Interventions for treating chronic pelvic pain in women (Review)

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ABSTRACT

Background

Chronic pelvic pain is common in women in the reproductive and older age groups and causes disability and distress. Often investigation by laparoscopy reveals no obvious cause for the pain. As the pathophysiology of chronic pelvic pain is not well understood its treatment is often unsatisfactory and limited to symptom relief. Currently the main approaches to treatment include counselling or psychotherapy, attempts to provide reassurance by using laparoscopy to exclude serious pathology, progestogen therapy such as medroxyprogesterone acetate, and surgery to interrupt nerve pathways.

Objectives

We aimed to identify and review treatments for chronic pelvic pain in women. The review included studies of patients with a diagnosis of pelvic congestion syndrome or adhesions but excluded those with pain known to be caused by i) endometriosis, ii) primary dysmenorrhoea (period pain), iii) pain due to active chronic pelvic inflammatory disease, or iv) irritable bowel syndrome.

Search strategy

We searched the Cochrane Menstrual Disorders and Subfertility Group Specialised Register of trials (searched 20th January 2005), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 1, 2005), and reference lists of articles.

Selection criteria

Randomised controlled trials (RCTs) with women who had chronic pelvic pain. The review authors were prepared to consider studies of any intervention including lifestyle, physical, medical, surgical and psychological treatments. Outcome measures were pain rating scales, quality of life measures, economic analyses and adverse events.

Data collection and analysis

For each included trial, information was collected including the method of randomisation, allocation concealment and blinding. Data were extracted independently by the two review authors using forms designed according to the Cochrane guidelines.

Main results

Nineteen studies were identified of which fourteen were of satisfactory methodological quality. Five studies were excluded. Progestogen (medroxyprogesterone acetate) was associated with a reduction of pain during treatment while goserelin gave a longer duration of benefit. Counseling supported by ultrasound scanning was associated with reduced pain and improvement in mood. A multidisciplinary approach was beneficial for some outcome measures. Benefit was not demonstrated for adhesiolysis (apart from where adhesions were severe), uterine nerve ablation, sertraline or photographic reinforcement after laparoscopy. Writing therapy and static magnetic field therapy showed some evidence of short-term benefit.

Authors' conclusions

The range of proven effective interventions for chronic pelvic pain remains limited and recommendations are based largely on single studies. Given the prevalence and healthcare costs associated with chronic pelvic pain in women, randomised controlled trials of other medical, surgical and psychological interventions are urgently required.

Chronic pelvic pain is common in women in the reproductive and older age groups and it causes disability and distress that result in significant costs to health services. The pathogenesis of chronic pelvic pain is poorly understood. Often investigation by laparoscopy reveals no obvious cause for the pain. There are several possible explanations for chronic pelvic pain including undetected irritable bowel syndrome, and central sensitisation of the nervous system. A vascular hypothesis proposes that pain arises from dilated pelvic veins in which blood flow is markedly reduced. As the pathophysiology of chronic pelvic pain is not well understood, its treatment is often unsatisfactory and limited to symptom relief. Currently the main approaches to treatment include counseling or psychotherapy, attempts to provide reassurance using laparoscopy to exclude serious pathology, progestogen therapy such as with medroxyprogesterone acetate and surgery to interrupt nerve pathways.

PLAIN LANGUAGE SUMMARY

Limited symptom relief is available for women with chronic pelvic pain

Chronic pelvic pain in women is a common problem. Symptoms include lower abdominal pain, and pain before and during sexual intercourse. Specific causes are difficult to identify and treatment is often limited to relief of symptoms. An ultrasound or internal examination using a laparoscope is done to rule out serious conditions and to provide reassurance. The review of trials found that a multidisciplinary approach helps alleviate symptoms. A high dose of progestogen therapy using medroxyprogesterone acetate also helps but goserelin has a longer duration of benefit. There is an indication of benefit from writing therapy for some patients.

BACKGROUND

Chronic pelvic pain is common in women in the reproductive age group. It causes disability and distress and results in significant costs to health services, estimated at over \$880 million in the USA (Mathias 1996). Consultations recorded in a UK general practice national database showed that the incidence and prevalence of chronic pelvic pain was similar to that of migraine, back pain and asthma, with monthly incidence and prevalence of 21.5/1000 and 1.58/1000 respectively (Zondervan 1999). The original protocol for this review limited the scope of the review to women in the reproductive age group, arising from the review author' clinical experience of consulting patterns in hospital gynaecology. However, Zondervan 1999 demonstrated that consulting rates for chronic pelvic pain in general practice were actually higher among older women, so the scope of the review was expanded to include studies of older participants.

The pathogenesis of chronic pelvic pain is poorly understood. Often investigation by laparoscopy reveals no obvious cause for the pain. Where some abnormality is present this may be coincidental rather than causal. A lesion such as adhesions following surgery or infection may not correlate with the site of the pain. This discrepancy is only partly explained by the complexity of the neurophysiology of visceral sensation (sensation arising from the internal organs). In a US population-based study (Mathias 1996), 61% of women with pelvic pain symptoms did not have a clear diagnosis.

In this review we did not consider pelvic pain known to be caused by i) endometriosis, which is also chronic in nature; ii) primary dysmenorrhoea, a recurrent acutely painful condition exclusively related to menstruation; iii) pain due to active chronic pelvic inflammatory disease, that is chronic low-grade sepsis in devitalised tubal tissue with acute exacerbations incompletely treated by antibiotics; or iv) irritable bowel syndrome.

Explanations for chronic pelvic pain in the absence of obvious pathology have included undetected irritable bowel syndrome, present in up to half of a group of women referred for gynaecological investigation (Prior 1989). Another explanation is provided by the vascular hypothesis, first postulated in the 1940s (Taylor 1949) and more recently by Beard (Beard 1984), where pain is thought to arise from dilated pelvic veins in which blood flow is markedly reduced. Other authors (Rapkin 1995) have suggested an alteration in processing of stimuli by the spinal cord and brain in women with chronic pelvic pain. This may be a feature shared by those with other chronic painful conditions, where normal bodily sensation comes to be perceived as painful. In specific subgroups such as those with pain arising following surgery, there may be a clear neuropathic element. Often the pathophysiology of chronic pelvic pain is not well understood so its treatment is unsatisfactory and limited to symptom relief.

Currently the main approaches to treatment include counseling or psychotherapy, attempts to provide reassurance using laparoscopy to exclude serious pathology, progestogen therapy such as with medroxyprogesterone acetate, and surgery to interrupt nerve pathways such as laparoscopic uterine nerve ablation and presacral neurectomy, or hysterectomy with or without removal of the ovaries. While less invasive, psychological approaches are time consuming and may not be acceptable to all women. Hormonal therapy is associated with side effects and impairs fertility during its use. Surgery, even if effective, is invasive and may be associated with the loss of reproductive capacity.

OBJECTIVES

We aimed to identify and review treatments for chronic pelvic pain in women. The scope of the review included those women with a diagnosis of pelvic congestion syndrome or adhesions but excluded those with pain known to be caused by i) endometriosis, which is also chronic in nature; ii) primary dysmenorrhoea (period pain), a recurrent acutely painful condition exclusively related to menstruation; iii) pain due to active chronic pelvic inflammatory disease, that is chronic low grade sepsis in devitalised tubal tissue with acute exacerbations incompletely treated by antibiotics; or iv) irritable bowel syndrome.

In chronic pelvic pain where pain is the main problem rather than a clearly identifiable progressive pathology, treatments need to be appropriate to the particular needs of individual women. This review aimed to combine information from studies using many different interventions and outcome measures to provide an overview of the most effective, acceptable and least invasive treatment options.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All truly randomised controlled trials.

Types of participants

Women with chronic pelvic pain including those with a diagnosis of pelvic congestion syndrome but excluding those with pain known to be caused by i) endometriosis, which is also chronic in nature; ii) primary dysmenorrhoea, a recurrent acutely painful condition exclusively related to menstruation; iii) pain due to active chronic pelvic inflammatory disease, that is chronic low grade sepsis in devitalised tubal tissue with acute exacerbations incompletely treated by antibiotics; or iv) irritable bowel syndrome.

Types of intervention

The reviewers were prepared to consider studies of any intervention. Those interventions about which research activity was anticipated were as follows.

Lifestyle: exercise, dietary, substance use.

Psychological: cognitive behaviour therapy, psychotherapy, counseling, meditation, biofeedback, ultrasonography as reassurance, hypnosis.

Physical therapy.

Medical: non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptive pill (OCP), oral and non-oral progestogen, danazol, GnRH analogues (alone or with 'add-back' oestrogen), progestogen-releasing intra-uterine contraceptive devices (IUCD),

drugs affecting blood vessels, antidepressants, anticonvulsants, analgesics, combined analgesic and caffeine preparations, local anaesthetic infiltration alone or in combination with corticosteroids.

Surgical: diagnostic laparoscopy, adhesiolysis, ventrosuspension, presacral neurectomy, laparoscopic uterine nerve ablation (LUNA), ovarian vein ligation (via surgery or radiology), hysterectomy, oophorectomy, ovarian drilling, wedge resection, endometrial ablation.

Other: transcutaneous nerve stimulation, complementary medicine, referral to standard versus multidisciplinary clinic setting, investigation and treatment protocols.

Types of outcome measures

Pain scores: visual analogue scales for pain, pain questionnaires such as the McGill long and short form, simple better or unchanged or worse rating scales, TOTPAR analysis.

Quality of life instruments: such as Euroquol and SF-36, mood

Quality of life instruments: such as Euroquol and SF-36, mood scales, sexual function, time off work.

Resource utilisation: by patients, family practitioners and hospitals.

Adverse outcomes: compliance with treatment, side effects of pharmacotherapy, short and long-term surgical complications, suicide, other mortality, morbidity arising from an unrecognised pathology.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched for all publications which describe (or might describe) randomised controlled trials of interventions for chronic pelvic or abdominal pain in women. The original search was performed in 1999. Updated searches were completed in 2005.

- (1) We searched the Menstrual Disorders and Subfertility Group Specialised Register for any trials (searched 20th January 2005). The Cochrane Menstrual Disorders and Subfertility Group Specialised Register is based on regular searches of MEDLINE, EMBASE, CINAHL and PsycINFO, the handsearching of 20 relevant journals and conference proceedings, and searches of several key grey literature sources. A full description is given in the Group's module on *The Cochrane Library*.
- (2) The citation lists of relevant publications, review articles, and included studies were also searched.

METHODS OF THE REVIEW

Two review authors (WS and YC) independently, and unblinded, assessed trials for inclusion in the review. A third assessor (FH) was available as an arbiter when there was uncertainty regarding eligibility. Additional information from investigators was sought where appropriate.

The quality of the included trials was assessed using a standard checklist, developed by the Review Group and based on guidelines in the Cochrane Handbook, and summarised in an overall quality score of A to C. In addition, the quality of allocation concealment was graded as either A (adequate), B (unclear) or C (inadequate). Any discrepancies were assessed by a third review author. Quality scores were recorded for each study in the Notes section of the Table of included studies and allocation concealment scores were also recorded in the Table.

For each included trial, information was collected regarding the method of randomisation, allocation concealment, blinding, whether an intention-to-treat analysis could be performed, the relevant interventions and outcomes (see previous sections). Data were extracted independently by two review authors, using forms designed according to Cochrane guidelines.

Where possible, results were analysed as dichotomous data by taking the number of women who achieved a certain degree of improvement in pain after treatment compared to the experience of women in the control groups. We used the definition of pain improvement specified by the authors in each trial, for example a 50% reduction in visual analogue scale or a five-point change in the McGill pain scale. Results from studies that measured pain on a continuous scale were collapsed into dichotomous data by this means. For dichotomous data, results for each study were expressed as an odds ratio with 95% confidence intervals and combined for meta-analysis with RevMan software using the Peto method and a fixed-effect model.

Where studies reported the results of pain scales as mean values in each group, these were treated as continuous data. Data from studies using different pain scales were standardised for meta-analysis using standardised mean differences.

Where sufficient trials were identified, the review authors tested for heterogeneity and calculated weighted estimates (fixed-effect model) of the typical treatment effect across trials (Peto odds ratio) using the Cochrane RevMan review package. They made specific reference to possible differences in the chronicity and severity of pain in the different studies.

DESCRIPTION OF STUDIES

Nineteen studies were identified. Of these, fourteen studies were included: six were undertaken in the UK, three in the Netherlands,

three in the USA, one in New Zealand and one in Turkey. Interventions identified as the subject of randomised controlled trials for chronic pelvic pain were progestogen (medroxyprogesterone acetate) alone or in combination with psychotherapy; goserelin; sertraline; lofexidine hydrochloride; ultrasound scanning as an aid to counseling and reassurance; intravenous dihydroergotamine for acute exacerbations of chronic pelvic pain; use of photographs to assist in post-operative patient consultation; static magnetic fields to improve pain; adhesiolysis via laparoscopy or laparotomy; LUNA versus no LUNA; writing exercises; chiropractic; and a multidisciplinary approach to investigation including physiotherapy, psychology, and attention to dietary and environmental factors. Five studies were excluded because of: insufficient information about outcomes (3), non-comparable evaluation points (1) and uncertainty about the study design (2).

The numbers of participants (N) in the included studies were: Brown 2002 (33); Engel 1998 (25); Farquhar 1989 (84); Ghaly 1994 (90); Johnson 2004 (56); Norman 2004 (48); Onwude 2004 (286); Peters 1991 (106); Peters 1992 (48); Reginald 1987 (6); Soysal 2001 (47); Stones 2001 (39); Swank 2003 (100); Walton 1992 (165), randomised from 14 centres.

Intravenous dihydroergotamine was used for the relief of acute exacerbations of pain associated with pelvic venous congestion (Reginald 1987). This study used a crossover design in which women presenting with two successive exacerbations of pain were given either dihydroergotamine or placebo. The results were presented as the difference in each woman's pain scores for each treatment and are not amenable to display in the same format as the other studies, which used parallel treatment and control or placebo groups. A similar approach was used in presenting the data from a study of sertraline versus placebo (Engel 1998), which also used a crossover design. Participants were randomised to receive placebo or sertraline for six weeks alternately. The effects of photographic reinforcement of the findings of the laparoscopy were tested in Onwude 2004 by showing women photographs of the findings at laparoscopy. The aim was to test whether reassurance about the findings would contribute to improved outcomes.

Study populations had a similar age distribution, with mean ages of 27 to 35 years, except in Peters 1992 and Swank 2003 where the patients were of an older age group (see Table of characteristics of included studies). All studies included only female patients except Swank 2003, where 88% were female patients; the participants included 12% men in whom the indication was abdominal pain rather than pelvic pain. Swank 2003 was included following discussion among the three review authors. We considered that the predominantly female patient population and the substantial clinical overlap between patients presenting with abdominal and pelvic pain with adhesions justified its inclusion. Eleven studies specified a six-month duration of symptoms prior to entry. Peters 1991 and Engel 1998 specified three months and Soysal 2001 did not state the duration of symptoms prior to entry. All studies except

four (Brown 2002; Engel 1998; Johnson 2004; Peters 1991) required prior laparoscopy. In Peters 1991 women were randomised to a 'standard investigation protocol' which included laparoscopy or to an 'integrated approach' where laparoscopy could be undertaken if indicated. In contrast to the other studies in this review, in Peters 1992 women were randomised after a laparoscopy showed evidence of adhesions. Adhesiolysis was performed via laparotomy in Peters 1992 whereas in Swank 2003 adhesiolysis was performed via laparoscopy. For Johnson 2004, this review entered data from those women who did not have endometriosis (56) out of a total of 123 women randomised before laparoscopy to receive LUNA or no LUNA. On these 56 women, 53 had non-menstrual pain, which justified the inclusion of this comparison in the review. The remaining three women (two in the control and one in the LUNA group) had dysmenorrhoea, dyspareunia, dyschezia alone or in combination.

All studies had comparable control and treatment groups with respect to age, parity and chronicity of pain except for Soysal 2001 where chronicity was not stated and Stones 2001 where the intervention group had higher parity. Outcomes were reported at the end of treatment in all studies and for post-treatment follow up in all except Engel 1998. The interval between the end of treatment and follow up ranged from 48 hours to one year.

For outcome measures, six studies (Farquhar 1989; Johnson 2004; Reginald 1987; Stones 2001; Swank 2003; Walton 1992) used visual analogue scales (VAS) for pain. Five studies (Brown 2002; Norman 2004; Ghalv 1994; Peters 1991; Peters 1992) used the McGill pain score. Four (Farquhar 1989; Peters 1991; Peters 1992; Walton 1992) also used a self-rating improvement scale. Ghaly 1994 and Soysal 2001 additionally used the Hospital Anxiety and Depression scale. Engel 1998 used a composite pain intensity score incorporating VAS, the Hamilton Depression Rating Scale, SF-36, work role items from the Social Adjustment Survey and the 12 somatization items from the Hopkins Symptom Checklist-90 (SCL-90). Soysal 2001 used venography scores, a modification of the Biberoglu and Behrman scale (Biberoglu 1981) that combines physical findings and symptoms and the revised Sabbatsberg Sexual Rating Scale (rSSRS) (Garratt 1995). Brown 2002 also used the pain disability index and clinical global impression scale. Swank 2003 included the SF-36.

METHODOLOGICAL QUALITY

Nine studies (Brown 2002; Engel 1998; Farquhar 1989; Ghaly 1994; Johnson 2004; Peters 1991; Peters 1992; Soysal 2001; Stones 2001) were of good methodological quality with inclusion criteria and outcome measures clearly defined. Allocation concealment was graded A either from the publications (Farquhar 1989; Johnson 2004; Soysal 2001; Stones 2001; Swank 2003) or following correspondence with the authors confirming that a robust method of randomisation was employed (Engel 1998; Peters 1991;

Peters 1992). Allocation concealment was uncertain (B) in Ghaly 1994.

Allocation concealment was graded C in Reginald 1987, a single blind study; graded B (used a deck of cards) in Norman 2004; and was uncertain (B) in Walton 1992. In all studies except Walton 1992 follow-up rates were very good with 10% or fewer lost to follow up. Intention-to-treat analyses were not performed in four studies. Outcome assessment was blinded to treatment allocation in all the included studies. It was justifiable in this review to include studies where participants were inevitably aware of their treatment allocation (Ghaly 1994; Norman 2004; Peters 1991; Peters 1992; Soysal 2001).

RESULTS

Two studies each reported results for treatment with progestogen (medroxyprogesterone acetate (MPA) versus placebo; and adhesiolysis versus expectant management or diagnostic laparoscopy. For the other interventions only single studies were identified. These interventions were: progestogen (MPA) with psychotherapy versus placebo, progestogen versus gosrelin, sertraline versus placebo, lofexidine hydrochloride versus placebo, ultrasound scanning as an aid to counseling versus conventional care, use of static magnetic field therapy versus placebo, a multidisciplinary compared to a conventional approach and dihydroergotamine versus placebo. Thus, it was not possible to combine data from different studies of these interventions. The combination of results from the two adhesiolysis studies should be treated with caution as one study used laparotomy and the other used laparoscopy.

Progestogen (MPA) was effective at the end of treatment as reflected in pain scores (OR 2.64, 95% CI 1.33 to 5.25, n=146) and a self-rating scale (OR 6.81, 95% CI 1.83 to 25.3, n=44), but benefit, measured nine months post-treatment, was not sustained. MPA plus psychotherapy was effective in terms of pain scores (OR 3.94, 95% CI 1.2 to 12.96, n=43) but not the self rating scale, at the end of treatment. Benefit was not sustained post-treatment (see Discussion).

No improvement in pain scores was seen in women taking sertraline when compared to placebo. The SF-36 subscale for Health perception showed a small improvement in the sertraline arm, while the Role functioning-emotional subscale showed a large fall in the sertraline arm (Engel 1998).

Other studies reported post-treatment results. Counseling supported by ultrasound scanning (Ghaly 1994) was effective both in terms of pain scores (OR 6.77, 95% CI 2.83 to 16.19, n = 90) and mood (OR 4.63, 95% CI 1.68 to 12.75). The use of a multidisciplinary approach (Peters 1991) led to a positive outcome in a self-rating scale (OR 4.15, 95% CI 1.91 to 8.99, n = 106) and daily activity but not in pain scores.

There was no evidence of difference in outcome for women undergoing adhesiolysis (OR 1.54, 95% CI 0.81 to 2.93, n=148) in one trial using laparotomy (Peters 1992) and in another performing the procedure via laparoscopy (Swank 2003). However, the small subgroup with severe adhesions did show a significant benefit for surgery (OR for self-rating scale 16.59, 95% CI 2.16 to 127.2, n=15) in Peters 1992.

The comparison between those who underwent LUNA and controls did not show evidence of a difference in pain scores at 3 or 12 months (OR for 50% reduction in VAS for pain at 12 months 1.16, 95% CI 0.35 to 3.79).

Pain scores after dihydroergotamine were reduced for up to 48 hours postinjection (Reginald 1987). The mean difference in pain score at this time point was 4.1 cm on a 10 cm scale, SD 2.4 (P value < 0.05).

There was no evidence of difference in outcomes between lofexidine hydrochloride and placebo (OR for reduction in pain on a VAS 2.5, 95% CI 0.6 to 10.3) (Stones 2001). Venography scores, symptom and examination scores, mood and sexual function were improved to a greater extent one year after treatment with goserelin compared to progestogen (Soysal 2001). Weighted mean differences (WMD) were for: venography, WMD 1.1 (95% CI 0.64 to 1.56); symptom score, WMD 3 (95% CI 2.08 to 3.92); HADS anxiety score, WMD 1 (95% CI 0.42 to 1.58); HADS depression score, WMD 0.3 (95% CI -0.34 to 0.94), HADS total score, WMD 1.3 (95% CI 0.42 to 2.18), rSSRS score, WMD 15.5 (95% CI 11.7 to 19.23).

Effects of static magnetic therapy versus placebo were analysed by the investigators using the Wilcoxon rank sum test. They showed no evidence of a difference in outcomes following two weeks of treatment but statistically significant differences with four weeks treatment as assessed by the Pain Disability Index, the Clinical Global Impression Scale but not the McGill pain questionnaire. For consistency in this review we presented the outcomes in terms of weighted mean differences, which showed no significant differences in the outcomes.

Photographic reinforcement after surgery did not appear to have any beneficial effect. The intervention group had a trend for greater baseline pain intensity compared to controls, which may have confounded possible beneficial effects of photographic reinforcement. Moreover, 233 women were entered into the trial compared to the target of 450 so the final comparisons were somewhat different to those originally planned.

Writing about the stress of pelvic pain as a therapeutic intervention showed small differences in outcome. The weighted mean differences (WMD) on the various subscales of the McGill Pain Questionnaire were: sensory pain, WMD 0.07 (95% CI -0.31to 0.45); affective pain, WMD -0.12 (95% CI -0.42 to 0.18); and evaluation pain, WMD -1.16 (95% CI -1.96 to -0.36). In a post hoc subgroup analysis reported in the study, but not presented

here, women with higher baseline "ambivalence about emotional expression" appeared to respond more positively to this intervention.

DISCUSSION

This review identified nineteen studies, of which fourteen were included, which evaluated a range of interventions. Data from two studies on progestogen and two of adhesiolysis could be combined. A large number of potential interventions for chronic pelvic pain have still not been tested in randomised trials. The inclusion of end points at the completion of treatment and at a later follow up, or only at a later follow up, is a necessary consequence of the different types of treatment available for pelvic pain. For example, it would be reasonable to expect a treatment acting primarily as an analgesic or pain suppressive agent to be effective only during treatment. On the other hand, for surgical treatments to be clinically useful they must have a sustained duration of benefit and evaluation immediately after the procedure is primarily to detect complications rather than treatment efficacy.

Combining the results of Farquhar 1989 with those of Walton 1992 for medroxyprogesterone acetate versus placebo resulted in a reduced odds ratio for pain improvement (at least 50% reduction in VAS for pain) at the end of treatment, compared to the results of Farquhar alone, but the 95% confidence intervals were smaller and the treatment effect remained significant. The latter study was fully reported in a company report made available to the review authors and had a very high dropout rate in both treatment and control arms. Nevertheless, the two studies are consistent in the direction of treatment effect. Dropout was substantial in Brown 2002 and Stones 2001, limiting the generalisability of the first study findings on static magnetic fields and reinforcing the lack of practical use of lofexidine in the second owing to a high incidence of drowsiness. In contrast, no dropouts or adverse events were reported in Soysal 2001. This was surprising given the strong likelihood of estrogen deficiency side effects during GnRH agonist therapy. The authors did not respond to a request for further information about adverse events. In the clinical setting, goserelin is a widely available treatment option. Many women will be concerned about possible adverse effects such as hot flushes and bone loss, which could be offset by the inclusion of estrogen 'add-back' therapy as is widely done for patients with endometriosis. Future studies could consider this combination. A possible over interpretation of the benefit of GnRHa therapy stems from the use of the modified Biberoglu and Behrman scale as an end point in this study. This scale depends on the assessment of pelvic tenderness by the physician and is also influenced by menstrual pain. Thus, any treatment that results in amenorrhoea will generate a spurious additive effect on the scale score during treatment. This objection does not apply to the final trial evaluation point one year after the end of therapy, by when normal menstruation would have resumed. Overall, while the scale has been widely used for industry

sponsored drug trials for regulatory purposes in endometriosis, the scale has not been tested for validity and reliability against modern psychometric standards and the review authors' view is that available reliable and valid pain measures are preferred in future research.

Progestogen remains an option for chronic pelvic pain, with efficacy during treatment. In practice it may be most acceptable among women unconcerned about possible weight gain, the most common adverse effect. Analysis of the data on progestogen (MPA) and psychotherapy (Farquhar 1989) for the present review was based on comparisons of two groups. Calculation of odds ratios showed a non-significant benefit for MPA and psychotherapy versus psychotherapy alone, post-treatment. The original paper reported the results of one-way analysis of variance and suggested a significant sustained benefit post-treatment in the MPA plus psychotherapy group. A possible explanation for the discrepancy in findings is the unexpectedly poor outcome in the placebo plus psychotherapy group. The authors hypothesised that the study conditions with ready access to the research staff might have masked the effect of providing psychological support, in addition to routine medical contact. This would be consistent with the results of other (non-randomised) studies showing benefit for psychological intervention in chronic pelvic pain, and with the results of Peters 1991 which provided evidence for the sustained effect of a multidisciplinary approach. In addition, the small numbers of patients in each group reduced the power of the study of Farquhar 1989 to detect treatment effects.

The review authors included Swank 2003 despite the inclusion of some men as participants in the study. The study authors did not respond to a request to provide outcome data by sex or to comment on the frequency of gynaecological pathologies such as endometriosis or pelvic inflammatory disease, seen at the time of adhesiolysis. However, in follow-up correspondence to the Lancet they presented a table of pain outcomes by type of previous surgery, which showed that similar numbers in the control and intervention groups had undergone previous gynaecological surgery and that the pain outcomes were very similar in this subgroup (Hop 2003). Our conclusions should be interpreted with caution given that the pathophysiology of abdominal and pelvic pain may differ between men and women, respectively; and the presence of gynaecological conditions such as endometriosis or pelvic inflammatory disease could, if left untreated, give rise to persistent pain. Thus there is still uncertainty about the place of adhesiolysis among patients presenting to gynaecologists and the conclusion of this review is that there is no evidence of benefit, rather than evidence of no benefit. Two possible conclusions may be drawn. Firstly, that further large trials of adhesiolysis that recruit gynaecological patients should be undertaken to provide the necessary level of evidence; Second, that given the uncertainties about pathophysiology it would be better for researchers to concentrate on careful observational studies, including full psychological assessment of participants, laboratory characterisation of adhesion tissues and physiological investigation of intraperitoneal inflammatory and nociceptive processes, in clinical subgroups such as those with adhesions involving the ovaries and others where the influence on outcomes of psychological and sociocultural variables may play a role.

Johnson 2004 tested the effect of LUNA in women with nonmenstrual chronic pelvic pain, dysmenorrhoea, dyspareunia and dyschezia. We included data from this study relating to the subgroup that did not have endometriosis; where there was no evidence of a difference in chronic pelvic pain outcomes at 12 months between the two groups. We did not consider the outcome data for dysmenorrhoea presented in the study report as this was outside the scope of the review. The sample size was insufficiently large to provide a definite answer on the role of LUNA and the results of the ongoing UK study (The LUNA Trial 2003) are awaited with interest.

The study of Reginald 1987 was very small and its major value was as a pathophysiological demonstration. In particular, the study should not be taken as a basis for current therapy as the systemic vasoconstrictor properties of dihydroergotamine have led to its withdrawal from the market. The single study of a selective serotonin reuptake inhibitor (SSRI) antidepressant (Engel 1998) did not show benefit with sertraline and identified a potential adverse effect on an aspect of quality of life. This was a small study with a short duration of treatment and as such was likely to be underpowered. There are no trials as yet on anticonvulsant agents such as carbamazepine or gabapentin. As the Cochrane review concludes, there is "still a need for high quality studies of the relative effectiveness of different anticonvulsants in chronic pain syndromes, and for comparisons of antidepressants with anticonvulsants" (Wiffen 2000.) Although Norman 2004 demonstrated benefit from women writing about the stressful consequences of their pain this was only in one pain subscale and outcomes were assessed after a short period of follow up. This study provides an interesting pointer to future interventions. The authors identified baseline psychological characteristics that indicated a more favourable response to an intervention facilitating emotional self disclosure. In the context of a multidisciplinary clinic, it is useful to be able to individualise treatment and psychologists working with women with chronic pelvic pain will find these observations of interest for planning approaches to pain management. Many clinicians are effective in struggling to integrate the disease-focussed aspects of care, addressing symptoms and managing distress arising from the impact of the condition; tools to increase women's capacity to cope are highly relevant.

AUTHORS' CONCLUSIONS

Implications for practice

Currently available information about treatment of women with chronic pelvic pain provides some support for the use of ultrasound scanning as an aid to counseling and reassurance, progestogen (medroxyprogesterone acetate) or goserelin for pelvic congestion and, with the aim of improved function and self rating, a multidisciplinary approach to assessment and treatment. Adhesiolysis is not shown to be of benefit other than in women with severe adhesions and LUNA is not shown to be effective. SSRI antidepressants have not been shown to be of benefit. Most of these conclusions are based on the outcome of single randomised trials and need replication. Writing therapy may have a place as part of a multidisciplinary programme.

Implications for research

This update of this review has again shown that a very limited range of interventions has been tested for the treatment of women with chronic pelvic pain. That only single studies have been undertaken on most of these interventions greatly limits the available evidence on which clinical practice can be based. Further work is required to confirm the findings of existing studies. Given the prevalence and healthcare costs associated with chronic pelvic pain in women randomised controlled trials of other medical, surgical and psychological interventions are urgently required. As causation and treatment of chronic pelvic pain is often complex, the design of research studies needs to adequately integrate baseline psycholog-

ical and clinical assessment. Studies currently needed include trials of radiological embolisation versus surgery for pelvic congestion, assessment of the value of neuropathic pain medications, and formal comparisons of outcomes from different packages of care. Most of the conclusions drawn are based on the outcomes of single randomised trials which are likely to be underpowered and need replication.

POTENTIAL CONFLICT OF INTEREST

One author (RWS) was also the first author of one study (Stones 2001).

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^{*}Indicates the major publication for the study

TABLES

Characteristics of included studies

Study	Brown 2002
Methods	Method of allocation: Blinded: double blind
	Number of centres: 1
	Design: double-blind, randomised, parallel group study
	Power calculation: yes
	Number of patients randomised: 33
	Number of patients analysed: 32
	Exclusion post randomisation: 0
	Losses to follow-up: 1
	Intention to treat analysis: no
	Source of funding: BIOflex Medical Magnets
Participants	Country: USA
	Number of participants: 32
	Inclusion criteria: Pelvic pain > 6 months despite other treatment, impaired social function, trigger/ circum-
	scribed tender point on examination, normal pelvic examination, normal cervical smears
	Age: 18 - 50 years
	Source of patients: gynaecology clinic
	Exclusion criteria: pregnancy, breast-feeding, medical disorders, metal/electronic device, BMI > 35.
Interventions	Treatment: Static magnetic fields
	control: no treatment
	Duration: 2-4 weeks
Outcomes	The McGill Pain questionaire, Pain Disability index, Clinical Global Impressions Scale
Notes	Variable duration of study. Subgroup analysis of women who continued to have 4 weeks of treatment showed significance. High discontinuation between 2-4 weeks (41% attrition rate). Quality score C.
Allocation concealment	B – Unclear
Study	Engel 1998
Methods	Method of allocation:
	Double-blinded
	Exclusions post randomisation: 2
	Losses to follow-up: 0
	Unusual study design: Crossover design
Participants	Country: USA
	Number of participants: 25
	Age: mean 29
	Sex: F
	Inclusion criteria:
	Pelvic pain for more than 3 months
	No psychoactive medication for previous 2 weeks
	Exclusion criteria:
	Laparoscopy within 3 months
	Failed 7-10 day placebo run-in phase

	ciuded studies (Continuea)
Interventions	Treatments: Sertraline 50 mg twice daily
	Control: Placebo
	Duration: 6 weeks
	Follow-up: end of treatment
Outcomes	Composite pain score
	SF-36
	Hamilton depression rating scale Social Adjustment Survey
	Hopkins Symptom Checklist Somatization items
	Pain
Notes	Quality score A
Allocation concealment	A – Adequate
Study	Farquhar 1989
Methods	Method of allocation: drug packs
	Double-blinded
	Exclusions post randomisation: 0
	Losses to follow-up: 7
	Unusual study design, eg factorial:
Participants	Country: England
	Number of participants: 102
	Age: mean 29.8 Sex: F
	Sex: F Inclusion criteria:
	Pelvic pain for more than 6 months
	No pathology on laparoscopy
	Venogram score 5 or more
	Exclusion criteria:
	Recent psychiatric disease
	History of thromboembolism
	Postmenopausal
	Previous hysterectomy
Interventions	Treatments: Medroxyprogesterone acetate (MPA) 50 mg daily
	MPA & psychotherapy
	Control: Placebo
	Placebo & psychotherapy
	Duration: 4 months
	Follow-up: 9 months
Outcomes	Visual analogue scale pain score
	Pain improvement rating scale
	Side effects
Notes	Not blinded to psychotherapy. Quality score A.
Allocation concealment	A – Adequate
Study	Ghaly 1994
Methods	Closed envelope system.
	Outcome assessed blind to allocation.
	Exclusions post randomisation: none
	Losses to follow-up: 10

Characteristics of inc	cluded studies (Continuea)
Participants	Country: Scotland Number of participants: 100 Age: 21-55
	Sex: F
	Inclusion criteria:
	> 6 months pain
	Negative laparoscopy
	Exclusion criteria:
	Previous malignant disease
	Mental retardation
	Medical treatment for pelvic pain at first visit Suspicion of malignant disease on pelvic examination
	Abnormal pelvic examination
T	
Interventions	Treatments: US Scan & education/counselling session
	Control: Wait & see policy Duration: 4-9 months reassessment
Outcomes	McGill pain score: at least 5 point improvement
Outcomes	Hospital anxiety depression scale: improvement in category (normal, borderline, depressed).
N	
Notes	Quality score A.
Allocation concealment	A – Adequate
0.1	7.1 000/
Study	Johnson 2004
Methods	Method of allocation: computer generated random number sequence Double blind
	Inclusion: women age 18-45, history of chronic pelvic pain, no change in medication for the three months
	prior to trial recruitment.
	Exclusion: previous hysterectomy, malignancy, LUNA, ovarian cysts, plan for pregnancy, change of medica-
-	tions, laparoscopic findings rendering surgery impossible
Participants	Country: New Zealand
	Number of participants: 56
	Age: 18-45
,	Sex : F
Interventions	Treatments: women without endometriosis at laparoscopy randomised to receive LUNA and or diagnostic
	laparoscopy alone.
Outcomes	50% reduction in VAS for pain
Notes	Quality score A.
Allocation concealment	A – Adequate
Study	Norman 2004
Methods	Method of allocation: Randomised by pack of cards
	Blinded: no
	Number of centres:1
	Design: prospective study
	Number of patients randomised: 60
	Power calculation: no
	Intention to treat analysis: no
Participants	Country: United States
	Number of participants: 78

	Age: 18-64
	Sex: F
Interventions	Treatments: Two groups of women wrote about their positive (control group) and their negative (disclosure group) experience of pain and their health status assessed at the end of 2 months.
Outcomes	McGill pain questionaire
Notes	Quality score B because of randomisation methodology.
Allocation concealment	B – Unclear
Study	Onwude 2004
Methods	Method of allocation: Sealed opaque envelopes to either patients to see or not to see polariod print taken, randomisation ratio of 1:1 in blocks of 8. Blinded: No Number of centres: 2 Design: RCT Power calculation: Yes. originally designed for sample size of 450, stratefied into 3 groups(normal pelvis, endometriosis and adhesions). As inadequate number of patients recrutied, study stratified into 2 ways (no pathology, pathology present) Number of patients randomised: 286 Number of patients analysed: 286 Intention to treat analysis: yes Exclusion post randomisation: see notes. Losses to follow-up: unclear Source of funding: Birthright
Participants	Country: United kingdom Number of participants: 233 Inclusion criteria: Pelvic pain > 3 months, women undergoing laparoscopy Age: study group 32, control group 33 years. Source of patients: Women undergoing laparoscopy in 2 teaching hospitals Exclusion criteria: none stated
Interventions	Intervention: polaroid print of pelvis taken after surgery and shown to patient post-operatively whilst surgeon explained findings Control: Print not shown to patient whilst surgeon explained findings Duration: not stated
Outcomes	Gynaecological pain questionnaire (Stout et al), McGill pain score, Pain beliefs and perceptions inventory (PBPI)
Notes	Intervention group had a trend for greater pain intensity compared to controls. 233 women were entered into the trial compared to the target of 450, so the final comparisons were somewhat different to those originally planned.
Allocation concealment	A – Adequate
Study	Peters 1991
Methods	Method of allocation: Sealed envelope Outcome assessed blind to allocation. Losses to follow-up: 6 unsuitable for laparoscpy
Participants	Country: Netherlands Participants: 106 Age: 16-58 Sex: F Inclusion criteria:

Characteristics of included studies (Continued)			
	Chronic pelvic pain > 3 months No problem with Dutch No mental retardation Exclusion criteria: No malignancy/disease requiring prompt gynae intervention No history of psychiatric/psychotherapeutic treatment for abdo pain No elaborate medical analysis re abdo pain in past 2 years		
Interventions	Treatments: Integrated Gynae surgery n=5 Drug Rx n=16 Diet/nutritional advice n=22 Physiotherapy n=28 Psychosocial n=43 Ultrasound scans Control: Laparoscopy & psychotherapy Ultrasound scans Duration: 6 months Follow up: 1 year		
Outcomes	General pain experience Disturbance of daily activities Associated symptoms McGill score		
Notes	Quality score A. Standard treatment laparoscopy findings were: n=32 NAD n=4 Endometriosis n=2 ov. cyst n=1 ut. fibroids n=9 adhesions n=1 varicosis pelvi.		
Allocation concealment	A – Adequate		
Study	Peters 1992		
Methods	Allocation: sealed envelope Blinded: no Exclusions post randomisation: none Losses to follow-up: none		
Participants	Country: Netherlands Number of participants: 48 Age: 21-58 Sex: F Inclusion criteria: Pelvic pain > 6 months Speak Dutch to answer questionnaire Adhesions at laparoscopy Exclusion criteria:		

Previous malignant disease

Medical Rx for pelvic pain at first clinic visit

Suspicion of malignant disease on examination

Psychiatric/psychotherapeutic Rx during 2 years preceding study

	Abnormal pelvic examination
Interventions	Treatments: Laparotomy
	Adhesiolysis
	Control: no surgery.
	Duration: 9-12 months follow-up
Outcomes	McGill pain score (Delta)
	Improvement
	Subjective improvement Disturbance of daily activities
Notes	
Notes	Quality score A. Stratification of results - benefit if adhesions were graded IV.
Allocation concealment	A – Adequate
Study	Reginald 1987
Methods	Method of allocation: not stated.
	Single blinded.
	Exclusions post randomisation: 0
	Losses to follow-up: 0.
D .: : .	Unusual study design: see notes.
Participants	Country: England. 6 women with 2 acute exacerbations of pain associated with venous congestion
Interventions	Dihydroergotamine 1 mg in 10 ml saline administered intravenously over 10 minutes, or saline alone.
Outcomes	Visual analogue scales for pain at 4 hrs, 8 hrs, 2,3, 4 and 5 days.
Notes	Data only entered into Data Tables for 4, 8 and 48 hours. Results non-significant at 3 and 5 days but significant at 4 days. Quality score B.
Allocation concealment	C – Inadequate
Study	Soysal 2001
Methods	Method of allocation: computer generated numbered opaque sealed envelopes.
	Blinding: some outcomes assessed double blind, more information awaited from investigators. Patients not
	blind owing to modes of drug administration.
	Exclusions post randomisation: 0
	Losses to follow-up: 0.
Participants	Country: Turkey.
T	47 women with pelvic pain and venographically demonstrated pelvic congestion.
Interventions	Goserelin 3.6 mg subcutaneous implant monthly for six months versus medroxyprogesterone acetate tablets 30 mg daily for six months.
Outcomes	Venography score, pelvic symptom and physical examination score (modified from Biberoglu and Behrman),
	Hospital Anxiety, Depression and Total Scores, Revised Sabbatsberg Sexual Rating Scale.
Notes	Quality score provisionally A, further information on blinding awaited from investigators. Note NO dropouts.
Allocation concealment	A – Adequate
Study	Stones 2001
Study Methods	Stones 2001 Sealed envelope system. Double blinded.

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Characteristics of file	citated stadies (Communa)
	Exclusion post randomisation: 0
	Losses to follow-up:
	10 women in treatment group did not complete the study due mainly to adverse events.
	Intention to treat analysis: Yes
Participants	Country: England.
	Number of participants: 39.
	Age: 25-35
	Sex: F
	Inclusion criteria: pelvic pain > 6 months, laparoscopy identified no pathology Exclusion criteria: Hysterectomised women
Interventions	Treatment: Lofexidine 200 mcg twice daily increasing to 600 mcg twice daily (first 3 weeks).
	Control: Placebo tablets.
	Duration: 8 weeks.
	Follow-up: Until the end of treatment.
Outcomes	Visual analogue scale pain score. Participant's self rating of pain as worst, unchanged, somewhat relieved,
	considerably relieved or completely relieved.
Notes	Note high drop out rate in treatment group (9 out of 14 completed 8 weeks treatment).
Allocation concealment	A – Adequate
Study	Swank 2003
Methods	Method of allocation: computer generated randomisation.
	Double blinded.
	Power calculation: Yes
	Number of patients randomised: 100
	1 lost to follow-up, 3 dropped out.
	Intention to treat analysis: yes
Participants	Country: Netherlands.
	Number of participants: 121
	Age: Study group: 45.4 (S.D. 14.5).
	Control group: 47.8 (S.D. 12.3)
	Sex: 88% F
	Inclusion Criteria: Abdominal pain > 6 months. Diagnostic laparoscopy confirmed presence of adhesions.
	Exclusion criteria: age<18 years, treated by psychiatrists, use of laxatives, sedatives, morphine, anti-psychotics,
	abnormal liver function tests, abnormal CT, ultrasonography, colonoscopy.
Interventions	Treatment: Laparoscopic adhesiolysis.
	Control: Diagnostic laparoscopy only. treatment.
Outcomes	Visual analogue scores at 3, 6 and 12 months, pain change score, use of analgesics and quality of life score.
Notes	Study was on abdominal pain rather than pelvic pain. No mention of exclusion of pathology such as en-
Allogation concealment	dometriosis in female patients, incomplete adhesiolysis in 9 patients.
Allocation concealment	A – Adequate
Study	Walton 1992
Methods	Method of allocation: not stated.
	Blinding not stated.
	Exclusions post randomisation: 0
	Losses to follow-up: 64 % of those taking active drug and 57% of those taking placebo completed the study.
Participants	Country: UK
	Number of participants: 165
	· · ·

	Age: not given. Sex: F Inclusion criteria: Pelvic pain for more than 6 months No pathology on laparoscopy Exclusion criteria: not given.
Interventions	Treatment: Medroxyprogesterone acetate 50 mg daily. Control: Placebo tablets. Duration: 4 months. Follow-up: only until end of treatment.
Outcomes	Visual analogue scale pain score Pain improvement rating: better/ not better.
Notes	Note very high dropout rate in MPA and placebo groups. Published report does not give SD for mean VAS, so data entered in Table are the numbers reporting 50% reduction in VAS at completion of the study. This allowed comparison with Farquhar 1989 as the drug, dose and duration of therapy are the same. Company study report obtained by the reviewers.
Allocation concealment	B – Unclear

Characteristics of excluded studies

Study	Reason for exclusion
Chung 2003	Method of selection of treatment unclear. Further information requested.
Elcombe 1997	Patients entered and evaluated at different time points in control and active groups making comparison between groups difficult.
Hawk 2002	Report as a pilot or feasibility study. Authors reported substantial deviation from study protocols and very inconsistent findings between study centres, which led them not to undertake analysis of outcomes.
Ouhilal 1999	Abstract only with no comparative data. Authors confirmed that the study was abandoned as the preliminary results did not suggest any benefit of LUNA.
Pearce 1986	Abstract only. No data available.

Characteristics of ongoing studies

Study	The LUNA Trial 2003
Trial name or title	The LUNA Trial Collaboration
Participants	Women with pelvic pain
Interventions	Laparoscopic ablation of the uterosacral ligaments
Outcomes	Pain and quality of life measures
Starting date	2003
Contact information	http://www.luna.bham.ac.uk/contact.htm
Notes	Initial analysis expected 2005

ANALYSES

Comparison 01. Progestagen versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome immediately after			Peto Odds Ratio 95% CI	Subtotals only
treatment 02 Outcome post treatment			Odds Ratio (Fixed) 95% CI	Subtotals only

Comparison 02. Progestagen and psychotherapy versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome immediately after			Peto Odds Ratio 95% CI	Totals not selected
treatment 02 Outcome post treatment			Peto Odds Ratio 95% CI	Totals not selected

Comparison 03. Psychotherapy versus placebo/ no treatment

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome immediately after			Peto Odds Ratio 95% CI	Totals not selected
treatment				
02 Outcome post treatment			Peto Odds Ratio 95% CI	Subtotals only

Comparison 04. Ultrasound scan and counselling versus "wait and see"

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in mood score			Peto Odds Ratio 95% CI	Totals not selected
02 Improvement in pain score			Peto Odds Ratio 95% CI	Totals not selected

Comparison 05. Multidisciplinary approach versus standard management

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in pain score			Peto Odds Ratio 95% CI	Totals not selected
02 Self rating: improved			Peto Odds Ratio 95% CI	Totals not selected
03 Daily activity score improved			Peto Odds Ratio 95% CI	Totals not selected
04 Associated (non-pain)			Peto Odds Ratio 95% CI	Totals not selected
symptoms improved				

Comparison 06. Adhesiolysis versus no surgery

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in pain score			Peto Odds Ratio 95% CI	Subtotals only
02 Self rating: improved			Peto Odds Ratio 95% CI	Totals not selected
03 Daily activity score improved			Peto Odds Ratio 95% CI	Totals not selected

Comparison 07. Dihydroergotamine versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome post injection			Other data	No numeric data

Comparison 08. Sertraline versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Change in SF-36 subscale			Other data	No numeric data
02 Change in pain, depression,			Other data	No numeric data
somatization and functional				
status				

Comparison 09. Goserelin versus progestagen

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome one year after			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
treatment				

Comparison 10. Lofexidine hydrochloride versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in pain score			Peto Odds Ratio 95% CI	Totals not selected

Comparison 11. Static magnetic field therapy versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
03 Outcome after 2 weeks			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
04 Outcome after 4 weeks			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 12. Photographic reinforcement after laparoscopy versus standard management

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Outcome at three months			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
02 Outcome at six months			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 13. Written emotional disclosure of negative versus positive aspects of chronic pelvic pain

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Improvement in pain scores			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 14. LUNA versus no LUNA

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 3 months: Greater or equal to 50% reduction in VAS score			Peto Odds Ratio 95% CI	Subtotals only
02 12 months: Greater or equal to 50% reduction in VAS for pain			Peto Odds Ratio 95% CI	Subtotals only

INDEX TERMS

Medical Subject Headings (MeSH)

Chronic Disease; Pelvic Pain [etiology; *therapy]; Randomized Controlled Trials

MeSH check wordsAdult; Female; Humans

COVER SHEET

Title Interventions for treating chronic pelvic pain in women

Authors Stones W, Cheong YC, Howard FM

Contribution of author(s)WS initiated the review, undertook data extraction and drafted the discussion section. YC

undertook data extraction, entered the data and wrote the updated text of the methods and results sections of the review. FH arbitrated on decisions about study inclusion and contributed to the discussion section. All authors have read and approved the final version.

Issue protocol first published 1996/3

Review first published 1998/3

Date of most recent amendment 24 August 2005

Date of most recent SUBSTANTIVE amendment

What's NewThis review was updated in March 2005. Seven new studies included (Brown 2002; Johnson

2004; Norman 2004; Onwude 2004; Soysal 2001; Stones 2001; Swank 2003). Four new studies were identified but excluded (Chung 2003; Elcombe 1997; Hawk 2002; Oulilal

1999).

25 March 2005

Date new studies sought but

none found

Information not supplied by author

Date new studies found but not

yet included/excluded

Information not supplied by author

Date new studies found and

included/excluded

27 July 2000

Date authors' conclusions

section amended

27 July 2000

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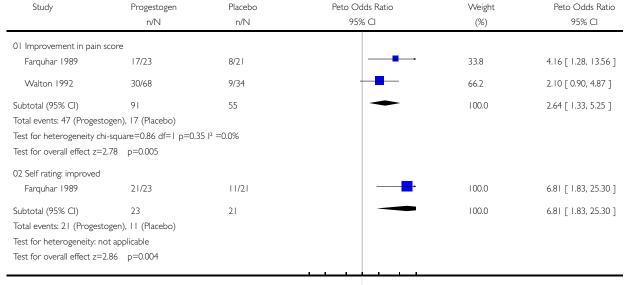
Editorial group code HM-MENSTR

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Comparison: 01 Progestagen versus placebo
Outcome: 01 Outcome immediately after treatment

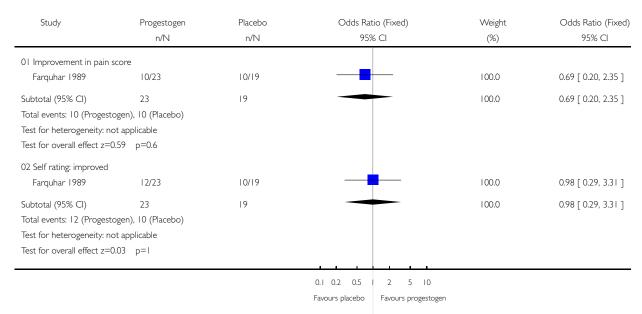


0.1 0.2 0.5 Favours placebo 2 5 10 Favours progestogen

Analysis 01.02. Comparison 01 Progestagen versus placebo, Outcome 02 Outcome post treatment

Review: Interventions for treating chronic pelvic pain in women

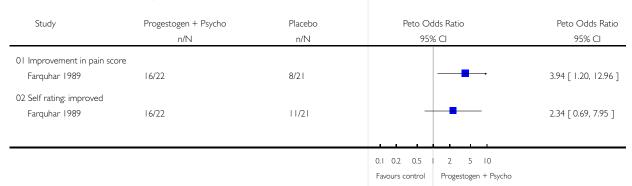
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Analysis 02.01. Comparison 02 Progestagen and psychotherapy versus placebo, Outcome 01 Outcome immediately after treatment

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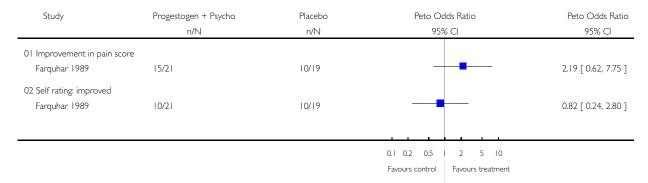
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Analysis 02.02. Comparison 02 Progestagen and psychotherapy versus placebo, Outcome 02 Outcome post treatment

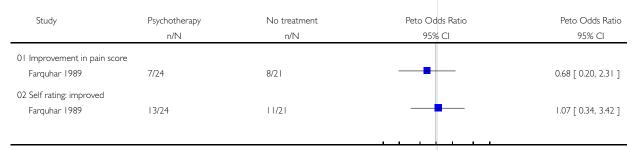
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Review: Interventions for treating chronic pelvic pain in women Comparison: 03 Psychotherapy versus placebo/ no treatment Outcome: 01 Outcome immediately after treatment

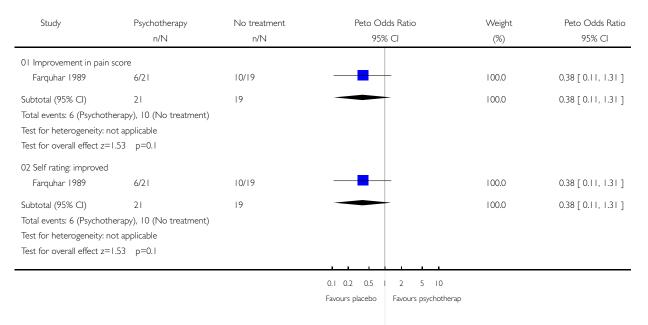


0.1 0.2 0.5 | 2 5 10 Favours placebo | Favours Psychotherap

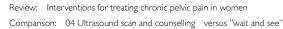
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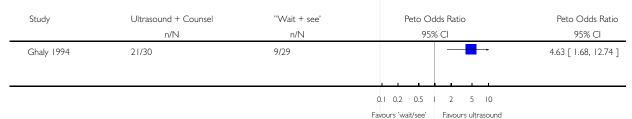
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Analysis 04.01. Comparison 04 Ultrasound scan and counselling versus "wait and see", Outcome 01 Improvement in mood score



Outcome: 01 Improvement in mood score

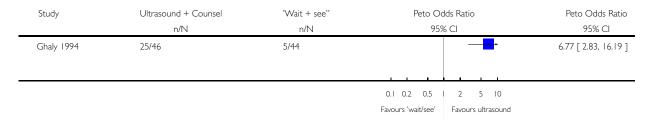


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Review: Interventions for treating chronic pelvic pain in women

Comparison: 04 Ultrasound scan and counselling versus "wait and see"

Outcome: 02 Improvement in pain score

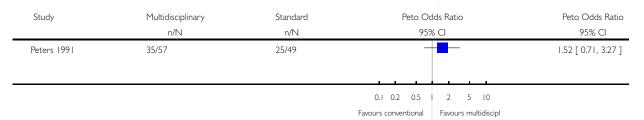


Analysis 05.01. Comparison 05 Multidisciplinary approach versus standard management, Outcome 01 Improvement in pain score

Review: Interventions for treating chronic pelvic pain in women

Comparison: 05 Multidisciplinary approach versus standard management

Outcome: 01 Improvement in pain score

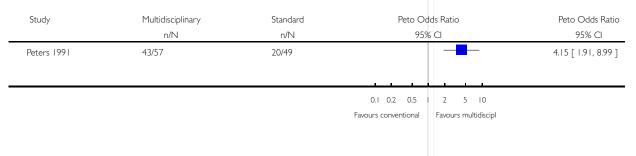


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Comparison: 05 Multidisciplinary approach versus standard management

Outcome: 02 Self rating: improved

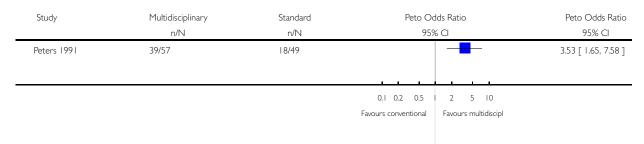


Analysis 05.03. Comparison 05 Multidisciplinary approach versus standard management, Outcome 03 Daily activity score improved

Review: Interventions for treating chronic pelvic pain in women

Comparison: 05 Multidisciplinary approach versus standard management

Outcome: 03 Daily activity score improved

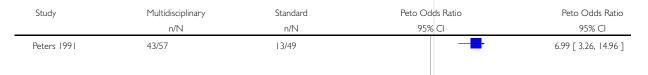


Analysis 05.04. Comparison 05 Multidisciplinary approach versus standard management, Outcome 04 Associated (non-pain) symptoms improved

Review: Interventions for treating chronic pelvic pain in women

Comparison: 05 Multidisciplinary approach versus standard management

Outcome: 04 Associated (non-pain) symptoms improved



0.1 0.2 0.5 | 2 5 10

Favours conventional Favours multidiscipl

Analysis 06.01. Comparison 06 Adhesiolysis versus no surgery, Outcome 01 Improvement in pain score

Review: Interventions for treating chronic pelvic pain in women

Comparison: 06 Adhesiolysis versus no surgery
Outcome: 01 Improvement in pain score

Study	Adhesiolysis n/N	No adhesiolysis n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
01 All patients					
Peters 1992	11/24	10/24	-	32.4	1.18 [0.38, 3.65]
Swank 2003	29/52	20/48	-	67.6	1.75 [0.80, 3.82]
Subtotal (95% CI)	76	72	•	100.0	1.54 [0.81, 2.93]
Total events: 40 (Adhes	iolysis), 30 (No adhesiol	vsis)			
Test for heterogeneity of	chi-square=0.31 df=1 p=	0.57 l ² =0.0%			
Test for overall effect z	=1.32 p=0.2				
02 Severe adhesions					
Peters 1992	8/9	1/6		100.0	16.59 [2.16, 127.20]
Subtotal (95% CI)	9	6		100.0	16.59 [2.16, 127.20]
Total events: 8 (Adhesia	olysis), I (No adhesiolysis	3)			
Test for heterogeneity:	not applicable				
Test for overall effect z	=2.70 p=0.007				
			<u> </u>		
			0.1 0.2 0.5 2 5 10		

0.1 0.2 0.5 | 2 5 10

No adhesiolysis | Favours adhesiolysis

Analysis 06.02. Comparison 06 Adhesiolysis versus no surgery, Outcome 02 Self rating: improved

Review: Interventions for treating chronic pelvic pain in women

Comparison: 06 Adhesiolysis versus no surgery

Outcome: 02 Self rating: improved

Study	Adhesiolysis n/N	No adhesiolysis n/N	Peto Odds Ratio 95% CI	Peto Odds Ratio 95% CI
01 All patients				
Peters 1992	10/24	9/24		1.19 [0.38, 3.73]
02 Severe adhesions				
Peters 1992	8/9	1/6	— 	16.59 [2.16, 127.20]

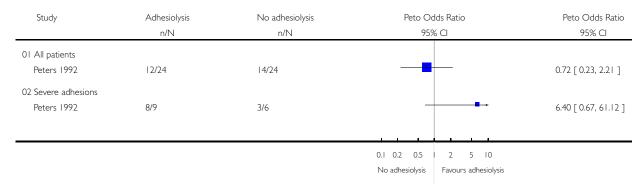
0.1 0.2 0.5 | 2 5 10

No adhesiolysis Favours adhesiolysis

Analysis 06.03. Comparison 06 Adhesiolysis versus no surgery, Outcome 03 Daily activity score improved

Review: Interventions for treating chronic pelvic pain in women

Comparison: 06 Adhesiolysis versus no surgery Outcome: 03 Daily activity score improved



Analysis 07.01. Comparison 07 Dihydroergotamine versus placebo, Outcome 01 Outcome post injection

Outcome post injection

Study

Reginald 1987 Mean difference in pain score (max 10 cm) at 4 hours for the same individual treated with dihydroergotamine on one occasion and placebo on another was 4.6 cm, SD 1.4.

Significance from Wilcoxon test of paired scores: P<0.05

Analysis 08.01. Comparison 08 Sertraline versus placebo, Outcome 01 Change in SF-36 subscale

Change in SF-36 subscale

Study	Health perception	Role emotional	Role functioning	Physical functioning	Social functioning	Mental health	Pain	Vitality
Engel 1998	3 point improvement, 95% CI 0.3 to 0.57	30.4 point decrement, 95%CI -50.3 to -10.6	4.3 decrement, 95% CI -16.4 to 7.7	0.2 point decrement, 95% CI -9.4 to 8.9	0.5 point decrement, 95% CI -5.6 to 4.5	1.6 point decrement, 95% CI -10.4 to 7.2	4.4 point decrement, 95% CI -15.2 to 6.4	1.5 point improve- ment, 95% CI -13.1 to 16.1

Analysis 08.02. Comparison 08 Sertraline versus placebo, Outcome 02 Change in pain, depression, somatization and functional status

Change in pain, depression, somatization and functional status

Study	Pain intensity (CPI)	Depression (HAM-D)	Somatization (SCL-90	Function (SAS-WR)
Engel 1998	0.02 point decrement, 95%	1 point decrement, 95% CI	0.04 point improvement,	0.3 point decrement, 95%
	CI -0.6 to 0.6	-3.5 to 1.5	95% CI -0.2 to 0.3	CI -0.9 to 0.2

Analysis 09.01. Comparison 09 Goserelin versus progestagen, Outcome 01 Outcome one year after treatment

Review: Interventions for treating chronic pelvic pain in women

Comparison: 09 Goserelin versus progestagen
Outcome: 01 Outcome one year after treatment

Study		Goserelin	F	Progestagen	Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	95% CI
01 Improvement in	ı venograph	y score				
Soysal 2001	23	5.30 (0.70)	24	4.20 (0.90)	-	1.10 [0.64, 1.56]
02 Improvement in	pelvic sym	ptom score				
Soysal 2001	23	7.70 (1.80)	24	4.70 (1.40)		3.00 [2.08, 3.92]
03 Improvement in	HADS anx	kiety score				
Soysal 2001	23	2.60 (0.80)	24	1.60 (1.20)	-	1.00 [0.42, 1.58]
04 Improvement in	HADS dep	oression score				
Soysal 2001	23	1.90 (0.90)	24	1.60 (1.30)	+	0.30 [-0.34, 0.94]
05 Improvement in	HADS tot	al score				
Soysal 2001	23	4.60 (1.10)	24	3.30 (1.90)		1.30 [0.42, 2.18]
06 Improvement in	rSSRS scor	re				
Soysal 2001	23	62.50 (5.00)	24	47.00 (7.80)	•	15.50 [11.77, 19.23]
					 	

-4.0 -2.0 0 2.0 4.0

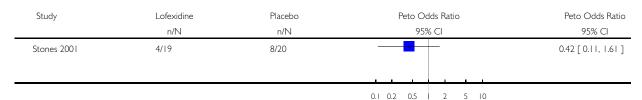
Favours progestagen

Favours goserelin

Analysis 10.01. Comparison 10 Lofexidine hydrochloride versus placebo, Outcome 01 Improvement in pain score

Review: Interventions for treating chronic pelvic pain in women Comparison: 10 Lofexidine hydrochloride versus placebo

Outcome: 01 Improvement in pain score



Favours placebo

Favours Lofexidine

Analysis I I.03. Comparison I I Static magnetic field therapy versus placebo, Outcome 03 Outcome after 2 weeks

Review: Interventions for treating chronic pelvic pain in women Comparison: I I Static magnetic field therapy versus placebo

Outcome: 03 Outcome after 2 weeks

Study	St	atic magnetic		Placebo	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 McGill Pain subsca	ale score	e (Present Pain Inte	nsity, PP	1)			
Brown 2002	15	3.30 (1.40)	17	2.90 (1.40)	=	100.0	0.40 [-0.57, 1.37]
Subtotal (95% CI)	15		17		+	100.0	0.40 [-0.57, 1.37]
Test for heterogeneit	y: not ap	oplicable					
Test for overall effect	z=0.81	p=0.4					
02 Pain Disabilty Inde	ex						
Brown 2002	15	39.80 (17.90)	17	38.80 (18.50)	 	100.0	1.00 [-11.63, 13.63]
Subtotal (95% CI)	15		17			100.0	1.00 [-11.63, 13.63]
Test for heterogeneit	y: not ap	oplicable					
Test for overall effect	z=0.16	p=0.9					
03 Clinical Global Im	pression	Scale scores					
Brown 2002	15	4.20 (1.10)	17	4.10 (0.90)	<u> </u>	100.0	0.10 [-0.60, 0.80]
Subtotal (95% CI)	15		17		+	100.0	0.10 [-0.60, 0.80]
Test for heterogeneit	y: not ap	oplicable					
Test for overall effect	z=0.28	p=0.8					

-10.0 -5.0 0 5.0 10.0 Favours magnet Favours placebo

Analysis I I.04. Comparison I I Static magnetic field therapy versus placebo, Outcome 04 Outcome after 4 weeks

Review: Interventions for treating chronic pelvic pain in women Comparison: II Static magnetic field therapy versus placebo

Outcome: 04 Outcome after 4 weeks

Study	Sta	atic Magnetic		Placebo	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 McGill Pain subsca	ale score	(Present Pain Inte	nsity, PP)			
Brown 2002	8	2.50 (1.60)	11	3.00 (1.50)		100.0	-0.50 [-1.92, 0.92]
Subtotal (95% CI)	8		11		•	100.0	-0.50 [-1.92, 0.92]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=0.69	p=0.5					
02 Pain disabilty inde	×						
Brown 2002	8	23.50 (20.60)	11	40.20 (16.70)		100.0	-16.70 [-34.05, 0.65]
Subtotal (95% CI)	8		П			100.0	-16.70 [-34.05, 0.65]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=1.89	p=0.06					
03 Clinical Global Im	pression	Scale scores					
Brown 2002	8	3.30 (1.50)	П	4.20 (1.20)	-	100.0	-0.90 [-2.16, 0.36]
Subtotal (95% CI)	8		П		•	100.0	-0.90 [-2.16, 0.36]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=1.40	p=0.2					

-10.0 -5.0 0 5.0 10.0 Favours magnet Favours placebo

Analysis 12.01. Comparison 12 Photographic reinforcement after laparoscopy versus standard management, Outcome 01 Outcome at three months

Review: Interventions for treating chronic pelvic pain in women

Comparison: 12 Photographic reinforcement after laparoscopy versus standard management

Outcome: 01 Outcome at three months

Study	Phot	o reinforcement	Stand	ard Management	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 VAS for Pain							
Onwude 2004	58	60.70 (48.00)	60	45.20 (41.60)	 	100.0	15.50 [-0.73, 31.73]
Subtotal (95% CI)	58		60			100.0	15.50 [-0.73, 31.73]
Test for heterogeneit	ty: not ap	oplicable					
Test for overall effect	z=1.87	p=0.06					
02 McGill 'sensory' so	core						
Onwude 2004	66	7.20 (7.30)	70	6.00 (7.00)	-	100.0	1.20 [-1.21, 3.61]
Subtotal (95% CI)	66		70		-	100.0	1.20 [-1.21, 3.61]
Test for heterogeneit	ty: not ap	oplicable					
Test for overall effect	z=0.98	p=0.3					
03 McGill 'affect' sco	re						
Onwude 2004	65	2.00 (3.10)	68	1.50 (2.90)	-	100.0	0.50 [-0.52, 1.52]
Subtotal (95% CI)	65		68		•	100.0	0.50 [-0.52, 1.52]
Test for heterogeneit	ty: not ap	oplicable					
Test for overall effect	z=0.96	p=0.3					
04 McGill 'present pa	ain inten	sity' score					
Onwude 2004	67	2.40 (1.60)	71	1.90 (1.60)	-	100.0	0.50 [-0.03, 1.03]
Subtotal (95% CI)	67		71		•	100.0	0.50 [-0.03, 1.03]
Test for heterogeneit	ty: not ap	oplicable					
Test for overall effect	z=1.83	p=0.07					

-10.0 -5.0 0 5.0 10.0

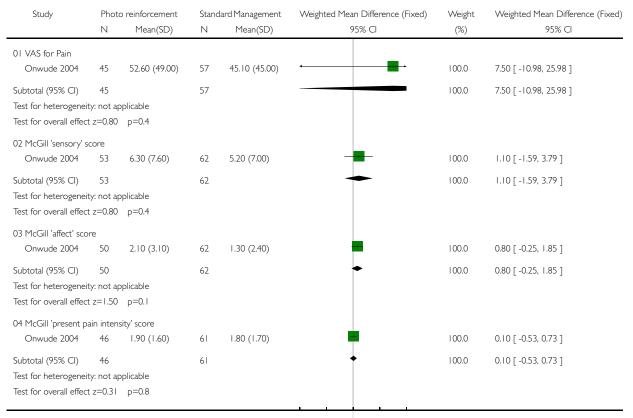
Photo reinforcement Standard management

Analysis 12.02. Comparison 12 Photographic reinforcement after laparoscopy versus standard management, Outcome 02 Outcome at six months

Review: Interventions for treating chronic pelvic pain in women

Comparison: 12 Photographic reinforcement after laparoscopy versus standard management

Outcome: 02 Outcome at six months



-10.0 -5.0 0 5.0 10.0

Photo reinforcement Standard management

Analysis 13.01. Comparison 13 Written emotional disclosure of negative versus positive aspects of chronic pelvic pain, Outcome 01 Improvement in pain scores

Review: Interventions for treating chronic pelvic pain in women

Comparison: 13 Written emotional disclosure of negative versus positive aspects of chronic pelvic pain

Outcome: 01 Improvement in pain scores

Study	Discl	osure negative	Discl	osure positive	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 MPQ sensory pair	า						
Norman 2004	28	-0.10 (0.68)	20	-0.17 (0.64)	•	100.0	0.07 [-0.31, 0.45]
Subtotal (95% CI)	28		20		•	100.0	0.07 [-0.31, 0.45]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=0.36	p=0.7					
02 MPQ affective pair	n						
Norman 2004	28	-0.11 (0.55)	20	0.01 (0.49)	•	100.0	-0.12 [-0.42, 0.18]
Subtotal (95% CI)	28		20		•	100.0	-0.12 [-0.42, 0.18]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=0.79	p=0.4					
03 MPQ evaluation p	ain						
Norman 2004	28	-1.11 (1.77)	20	0.05 (1.05)	-	100.0	-1.16 [-1.96, -0.36]
Subtotal (95% CI)	28		20		•	100.0	-1.16 [-1.96, -0.36]
Test for heterogeneit	y: not ap	plicable					
Test for overall effect	z=2.84	p=0.005					

-10.0 -5.0 0 5.0 10.0 Favours negative Favours positive

Analysis 14.01. Comparison 14 LUNA versus no LUNA, Outcome 01 3 months: Greater or equal to 50% reduction in VAS score

Review: Interventions for treating chronic pelvic pain in women

Comparison: 14 LUNA versus no LUNA

Outcome: 01 3 months: Greater or equal to 50% reduction in VAS score

Study	LUNA	Placebo	Peto Odds Ratio	Weight	Peto Odds Ratio
	n/N	n/N	95% CI	(%)	95% CI
Johnson 2004	10/19	15/32	-	100.0	1.25 [0.41, 3.86]
Subtotal (95% CI)	19	32		100.0	1.25 [0.41, 3.86]
Total events: 10 (LUNA),	15 (Placebo)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	0.39 p=0.7				
			0.1 00 05 10		

Analysis 14.02. Comparison 14 LUNA versus no LUNA, Outcome 02 12 months: Greater or equal to 50% reduction in VAS for pain

Review: Interventions for treating chronic pelvic pain in women

Comparison: 14 LUNA versus no LUNA

Outcome: 02 I2 months: Greater or equal to 50% reduction in VAS for pain

Study	LUNA n/N	Placebo n/N	Peto Odds Ratio 95% Cl	Weight (%)	Peto Odds Ratio 95% CI
Johnson 2004	8/17	13/30	——————————————————————————————————————	100.0	1.16 [0.35, 3.79]
Subtotal (95% CI)	17	30		100.0	1.16 [0.35, 3.79]
Total events: 8 (LUNA),	I 3 (Placebo)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	0.24 p=0.8				

0.1 0.2 0.5 | 2 5 10 Favours placebo Favours LUNA