (25580)
39 or/30-38 (380903)
40 exp animals/ not humans.sh. (446220)
41 39 not 40 (359514)
42 8 and 29 and 41 (216)

Appendix 4. Embase search strategy

Ovid platform

Searched from 1980 to 23 April 2021

1 exp pelvis pain syndrome/ or pelvic pain/ (19927)
2 (Pelv* adj5 Pain*).tw. (19372)
3 (Pelv* adj5 congest*).tw. (729)
4 pelvi* condition*.tw. (92)
5 ovar* vein syndrome*.tw. (65)
6 abdomin* pain*.tw. (103862)
7 or/1-6 (128705)
8 exp gynecologic surgery/ (151812)
9 (laparoscop* or hysteroscop*).tw. (223557)
10 exp endometrium ablation/ (2698)
11 exp ovariectomy/ (34711)
12 exp salpingooophorectomy/ (15774)
13 exp minimally invasive surgery/ (44086)
14 adhesiolys*.tw. (3149)
15 ((resect* or excis* or surg*) adj5 adhesion*).tw. (4709)
16 (hysterectom* or oophorectom* or Ovariectom* or salpingooophorectomy).tw. (96398)
17 (Endometri* adj3 Ablat*).tw. (2471)
18 (minilaparoscop* or microlaparoscop*).tw. (567)
19 ventrosuspension*.tw. (26)
20 presacral neurectom*.tw. (115)
21 PSN.tw. (1082)
22 uter* nerve ablation*.tw. (80)
23 (LUNA or UNA).tw. (4188)
24 (ovar* adj2 vein ligation*).tw. (16)
25 (ureterolysis or ureterostom*).tw. (1739)
26 (ovar* adj3 drill*).tw. (493)
27 (ovar* adj3 wedge resection*).tw. (233)
28 (uter* adj2 ligament*).tw. (2449)
29 (resect* adj3 uterosacral ligament*).tw. (50)
30 (USL adj3 resect*).tw. (5)
31 or/8-30 (411395)
32 Clinical Trial/ (1021215)
33 Randomized Controlled Trial/ (665600)
34 controlled clinical trial/ (469700)
35 multicenter study/ (295631)
36 Phase 3 clinical trial/ (54131)
37 Phase 4 clinical trial/ (4325)
38 exp randomization/ (92802)
39 Single Blind Procedure/ (42813)
40 Double Blind Procedure/ (182234)
41 Crossover Procedure/ (66858)
42 Placebo/ (356442)
43 Randomi?ed controlled trial$.tw. (258430)
44 Rct.tw. (41839)
45 (random$ adj2 allocat$).tw. (46671)
46 Single blind$.tw. (26775)
47 Double blind$.tw. (214971)
48 ((treble or triple) adj blind$).tw. (1332)
49 placebo$.tw. (322490)
50 prospective study/ (681655)
51 or/32-50 (2502604)
52 case study/ (81637)
53 case report.tw. (439329)
54 abstract report/ or letter/ (1175251)
55 Editorial.pt. (689139)
56 Letter.pt. (1166544)
57 Note.pt. (861459)
58 or/52-57 (3293585)
59 51 not 58 (2371883)
60 7 and 31 and 59 (1828)

Appendix 5. PsycINFO search strategy

Ovid platform

Searched from 1806 to 23 April 2021

1 (Pelv$ adj5 Pain$).tw. (763)
2 (Pelv$ adj5 congest$).tw. (11)
3 (abdomin$ adj5 congest$).tw. (4)
4 or/1-3 (772)
5 exp Surgery/ (73991)
6 laparoscop$.tw. (533)
7 adhesiolysis.tw. (19)
8 LUNA.tw. (146)
9 hysterectomy.tw. (756)
10 oophorectom$.tw. (245)
11 wedge resection.tw. (4)
12 endometri$ ablation.tw. (7)
13 exp Hysterectomy/ (455)
14 exp Ovariectomy/ (1309)
15 Ovariectom$.tw. (3785)
16 or/5-15 (77067)
17 random.tw. (61337)
18 control.tw. (462714)
19 double-blind.tw. (23582)
20 clinical trials/ (11891)
21 placebo/ (5976)
22 exp Treatment/ (1089476)
23 or/17-22 (1501525)
24 4 and 16 and 23 (50)

WHAT'S NEW

Date	Event	Description
13 January 2022	Amended	Adding missing CI data to abstract reporting effectiveness of treatment as 12 months

HISTORY

Protocol first published: Issue 1, 2010
Review first published: Issue 12, 2021

Date	Event	Description
9 May 2021	New citation required but conclusions have not changed	Updated search; unchanged conclusion
5 May 2020	New search has been performed	Updated protocol
25 April 2013	New search has been performed	updated review with new conclusions

CONTRIBUTIONS OF AUTHORS

All authors were involved in design and approval of the protocol.

TG and AC were responsible for independent review of included and excluded studies.

MA led on the analysis.

ML led the protocol redevelopment and write-up.

All authors contributed to the final write-up.

DECLARATIONS OF INTEREST

ML: no conflicts to declare.

MA: no conflicts to declare.

TG: no conflicts to declare.

AC: no conflicts to declare.

SAS: has received educational event support from Pfizer/Myovant Sciences, consulting fees from Abbvie, Myovant Sciences, Pfizer and Bayer, and receives royalties as author or co-author of chapters in an online medical resource on pelvic pain.

GC: no conflicts to declare.

YCC: was the lead author of included study Cheong 2014. She took no part in selection, assessment or extraction of data for this study. YCC has received conference support and honoraria from Merck Serono, Ferring and Nordic. She has a minor shareholding in a private fertility clinic. She has contributed to advisory boards for Ferring and Merck.

SOURCES OF SUPPORT

Internal sources

- None, Other

  N/A

External sources

- None, Other

  N/A

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review revises and updates the previous review entitled 'Interventions for women with chronic pelvic pain' (Stones 2005), which has been withdrawn. This review focuses on women with chronic pelvic pain syndrome, which is the clinical entity when no clear aetiology of chronic pelvic is identified. This change from the original review was declared in the updated study protocol, which was not formally published. Otherwise, changes to the updated protocol involved updated components of the methods section to current Cochrane standards including provision for summary of findings tables and planned sensitivity/subgroup analyses. There were no differences between the protocol and review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Chronic Pain [etiology] [therapy]; *Endometriosis; *Laparoscopy; Pelvic Pain [etiology] [surgery]; Quality of Life

MeSH check words

Female; Humans