Effectiveness of embolization or sclerotherapy of pelvic veins for reducing chronic pelvic pain: a systematic review

Daniels, Jane; Champaneria, Rita; Shah, Laila; Gupta, Janesh; Birch, Judy; Middleton, Lee; Moss, Jonathan G

Effectiveness of embolization or sclerotherapy of pelvic veins for reducing chronic pelvic pain: a systematic review

JP Daniels, [1] R Champaneria,[1] L Shah, [1] JK Gupta, [1] J Birch, [2] LJ Middleton, [1] J Moss, [3]

1 University of Birmingham, Birmingham, UK

2 Pelvic Pain Support Network

3 North Glasgow University Hospitals, Glasgow, UK

Corresponding author: Dr JP Daniels, Birmingham Clinical Trials Unit, Institute of Applied Health Research, University of Birmingham, Edgbaston, Birmingham, UK. B15 2TT. Email: j.p.daniels@bham.ac.uk

Short title: Pelvic congestion syndrome treatment review

PROSPERO 2012: CRD42012002238

Protocol available at

http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0004/56092/PRO-11-29-01.pdf

Disclosure of Interests

Jonathan Moss is a member of the NIHR Health Technology Assessment Interventional Procedures Panel, which prioritized the review question for funding. All other authors have no competing interests to declare.

Funding acknowledgement

This project was funded by the National Institute for Health Research Health Technology Assessment programme (project number 11/29/01)

Department of Health Disclaimer: The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Health Technology Assessment programme, NIHR, NHS or the Department of Health.

Abstract

Purpose

Chronic pelvic pain (CPP) in the presence of dilated and refluxing pelvic veins is often described as pelvic congestion syndrome (PCS), although the causal relationship between pelvic vein incompetence and CPP has not been established. Percutaneous embolization is the principal treatment for PCS, with high success rates cited. Our objective was to systematically and critically review the effectiveness of embolization of incompetent pelvic veins.

Materials and Methods

A comprehensive search strategy encompassing various terms for pelvic congestion, pelvic pain and embolization was deployed in 17 bibliographic databases, with no restriction on study design. Methodological quality was assessed. The quality and heterogeneity generally precluded meta-analysis. Results were tabulated and described narratively.

Results

21 prospective case series and one poor quality randomized trial of embolization (involving 1308 women) were identified. Early substantial relief from pain was observed in approximately 75% of women undergoing embolization, which generally increased over time and was sustained. Where pain was measured on a visual analogue scale, statistically significant reductions following treatment were observed in all studies. Re-intervention rates were generally low. There were few data on the impact on menstruation, ovarian reserve or fertility, but no concerns were noted. Transient pain was common following foam embolization, whilst there was a <2% risk of coil migration.

Conclusions

Embolization appears to provide symptomatic relief of chronic pelvic pain in the majority of women and is safe, although the quality of the evidence is low.

Introduction

Pelvic congestion syndrome (PCS) is described as chronic pelvic pain arising from dilated and refluxing incompetent pelvic veins. The diagnosis is based on patient reported symptoms, clinical examination, anatomical features, and venographic findings. There are no generally accepted, well-defined clinical criteria for the diagnosis of PCS, reflecting the residual uncertainty that there is a causal relationship between pelvic vein incompetence (PVI) and chronic pelvic pain (CPP).

Elimination of the blood flow is a recognized strategy for treating incompetent veins. This can be achieved surgically, by ligation of a vein or since the early 1990s, via percutaneous introduction of an embolic agent upstream downstream of the dilated or refluxing veins.(1) Once the incompetent vein is occluded, blood is diverted via other veins, and in time, new vessels can form in the place of the original, although in theory these too could become incompetent. Whether recurrence of symptoms is a result of failure of the original embolization, or due to collateral or recanalized veins diverting the flow to the internal iliac vein (IIV) or elsewhere, , or through untreated or *de novo* varices, is unclear.

The objective of this systematic review of the literature was to assess the effectiveness of percutaneous embolization of incompetent pelvic veins in reducing CPP in women. Secondary objectives were to assess radiological features, impact on fertility and adverse events.

Materials and methods

The systematic review was conducted based on a protocol developed prior to commencing the review and it has also been registered with the PROSPERO database. Ethics approval was not needed as no patients or patient identifiable data were involved.

Search strategy

A comprehensive search strategy was developed. This was used in the following bibliographic databases: Web of Knowledge, British Nursing Index, CINAHL, Cochrane Library, DARE, Embase, MEDION, Medline and Web of Science. The foreign databases, AIM, IMEMR, IMSEAR, LILACS, PAHO, Popline, SciELO and WPRIM held on the World Health Organisation portal were also searched, from database inception to November 2013. Bibliographies of all relevant primary articles and reviews were hand searched to identify articles missed by the electronic searches. No language or study design restrictions were applied in the searching phase.

Search terms for the condition included pelvic pain, pelvic congestion, pelvic or ovarian vein, incompetence or reflux, and variations of these as keywords and text. Search terms for the intervention included treatment, endovascular therapy, interventional radiology, embolization, sclerotherapy, ligation or occlusion, and variations of these as keywords and text. Wild card characters were used to capture alternative spellings and stems of words. The condition and treatments terms were each combined using the "or" term to broaden the search and the two components combined using the "and" function. See *Supplementary Appendix 1*.

Study selection and data extraction

Studies were selected for inclusion in the review in a three-step process (see Figure 1) if they fulfilled the following criteria:

1. Population: Women with a clinical diagnosis of PCS and/or radiological diagnosis of PVI, with or without CPP. No restriction was placed on any previous treatment, age of the participants, duration of symptoms, co-morbidity (including co-presence of endometriosis or other gynecological cause) or severity of the complaint in selection of the studies or on the method of identification of the pelvic varices to be embolized.

2. Interventions: Coil embolization or sclerotherapy of pelvic veins, using any method.
3. Outcomes: Studies reporting subjective assessment of pain or improvement in pain symptoms.
4. Study design: Ideally, only reports of well designed, randomized controlled trials would be included, but preliminary searching indicated that these would be scarce. Primary reports of observational studies were therefore included, but restricted to those where participants were recruited prospectively. Case reports or small series with fewer than 6 participants were excluded. Where it was ambiguous as to whether the data was collected prospectively or retrospectively, a judgement was made based on the timeframe of the follow-up assessments. Where participants were reassessed at particular time-points, it was accepted that they were recruited into the study prospectively. If the duration of follow-up was reported as a wide time frame, it was assumed that participants had been identified retrospectively and the follow-up was a cross-sectional survey, therefore were excluded.

Methodological quality assessment

All studies selected for inclusion were assessed for their methodological quality in duplicate. For any eligible randomized trials, the Cochrane Collaboration risk of bias tool was used.(2) There are no universally accepted quality criteria and reporting standard for case series, as systematic reviews usually tend to exclude studies of this design, and there are no reporting standards. The quality of case series was assessed using criteria adapted from a published checklist.(3),

Data synthesis

Standard meta-analytical methods were used to estimate the overall proportion with a symptomatic improvement following embolization, using the proportions reported in

individual studies under both fixed and random effects assumptions. Plots were generated in MedCalc software (version 14.10.2. Ostend, Belgium). For other outcomes, studies were extracted in duplicate, tabulated and described narratively.

Results

Studies selection for the review

A total of 2858 citations were identified through the electronic bibliographic database searches. Of these 2718 were excluded after reading of titles and abstracts, mainly because they referred to varicose veins of the lower limbs. From 140 citations whose full papers were retrieved, further exclusions were made: seven studies investigated pelvic vein ligation, three studies were considered retrospective but reported on medium to long term outcomes, so were considered for this outcome, (4-6) and two studies, with a total of 37 women, although prospective in design, reported only on technical success and complications.(7, 8) This left 22 studies,(5, 9-29) reporting on 1308 women. A summary of the characteristics of the included studies is given in *Table 1*.

Description of study characteristics

The mean age of the study population was reported in 20 of the studies (5, 9-16, 18-23, 25-29), and ranged between 32 and 51 years,.. Sixteen studies reported the reproductive status of the treated women in some format, (9-12, 14, 18-23, 25-29) usually as the mean parity, which ranged from 0.9 to 3.5. See *Supplementary Table S1*. There was no consistent reporting of any other demographic data e.g. body mass index, history and duration of symptoms.

Bilateral embolization was conducted on 478 women, whilst 384 had only left-sided embolization, six only right-sided embolization, whilst for 440 women it was unclear. The total number of veins embolized and number or proportion of women who had either ovarian or internal iliac vein embolized is indeterminable. One of the larger series of 218 women (23), reported the distribution of the 526 veins treated as 27% right IIV, 23% left IIV, 7% right OV and 32% left OV, but the degree of multiple vein embolization could not be extracted from the study report.

Embolization of pelvic veins was achieved using a sclerosant in 229 women, by use of metal coils (stainless steel or platinum) in 660 women and a combination of both in 405, with the method unclear in the remaining 13 women. The sclerosant used varied considerably and included 1-3% sodium tetradecyl sulphate, (12, 15, 22, 24) 2-3% aetoxisclerol (17, 20, 25, 27) or enbucrilate.(9, 28) There was no apparent trend towards or away from using either technique, either over time or between countries.

Quality assessment

There were 20 case series included in the review, see *Supplementary Tables, Table S2* with one further study being unable to be reliably assessed due to uncertainty after translation.(24) Whilst the aims and embolization techniques were clearly stated, a third did not clearly describe the intended outcome measures and how they were to be collected. Although we sought only prospective trials, it was still not clear in 40% that consecutive patients were included: this was reinforced by poor descriptions of the criteria with which women were referred for venography and inadequate reporting of losses to follow-up.

The sole randomized trial was likely to be subject to selection, performance, measurement and attrition biases and was deemed of low internal validity.

Symptomatic Improvement

Subjective symptom relief was reported on ordinal scales of complete, moderate/ partial or no relief of CPP symptoms in six studies.(9-12, 24, 28) Early reporting of complete symptom relief, less than two months, ranged from 33% (24) to 80% (12) of study participants.)Pooling rates of complete, excellent or moderate improvement from these studies gave an overall improvement rate of 75% (95%CI 64 to 85%, I^2 statistic 42%) at 4-8 weeks post-procedure. See Figure 2.

Few studies reported symptoms at two time-points. Van der Vleuten *et al* assessed all women twice and found 67% of women had moderate or obvious improvement at two months post-operatively, which increased to 76% at an average of 18 months (+/- 12 months) later.(10) Other studies report 85% of women had some symptom improvement at 6 months (17, 25), which again increased to 95% after 12 months in the smaller study (Tropeano *et al*). At an average of 45 months of follow-up, relief rates of over 80%

were reported by two studies (16, 21) but sustained relief in only 47% in a third study.(26)

Studies reported treatment failures either as residual symptoms, unsatisfactory improvement or as the number of repeat embolizations performed. In a larger study, 22 of 193 of women (11%) had mild or moderate residual symptoms at 6 weeks (23), whilst another reported only 2.2% found their improvement unsatisfactory.(24) Re-intervention by 3-6 months due to unresolved symptoms was reported in 5.7% of women by D'Archambeau *et al* (5), lower than the 15% at 3 months cited by Tropeano *et al*.(25)

No study reported quality of life using a generic instrument. Chung and Huh *et al* deployed a social readjustment rating scale (30) to compare stress between women who had embolization or hysterectomy but found no significant differences.(14)

Pain Scores

Nine studies report on pelvic pain scores from 0-10cm visual analogue scales, although at varying time-points after embolization.(13, 14, 16, 18, 19, 22, 25, 26, 29) In all cases, the pain score reduces significantly from a baseline and were generally sustained in those trials. See Figure 3.

Five studies undertook paired t-tests of pain scores before and after embolization and reported the reductions as being statistically significant, with sufficient data that this could be verified by the reviewers.(16, 18, 22, 26, 29) There were insufficient studies with all necessary data to perform a meta-analysis. See *Supplementary Tables, Table S3*.

Several studies reported on different pain symptoms. Kim *et al* noted statistically significant score reductions in pain on standing, lying down, dyspareunia and dysmenorrhea, as well as the amount of pain relief required, (16) whilst Venbrux *et al* also observed similar reductions in all symptoms except dysmenorrhea.(13) Gandini *et al* reported statistically significant reductions in dyspareunia and dysmenorrhea (22); Creton *et al* also considered pain at the site of pelvic varices occurring specifically before or during menstruation, which decreased from a mean of 6.0 to 1.7 at 45 days post embolization and remained low.(19) Van der Vleuten *et al* reported on the widest

range of symptoms, observing statistically significant improvements in scores at 2 months and an average of 18 months (SD 12 months) for dysmenorrhea, dyspareunia, worsening of symptoms with walking, standing or sitting, varicose veins and pain in varicose veins.(28)

Impact on pelvic vein reflux and diameter.

Only two studies quantified the diameter of the pelvic veins before and after the procedure. One study measured the mean diameter of varices in supine patients, decreasing from 6.3 mm to 4.4mm and 4.5mm to 3.1mm for the left and right OV respectively, both statistically significant reductions.(15) In another study, left and right OV diameters reduced from a mean of 6.9mm (SD 2.1) and 5.1mm (SD1.4) to less than 4.5mm on both sides in all cases.(27) Pieri *et al* noted that symptoms persisted in women in whom, although their OV varicosities decreased in diameter from pre-procedure measurements, remained over 5mm at rest.(15)

Ratnam *et al* was able to perform a repeat transvaginal ultrasound (TVUS) at 6-8 weeks in 193 patients, observing residual mild reflux in 16 (8.3%).(23) Nine women had a second procedure dictated by the ultrasound: six patients due to moderate persistent reflux and three because of new reflux. Tropeano *et al* also repeated the TVUS at 3, 6 and 12 months and observed an absence of reflux and reduced (<5mm) pelvic vein diameter in 17 of 20 (85%) women.(25) The remaining 3 women who showed recurrence or persistent left sided reflux, were also those who did not report a symptomatic improvement, and had a successful repeat procedure performed at 4-5 months and were reported as symptom free after a median follow-up of 15 months.

Impact on future fertility, menstruation and ovarian reserve

Venbrux *et al* captured information on menstruation between 6 and 24 hours post-procedure, in 24 of 56 participants, finding no significant difference in the interval or length of menstruation compared to before the embolization.(13) Kim *et al* measured follicular stimulating hormone, estradiol, and luteinizing hormone at baseline, six and 12 months and reported no statistically significant differences before and after the procedure.(16)

No study explicitly included or excluded women based on their desire for a future pregnancy, nor specifically mentioned active follow-up of future pregnancies. Therefore, reports of pregnancies are likely not to have been systematically collected. Three studies report six successful pregnancies.(9, 13, 16)

Adverse events of embolization

Six studies did not report any adverse events in their population, although it is not clear whether this equates to technical success in all cases. Of the remaining 938 women, in total there were 10 cases of vein perforation causing extra-vascular leakage of contrast media during the insertion of coils. Transient pain following the embolization was reported in between 8% and 100% of cases and only appeared to occur in the studies using sclerotherapy, with or without coils. One large study of 239 women described early adverse symptoms as a "post-embolization syndrome", reporting that 129 (54%) had transient gluteal or lumbar pain, 61 (26%) general achiness, 30 (12%) transient fever (≥38°C) and 21 (9%) had mechanical superficial phlebitis at the point of venous access in the arm.

Coil migration after placement was reported in 11 cases, being displaced to the lung in eight cases, the renal vein in two cases and one report of coil protrusion into the femoral vein. In all cases, the coil was retrieved by a catheterized snare without any lasting harm to the woman.

Discussion

This systematic review of embolization for PVI found no high quality studies, so all estimates of effectiveness are derived from presumed prospective case series reporting on 1308 women, the majority of whom were of reproductive age and parous.

Early substantial relief from pain symptoms was observed in approximately 75% of 162 women in six case series, which generally increased over time and was sustained. Where pain was measured on a visual analogue scale, statistically significant reductions following treatment were observed in all studies. Re-intervention rates were generally low. Where measured, embolization reduced the diameter of dilated veins to a significant degree, with minimal residual reflux.

There was little data on menstruation, ovarian reserve or fertility, but no concerns were noted. Transient pain was a common occurrence following foam embolization, whilst there was a <2% risk of coil migration.

The review followed a registered protocol and focused on a clear question for the assessment of effectiveness. The comprehensive search strategy is the broadest ever applied in a review of PCS. All outcomes identified *a priori* were reported upon to the extent that data were available. The embolic techniques employed were generally well described and follow-up data was available for the majority of participants.

The most significant limitation, which prevents firm conclusions being drawn from the data and recommendations being made, is the quality of the studies identified. There is only one randomized controlled trial of embolization in the literature, with hysterectomy as a comparison, which was in itself not free of potential biases. The majority of the studies were relatively small case series, with the inherent high risk of bias, with no comparative group and frequently ill-defined inclusion criteria. In comparison to other reviews in this area, we attempted to restrict the studies included to those where participants were prospectively enrolled, in order to reduce selection bias, unlike other reviews.(31). However, in some studies it was impossible to be completely certain, from the methodology used, that included participants were not retrospectively identified from medical records.

The effect of embolization on pain was generally described either in terms of symptomatic improvement or as pain scores, reducing the amount of information available for either outcome. We cannot be certain these outcomes were not collected across all studies but not reported if they failed to show statistical significance or consistent results. We performed a meta-analysis to get a pooled estimate of improvement rates, but may be criticized for doing so using such low quality data. Few studies sought pain data on individual pain symptoms, such as dyspareunia or pain on standing, preventing reflection on whether embolization reduces specific symptoms thought to be particularly indicative of pelvic vein congestion.

The pooled estimate of moderate to complete symptomatic improvement following embolization is consistent with previous limited reviews, as are the rates of coil

migration, although these too draw upon low quality case series. (31, 32) Technical success is high, although dependent on pelvic anatomy, and has been widely adopted around the world. Few studies addressed the impact on menstruation and fertility. This contrasts starkly with uterine artery embolization for the uterine fibroids, where there is considerable debate regarding the impact on ovarian function and pregnancy rates.(33, 34)

Whilst the data appears supportive, the quality of evidence is poor. Under the GRADE criteria, the methodological quality is very low and there is no direct comparative evidence against no embolization.(35) Some reflection on the only randomized controlled trial is warranted. The study population excluded those whose pain could be attributable to organic pathology or who responded to medroxyprogesterone, and who did not wish to retain their uterus and ovaries. The 118 patients were randomized to either embolization or hysterectomy with bilateral oophorectomy, plus hormone replacement therapy, or hysterectomy with unilateral oophorectomy, on the predominantly congested side.(14) The study reported that the embolization group and the hysterectomy with bilateral oophorectomy group had statistically significant improvement in pain reported on a visual analogues scale at 3, 6 and 12 months, whereas those with only unilateral oophorectomy did not, but these assertions have not be replicated. Furthermore, the method of randomization was unclear and there were substantial post-randomization exclusions, which undermine the credibility of the trial results.

We were unable to investigate heterogeneity of results across studies other than for the outcome of moderate to complete symptomatic improvement, reported in 6 studies, where moderate heterogeneity was identified. This could arise from the embolization technique, the way in which the question of improvement was presented and categorized or from the population included in the study.

The precision of the estimates for this outcome is moderate, due to the relatively small number of studies and participants per study, with a confidence interval of ±10% around the pooled rate of substantial symptomatic improvement of 75% in the short term. This would probably encompass a range of response rates that would be acceptable to women, given the low incidence of adverse events. However, we cannot be certain that

publication bias does not exist and that this results is not an overestimation of the true effect.

If we can accept that embolization provides pain relief, despite the limitations of the literature, the next questions are whether particular presenting characteristics can predict a successful outcome, and what the optimal technique is. A retrospective case series of 41 women access the relationship between technique (bilateral or unilateral), parity and location of varices (thigh or labial compared to pelvic) and clinical outcome. There was no statistically significant predictor of a successful outcome amongst these variables, although a trend towards a higher rate of success in grand multiparous women was noted. No association between these variables and treatment failure was observed, but in both circumstances, it may just be that there are too few women to observe a small association.(4)

No apparent trend for either metal coils or sclerosant has emerged. Stratification of the meta-analysis of symptomatic improvement by method is limited by the amount of data but seems to suggest the overall rate of substantial improvement is reflective of the studies using sclerosant at about 75%, whereas the two studies using solely coils had higher rates, at 89% and 100% respectively.(10, 11) No obvious differences between methods on the reduction in pain scores were seen. It may indeed be that the presentation of the varices and anatomy of the veins are the key determinants of successful elimination of reflux, with perhaps both methods being requiring for the most dilated veins.

Complications of embolization appear to be limited to short-term pain and fever in a reasonable proportion of sclerosant cases, or an uncommon incidence of coil migration. Coil placement is a relatively straightforward procedure but may be subject to recanalization or development of collaterals, as has been observed in male varicocele.(36) Some radiologists prefer liquid sclerosants the perception being that a more extensive embolus is produced, and also due to their cost compared with metal coils.(4)

Women should be counselled that the embolization, whilst apparently safe, may not provide complete relief of symptoms. There is scope for considerable further research

into the condition known as pelvic congestion syndrome, and in particular, an adequately powered randomized trial is essential to provide the necessary data on the effectiveness of embolization, but faces methodological challenges.

References

1. Edwards RD, Robertson IR, MacLean AB, Hemingway AP. Pelvic pain syndrome - Successful treatment of a case by ovarian vein embolization. Clin Radiol. 1993;47(6):429-31.

2. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration, 2011.

3. Moga C, Guo B, Schopflocher D, Harstall C. Development of a quality appraisal tool for case series studies uisng a modified delphi technique. 2012.

4. Maleux G, Stockx L, Wilms G, Marchal G. Ovarian vein embolization for the treatment of pelvic congestion syndrome: long term technical and clinical results. J Vasc Interv Radiol. 2000;11(7):859-64.

5. D'Archambeau O, Voormolen M, Frangois O, De Schepper A, Parizel P. Is bilateral ovarian vein embolization necessary and is coil embolization alone sufficient for the treatment of pelvic varicosities? J Vasc Interv Radiol. 2010;21(5):May.

6. Laborda A, Medrano J, de Blas I, Urtiaga I, Carnevale FC, MA DG. Endovascular Treatment of Pelvic Congestion Syndrome: Visual Analog Scale (VAS) Long-Term Follow-up Clinical Evaluation in 202 Patients. Cardiovasc Intervent Radiol 2013;36(4):1006-14.

7. Garrett JP, Wetton CWN, Tyrrell MR. Ovarian vein embolisation as an adjunct in the treatment of vulval and atypical leg varicosities. Phlebology. 2002;17(1):3-9.

8. Ashour MA, Soliman HET, Khougeer GA. Role of descending venography and endovenous embolization in treatment of females with lower extremity varicose veins, vulvar and posterior thigh varices. Saudi Med J. 2007;28(2):206-12.

9. Capasso P, Simons C, Trotteur G, Dondelinger RF, Henroteaux D, Gaspard U. Treatment of symptomatic pelvic varices by ovarian vein embolization. Cardiovasc Intervent Radiol 1997;20(2):107-11.

10. Tarazov PG, Prozorovskij KV, Ryzhkov VK. Pelvic pain syndrome caused by ovarian varices. Treatment by transcatheter embolization. Acta Radiol 1997;38(6):1023-5.

11. Cordts PR, Eclavea A, Buckley PJ, DeMaioribus CA, Cockerill ML, Yeager TD. Pelvic congestion syndrome: Early clinical results after transcatheter ovarian vein embolization. J Vasc Surg 1998;28(5):862-8.

12. Scultetus AH, Villavicencio JL, Gillespie DL, Kao TC, Rich NM. The pelvic venous syndromes: Analysis of our experience with 57 patients. J Vasc Surg 2002;36(5):881-8.

13. Venbrux AC, Chang AH, Kim HS, Montague BJ, Hebert JB, Arepally A, et al. Pelvic congestion syndrome (pelvic venous incompetence): Impact of ovarian and internal iliac vein Embolotherapy on menstrual cycle and chronic pelvic pain. J Vasc Interv Radiol. 2002;13(2):171-8.

14. Chung MH, Huh CY. Comparison of treatments for pelvic congestion syndrome. Tohoku J Exp Med 2003;201(3):131-8.

15. Pieri S, Agresti P, Morucci M, de Medici L. Percutaneous treatment of pelvic congestion syndrome. Radiol Med 2003;105(1-2):76-82.

16. Kim HS, Malhotra AD, Rowe PC, Lee JM, Venbrux AC. Embolotherapy for pelvic congestion syndrome: Long-term results. J Vasc Interv Radiol. 2006;17(2):289-97.

17. Leal Monedero J, Zubicoa Ezpeleta S, Castro Castro J, Calderon Ortiz M, Sellers Fernandez G. Embolization treatment of recurrent varices of pelvic origin. Phlebology. 2006;21(1):3-11.

18. Richardson GD, Driver B. Ovarian vein ablation: coils or surgery? Phlebology. 2006;21(1):16-23.

19. Creton D, Hennequin L, Kohler F, Allaert FA. Embolisation of symptomatic pelvic veins in women presenting with non-saphenous varicose veins of pelvic origin - three-year follow-up. Eur J Vasc Endovasc Surg 2007;34(1):112-7.

20. Greiner M, Gilling-Smith GL. Leg varices originating from the pelvis: Diagnosis and treatment. Vascular. 2007;15(2):70-8.

21. Kwon SH, Oh JH, Ko KR, Park HC, Huh JY. Transcatheter ovarian vein embolization using coils for the treatment of pelvic congestion syndrome. Cardiovasc Intervent Radiol 2007;30(4):655-61.

22. Gandini R, Chiocchi M, Konda D, Pampana E, Fabiano S, Simonetti G. Transcatheter foam sclerotherapy of symptomatic female varicocele with sodium-tetradecyl-sulfate foam. Cardiovasc Intervent Radiol 2008;31(4):778-84.

23. Ratnam L, Marsh P, Holdstock J, Harrison C, Hussain F, Whiteley M, et al. Pelvic Vein Embolisation in the Management of Varicose Veins. Cardiovasc Intervent Radiol 2008;31(6):1159-64.

24. Sukovatykh BS, Rodionov OA, Sukovatykh MB, Khodykin SP. Diagnosis and treatment of atypical forms of varicose disease of pelvic veins. [Russian]. Vestn Khir Im I I Grek 2008;167(3):43-5.

25. Tropeano G, Di Stasi C, Amoroso S, Cina A, Scambia G. Ovarian vein incompetence: a potential cause of chronic pelvic pain in women. Eur J Obstet Gynecol Reprod Biol 2008;139(2):215-21.

26. Asciutto G, Asciutto KC, A M, Geier B. Pelvic venous incompetence: reflux patterns and treatment results. Eur J Vasc Endovasc Surg 2009;38(3):381-6.

27. Tinelli A, Prudenzano R, Torsello M, Malvasi A, De Nunzio G, De Mitri I, et al. Suprapubic percutaneous sclero-embolization of symptomatic female pelvic varicocele under local anesthesia. Eur Rev Med Pharmacol Sci 2012;16(1):111-7.

28. Van Der Vleuten CJM, Van Kempen JAL, Schultze-Kool LJ. Embolization to treat pelvic congestion syndrome and vulval varicose veins. Int J Gynaecol Obstet 2012;118(3):227-30.

29. Meneses L, Fava M, Diaz P, Andia M, Tejos C, Irarrazabal P, et al. Embolization of Incompetent Pelvic Veins for the Treatment of Recurrent Varicose Veins in Lower Limbs and Pelvic Congestion Syndrome. Cardiovasc Intervent Radiol 2013;36(1):128-32.

30. Hobson CJ, Kamen J, Szostek J, Nethercut CM, Tiedmann JW, Wojnarowicz S. Stressful life events: A revision and update of the Social Readjustment Rating Scale. International Journal of Stress Management. 1988;5:1-23.

31. . Hansrani V, Abbas A, Bhandari S, Caress AL, Seif M, McCollum CN.Trans-venous occlusion of incompetent pelvic veins for chronic pelvic pain in women: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2015;185:156-63

32. Tu FF, Hahn D, Steege JF. Pelvic congestion syndrome - associated pelvic pain: a systematic review of diagnosis and management. Obstet Gynecol Surv 2010;65(5):322-40.

33. Torre A, Paillusson B, Fain V, Labauge P, Pelage JP, Fauconnier A. Uterine artery embolization for severe symptomatic fibroids: effects on fertility and symptoms. Hum Reprod 2014;29(3):490-501.

34. Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, O S. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. Cardiovasc Intervent Radiol 2008;31(1):73-85.

35. Atkins D, Eccles M, Flottorp S, Guyatt GH, Henry D, Hill S, et al. Systems for grading the quality of evidence and the strength of recommendations I: Critical

appraisal of existing approaches The GRADE Working Group. BMC Health Serv Res. 2004;4(1):38.

36. Goffette P, Hammer F, Mathurin P, Wese FX, RJ O, De Cooman S, et al. Recurrence of varicocele after spermatic vein embolization in young patients: radiological aspects. Acta Urol Belg 1995;63:55-6.

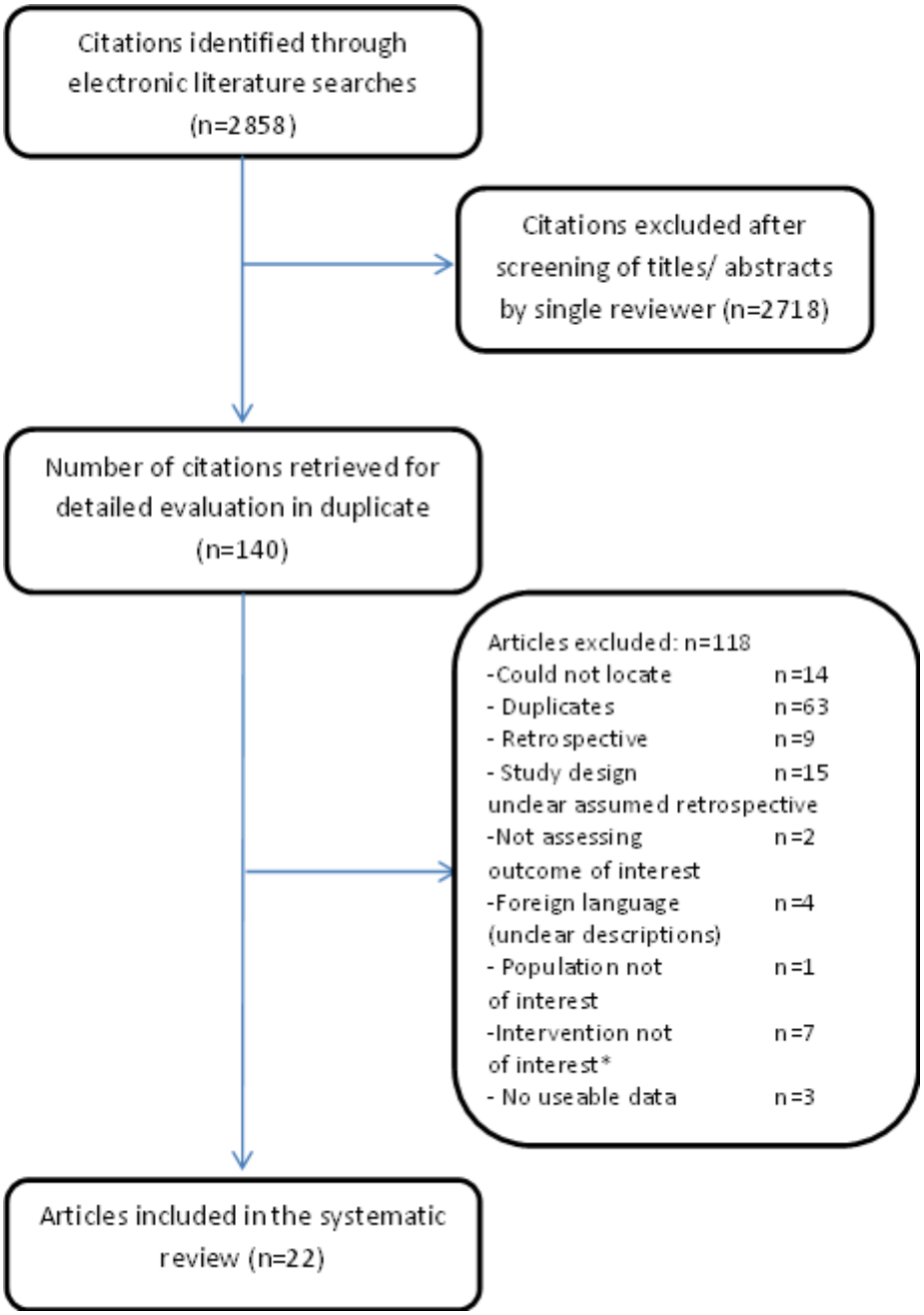

Figure 1: Flow diagram showing the study selection process for the systematic review of embolization and sclerotherapy for reducing chronic pelvic pain

Footnote:

* Seven studies of OV ligation were identified in an initial scoping search. We made a decision after registration on the PROSPERO database to exclude studies of ligation from this review, as it is rarely performed in current practice now that the technically less demanding and lower risk option of percutaneous vein embolization is widely available.

Table 1 Characteristics and key outcomes of studies selected for inclusion in systematic review of effectiveness of embolization of pelvic vein incompetence

Author, date, country	**Number**	**Treatment**	**Study type**	**Outcomes, follow up period**	**Key results**
Capasso 1997 Belgium	19	OV vein glue, coil or combined embolization	Prospective observational study	Subjective assessment of pain relief within 4 weeks. Trans-abdominal Doppler ultrasound at 5 weeks. Average 15 month follow up for recurrence.	Early outcomes: 74% had improvements in pain symptoms (complete relief in 58%, partial in 16%). Improvement correlated with ultrasonographical evidence of complete thrombosis of varices. Dyspareunia (n=5) persisted. N=5 with persistent pain had re-intervention. 2 venous perforations that resolved.
Tarazov 1997 Russia	6	OV coil embolization.	Not stated	Subjective reporting of symptom Improvement, follow-up duration 1-4	Complete alleviation of CPP in all women within 4 weeks. Improved menstrual symptoms I 2 women with dysmenorrhea. No serious complications.

				years.	
Cordts 1998 USA	9	OV coil embolization.	Consecutive case series	Numerical rating scale of symptom relief, mean follow-up 13 months	8 women (88.9%) had >80% immediate symptom relief. Two women had a mild or moderate return of the symptoms at 6 and 22 months respectively. One lower lobe coil pulmonary embolus.
Scultetus 2002 USA	15 (treated with sclerotherapy)	Sclerotherapy of varices alone or with excision of varices.	Prospective observation study	VAS of improvement. Mean follow-up 2.3 years.	12 had excellent improvement, 3 had moderate improvement. No deep vein thrombosis reported.
Venbrux 2002 USA	56	OV and subsequent IIV coil embolization	Prospective observational study	VAS for pain, menstrual cycle questionnaire at 3, 6 and 12 months post procedure.	Mean pain 7.8 at baseline decreased to 4.2 at 3-months, 3.8 at 6 months, 2.7 at 12 months ($p<0.001$ for all comparisons). No significant changes in cycle length.

Chung 2003 South Korea	106, of whom 52 treated with emboliz ation	OV or IIV coil embolization, Hysterectomy with uni or bilateral oophorectomy	Randomized control trial	VAS at 3, 6, and 12 months post-procedure, patient global impression of change.	Statistically significant decrease from baseline and between embolization and hysterectomy groups at all time-points.
Pieri 2003 Italy	33	OV foam sclerotherapy	Prospective observational study	Subjective rating of various pain symptoms at 1 month. Clinical assessment and mean venous diameter by ultrasound at 6 months.	Improvement in pain in 61%. Mean OV diameter at baseline right 4.5mm and left 6.3mm reduced to 3.10 and 4.4mm respectively at follow-up. Seven patients had transient flank pain.
Kim	127	OV	Retrospectivel	Visual analogue scale	Mean pelvic pain at baseline 7.6 (SD 1.8) and 2.9

2006 USA		coil/sclerosant embolization, +/- subsequent IIV sclerosant embolization	y identified women followed-up prospectively.	and composite clinical assessment at 3 and 6 months and annually thereafter.	(SD 2.8) ($p < 0.0001$) and 80% had significant improvement at mean 45 months follow-up. All pain symptoms significantly improved. Two coil migrations.
Leal Monedero 2006 Spain	239	Coil embolization +/- foam, of OV or IIV	Observational study	Clinical assessment at 6 months post-procedure.	Complete resolution of pain symptoms in 120/ 239 (50.2%) and partial relief in 95/239 (36.8%). Superficial phlebitis at point of venous access in 21 women. No coil migrations.
Richardson 2006 Australia	26	OV coil embolization, +/- foam.	Prospective case series, with historical control group undergoing	Visual analogue scale for pain symptoms and patient overall satisfaction. Mean follow-up 22±13	No significant difference between groups in demographics and presenting symptoms. Coil group pain score statistically significantly reduced from 6.6 (SD 1.9) to 4.0 (SD 2.8), from baseline. No statistically significant difference in pain reduction

			OV ligation.	months.	between ligation and embolization groups nor in overall satisfaction. No coil migration within 6 weeks, one coil perforation detected at 5 months.
Creton 2007 France	24	OV or IIV coil embolization	Prospective observational study	VAS for dysmenorrhea, dyspareunia and venous pain (individually and total); clinical assessment at 45 days and 1,2 and 3 years follow up	Statistically significant decreases in all three pain symptoms and improvements in clinical assessment maintained. One coil migration.
Greiner 2007 France	13 (of 24 embolized)	Coil or glue or combined embolization of OV and IIV.	Observational study (assumed prospective)	Repeat TVUS at 1 and 6 months, 1 and 4 years. Repeat clinical assessment and venography at 4 years.	Complete resolution of symptoms in 10/13 and significant improvement in 3/13. No recurrence of PVI.

Kwon 2007 South Korea	67	OV coil embolization	Prospective study of outcome with baseline pain determined by telephone interview or medical note review	Categorical pain severity scale. Mean follow up 45 months	82% reported total or significant pain reduction. Two coil migrations.
Gandini 2008 Italy	38	OV foam sclerotherapy	Described as retrospective but included all patients at 3 defined time-points	VAS for 4 pain symptoms at 1, 3, 6 and 12 months follow up	Mean VAS for CPP showed decrease from 7.8 (SD 1.8) to 2.7(SD 2.8), from 4.9(SD 4.2) to 2.2(3.1) for menstrual pain, from 3.3(SD 3.7) to 1.5(SD 2.7) for dyspareunia and 3.5(SD 3.9) to 1.5(SD 3.0) for urinary urgency at 12 months, all statistically significant.

Ratnam 2008 UK	218	Coil embolization of OV and IIV	Prospective inclusion, retrospective data extraction from medical notes.	Repeat TVUS at 6-8 weeks	Of 193 with follow-up, 16 had residual mild reflux, 6 had marked reflux and 3 had new reflux. Two coil migrations, one misplacement, one case of perineal thrombophlebitis.
Sukovatykh 2008 Russia	59	Sclerotherapy	Not stated	Clinical examination, USS and self-reported quality of life	Improvements (not defined) were classified as excellent in 32.6%, good in 46.1%, satisfactory in 19.1% and unsatisfactory in 2.2% of the patients.
Tropeano 2008 Italy	20	Sclerotherapy of the OV	Prospective observational study	VAS for pain, menstrual cycle questionnaire and ultrasound at 3, 6 and 12 months post procedure.	Three women had repeat embolization after 3 months due to no change in symptoms and residual PVI on ultrasound. 17 (85%) achieved marked to complete relief until 6 months, with 2 describing a reduction in relief by 12 months,

					Median VAS pain scores decreased from at 8.0 (range 6.0 to 10.0) at baseline to 2.0 (1.0 – 5.0), 2.5 (1.5 - 5.0), and 3.0 (2.0 – 6.0) at 3, 6 and 12 months respectively, all statistical significantly reductions (p<.001).
Asciutto 2009 Germany	35 (26 also had concurrent VV surgery)	OV, IIV or both with coil embolization	Prospective observational study	VAS of pain at 1,2,3 years of follow up	VAS scores for isolated OVI: baseline mean 5.2 (SD 3.5) and 1.2 (SD 0.9) at 3 years; p<0.0001, non-statistically significant reduction for combined OVI and IIV or isolated IIV alone. At mean follow-up 45 months, overall 47% had sustained improvement. 3 venous perforations that resolved.
D'Archambeau 2010 Belgium	193 (130 had PVI)	Coil embolization of OV	Prospective observational study	Symptom rating on VAS before procedure and at 1 year.	11 (5.7%) were re-embolized between 3 months and 6 years. 91/102 (89.2%) patients with PCS symptoms reported improvement in symptoms on VAS.

Tinelli 2012 Italy	28	OV foam sclerotherapy	Not stated but follow-up at specific time-points.	VAS for pain, clinical examination and USS at 10 days, 1 and 6 months post procedure.	At 1 month, 6 (21%) reported PVI symptoms, which resolved by 6 months. Reduction in varicosity size from 6.9mm (SD 2.1mm) on left and 5.1mm (SD1.4mm) on right to <4.5mm in all embolized veins. 100% technical success with no adverse events beyond minor analgesics needs in 6 (21%) patients.
van der Vleuten 2012 Netherlands	21 who responded follow-up survey	Sclerotherapy of OV.	Prospective observational study	5 point ordinal scale of 8 pain symptoms and pelvic varices and hemorrhoids, and global impression of change.	14 (66.7%) and 16 (76.2%) women had moderate or obvious improvement or no symptoms, at 2 months and cross sectional follow-up at mean 18 ±122 months survey, respectively. All pain symptoms except backache or urinary symptoms showed statistically significant improvements. Nine (42.9%) women had a second embolization.
Meneses	10	Combined OV	Prospective	Venous clinical severity	Significant decrease in pain from 8.2 at baseline to

2013 Chile		and/or IIV embolization, using sclerosant and coil.	observational study	score (VCSS) and VAS for pain at 3 months follow-up.	4.0 at 3 months ($p<0.001$). Significant decrease in VVCS from 8.4 at baseline to 3.6 at 3 months follow-up ($P<0.001$). No VV recurrence by 6 months.

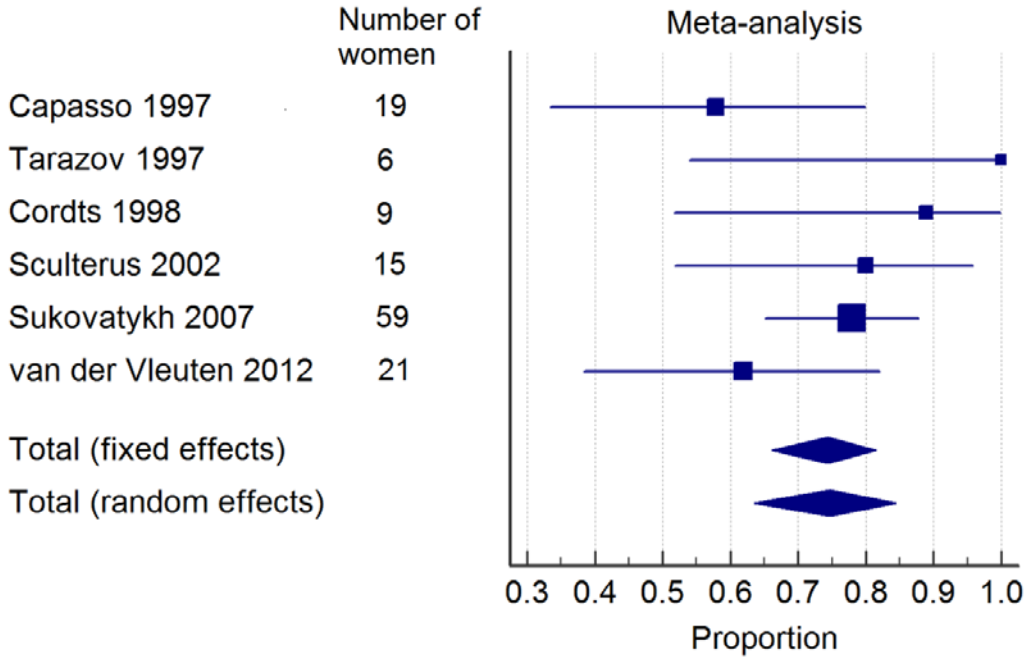

Figure 1 Meta-analysis of rates of complete, excellent or moderate (combined) improvement 4-8 weeks following embolization

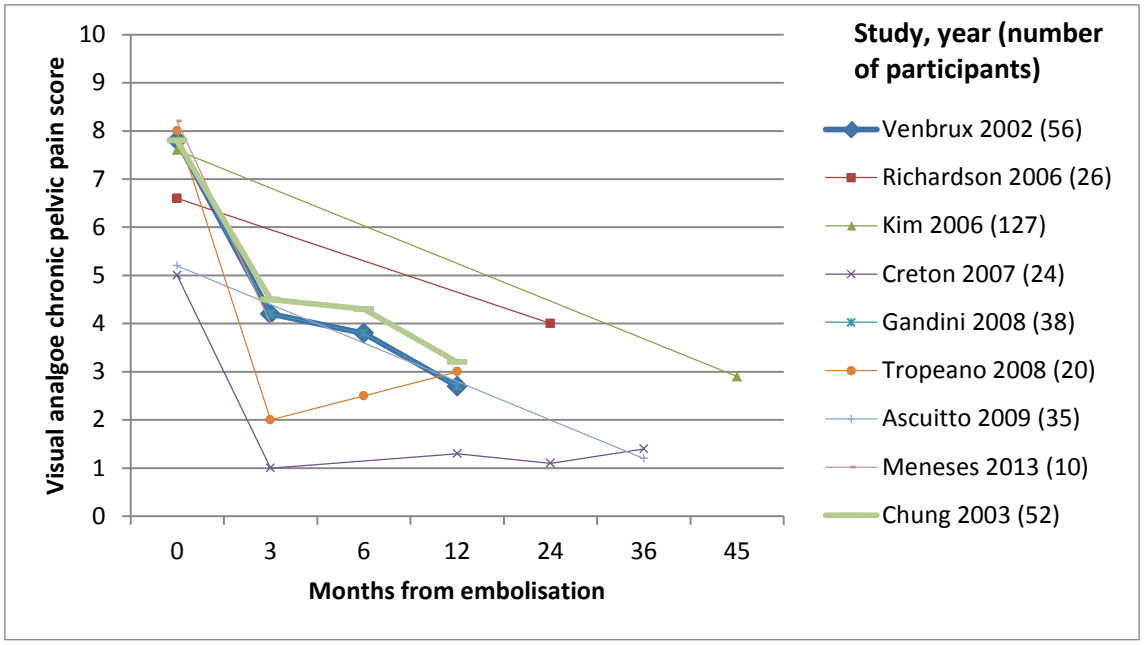

Figure 2 Time course of pain scores following embolization for pelvic vein incompetence

Table S1 Characteristics of studies selected for inclusion in systematic review of effectiveness of embolization of pelvic vein incompetence

Author, date, country	Number	Patient group	Treatment	Study type	Outcomes, follow up period	Key results
Capasso 1997 Belgium	19	Women with clinical and ultrasonographical or radiological evidence of PVI.	OV vein glue (n=24), coil (n=2) or combined (n=4) embolization; left OV only n=13, bilateral n=6.	Prospective observational study	Subjective assessment of pain relief within 4 weeks. Trans-abdominal Doppler ultrasound at 5 weeks. Average 15 month follow	Early outcomes: 74% had improvements in pain symptoms (complete relief in 58%, partial in 16%). Improvement correlated with ultrasonographical evidence of complete thrombosis of varices.

					up for recurrence.	Dyspareunia (n=5) persisted. N=5 with persistent pain had re-intervention. 2 venous perforations that resolved.
Tarazov 1997 Russia	6	Women with clinical and radiological evidence of PVI	Bilateral n=1 or left unilateral n=5 OV coil embolization.	Not stated	Subjective reporting of symptom Improvement, follow-up duration 1-4 years.	Complete alleviation of CPP in all women within 4 weeks. Improved menstrual symptoms I 2 women with dysmenorrhea. No serious complications.
Cordts	9	Women with	Bilateral n=4 or	Consecutive	Numerical	8 women (88.9%) had

1998 USA		clinical and ultrasonographic and/or radiological evidence of PVI.	left unilateral n=4 OV coil embolization.	case series	rating scale of symptom relief, mean follow-up 13 months	>80% immediate symptom relief. Two women had a mild or moderate return of the symptoms at 6 and 22 months respectively. One lower lobe coil pulmonary embolus.
Scultetus 2002 USA	15 (treated with sclerotherapy)	Women with “mild” discomfort, small varies and mild reflux by Doppler ultrasound.	Sclerotherapy of varices alone or with excision of varices.	Prospective observation study	VAS of improvement. Mean follow-up 2.3 years.	12 had excellent improvement, 3 had moderate improvement. No deep vein thrombosis reported.

Venbrux 2002 USA	56	Women with clinical and ultrasonographic and/or radiological evidence of PVI.	Bilateral OV (100%) and subsequent IIV (77%) coil embolization	Prospective observational study	VAS for pain, menstrual cycle questionnaire at 3, 6 and 12 months post procedure.	Mean pain 7.8 at baseline decreased to 4.2 at 3-months, 3.8 at 6 months, 2.7 at 12 months ($p<0.001$ for all comparisons). No significant changes in cycle length.
Chung 2003 South Korea	106, of whom 52 treated with embolization	Pre-menopausal women with idiopathic CPP and a score of ≥5 on a modified venography	a) OV or IIV coil embolization (n=52) b) Hysterectomy with bilateral oophorectomy (n=27) c)	Randomized control trial	VAS at 3, 6, and 12 months post-procedure, patient global impression of change.	Statistically significant decrease from baseline and between embolization and hysterectomy groups at all time-points.

		scale, refractory to MPA.	Hysterectomy with unilateral oophorectomy (n=27)			
Pieri 2003 Italy	33	Women with clinical and ultrasonographical evidence of PVI.	OV foam sclerotherapy (64% bilaterally)	Prospective observational study	Subjective rating of various pain symptoms at 1 month. Clinical assessment and mean venous diameter by ultrasound at 6 months.	Improvement in pain in 61%. Mean OV diameter at baseline right 4.5mm and left 6.3mm reduced to 3.10 and 4.4mm respectively at follow-up. Seven patients had transient flank pain.
Kim	127	Women with	Bilateral (85%) or	Retrospectivel	Visual analogue	Mean pelvic pain at

2006 USA		clinical and radiological evidence of PVI, including 25 with hysterectomy.	unilateral (15%) OV coil/sclerosant embolization, with 85% having subsequent IIV sclerosant embolization	y identified women followed-up prospectively.	scale and composite clinical assessment at 3 and 6 months and annually thereafter.	baseline 7.6 (SD 1.8) and 2.9 (SD 2.8) ($p < 0.0001$) and 80% had significant improvement at mean 45 months follow-up. All pain symptoms significantly improved. Two coil migrations.
Leal Monedero 2006 Spain	239	Women with clinical and radiological evidence of PVI (with or without	Coil embolization with or without foam, of OV or IIV, with VV surgery where	Observational study (unclear whether prospective or retrospective)	Clinical assessment at 6 months post-procedure.	Complete resolution of pain symptoms in 120/239 (50.2%) and partial relief in 95/239 (36.8%). Superficial

		CPP) and lower limb VV	indicated s			phlebitis at point of venous access in 21 women. No coil migrations.
Richardson 2006 Australia	26	Women with CPP and ultrasonographic evidence of PVI.	Coil embolization, with or without foam, of OV.	Case series, with historical control group undergoing OV ligation. Patient information suggests prospective.	Visual analogue scale for pain symptoms and patient overall satisfaction. Mean follow-up 22±13 months.	No significant difference between groups in demographics and presenting symptoms. Coil group pain score statistically significantly reduced from 6.6 (SD 1.9) to 4.0 (SD 2.8), from

						baseline. No statistically significant difference in pain reduction between ligation and embolization groups nor in overall satisfaction. No coil migration within 6 weeks, one coil perforation detected at 5 months.
Creton 2007 France	24	Pre-menopausal women with dysmenorrhea/	OV or IIV coil embolization	Prospective observational study	VAS for dysmenorrhea, dyspareunia and	Statistically significant decreases in all three pain symptoms and

		dyspareunia and radiological evidence of PVI.			venous pain (individually and total); clinical assessment at 45 days and 1,2 and 3 years follow up	improvements in clinical assessment maintained. One coil migration.
Greiner 2007 France	13 (of 24 embolized)	Women with clinical and ultrasonographical evidence of PVI with CPP and lower limb VV.	Bilateral and unilateral coil or glue or combined embolization of OV and IIV.	Observational study (assumed prospective)	Repeat TVUS at 1 and 6 months, 1 and 4 years. Repeat clinical assessment and venography at 4 years.	Complete resolution of symptoms in 10/13 and significant improvement in 3/13. No recurrence of PVI.

Kwon 2007 South Korea	67	Women with clinical and radiological evidence of PVI	OV coil embolization (96% left OV only)	Prospective study of outcome with baseline pain determined by telephone interview or medical note review	Categorical pain severity scale. Mean follow up 45 months	82% reported total or significant pain reduction. Two coil migrations.
Gandini 2008 Italy	38	Women with CPP and ultrasonographic evidence of PVI.	Bilateral OV foam sclerotherapy (3% STSF)	Described as retrospective but included all patients at 3 defined time-points	VAS for 4 pain symptoms at 1, 3, 6 and 12 months follow up	Mean VAS for CPP showed decrease from 7.8 (SD 1.8) to 2.7(SD 2.8), from 4.9(SD 4.2) to 2.2(3.1) for menstrual pain, from

						3.3(SD 3.7) to 1.5(SD 2.7) for dyspareunia and 3.5(SD 3.9) to 1.5(SD 3.0) for urinary urgency at 12 months, all statistically significant.
Ratnam 2008 UK	218	Women with ultrasonographical evidence of PVI and veins communicating with lower limb VV	Bilateral and unilateral coil embolization of OV and IIV, with VV surgery deferred to >8 weeks post procedure.	Prospective inclusion, retrospective data extraction from medical notes.	Repeat TVUS at 6-8 weeks	Of 193 with follow-up, 16 had residual mild reflux, 6 had marked reflux and 3 had new reflux. Two coil migrations, one misplacement, one case of perineal

						thrombophlebitis.
Sukovatykh 2008 Russia	59	Women with clinical and ultrasonographic and/or radiological evidence of PVI	Sclerotherapy	Not stated	Clinical examination, USS and self-reported quality of life	Improvements (not defined) were classified as excellent in 32.6%, good in 46.1%, satisfactory in 19.1% and unsatisfactory in 2.2% of the patients.
Tropeano 2008 Italy	20	Women with CPP and ultrasonographic evidence of PVI, with no pelvic pathology seen	Sclerotherapy of the OV (15% bilateral)	Prospective observational study	VAS for pain, menstrual cycle questionnaire and ultrasound at 3, 6 and 12 months post	Three women had repeat embolization after 3 months due to no change in symptoms and residual PVI on ultrasound. 17

		at laparoscopy and embolization possible anatomically.			procedure.	(85%) achieved marked to complete relief until 6 months, with 2 describing a reduction in relief by 12 months, Median VAS pain scores decreased from at 8.0 (range 6.0 to 10.0) at baseline to 2.0 (1.0 – 5.0), 2.5 (1.5 - 5.0), and 3.0 (2.0 – 6.0) at 3, 6 and 12 months respectively, all statistical

						significantly reductions (p<.001).
Asciutto 2009 Germany	35 (26 also had concurrent VV surgery)	Women with clinical and radiological evidence of PVI.	OV (n=28), IIV(n=5) or both (n=2) with coil embolization	Prospective observational study	VAS of pain at 1,2,3 years of follow up	VAS scores for isolated OVI: baseline mean 5.2 (SD 3.5) and 1.2 (SD 0.9) at 3 years; p<0.0001, non-statistically significant reduction for combined OVI and IIV or isolated IIV alone. At mean follow-up 45 months, overall 47% had sustained improvement. 3

						venous perforations that resolved.
D'Archambeau 2010 Belgium	193 (130 had PVI)	Women with clinical and radiological evidence of PVI.	Bilateral (4.7%) or unilateral coil (94.3% left, 1% right) coil embolization of OV	Prospective observational study	Symptom rating on VAS before procedure and at 1 year.	11 (5.7%) were re-embolized between 3 months and 6 years. 91/102 (89.2%) patients with PCS symptoms reported improvement in symptoms on VAS.
Tinelli 2012 Italy	28	Women with ultrasonographic and radiological evidence of PVI	OV foam sclerotherapy (29% bilaterally)	Not stated but follow-up at specific time-points.	VAS for pain, clinical examination and USS at 10 days, 1 and 6 months	At 1 month, 6 (21%) reported PVI symptoms, which resolved by 6 months. Reduction in

					post procedure.	varicosity size from 6.9mm (SD 2.1mm) on left and 5.1mm (SD1.4mm) on right to <4.5mm in all embolized veins. 100% technical success with no adverse events beyond minor analgesics needs in 6 (21%) patients.
van der Vleuten 2012 Netherlands	21 who responded follow-up	Women with CPP and radiological evidence of PVI	Bilateral or unilateral sclerotherapy of OV.	Prospective observation study for 2 month follow-	5 point ordinal scale of 8 pain symptoms and pelvic varices	14 (66.7%) and 16 (76.2%) women had moderate or obvious improvement or no

	survey	with or without lower limb VV		up, with cross sectional follow-up at mean 18 ±122 months	and hemorrhoids, and global impression of change.	symptoms, at 2 months and at the survey, respectively. All pain symptoms except backache or urinary symptoms showed statistically significant improvements. Nine (42.9%) women had a second embolization.
Meneses 2013 Chile	10	Women undergoing repeat surgery for VV recurrence and	Combined OV and/or IIV embolization, using sodium morrhuate	Prospective observational study	Venous clinical severity score (VCSS) and VAS for pain at 3 months	Significant decrease in pain from 8.2 at baseline to 4.0 at 3 months ($p<0.001$). Significant decrease in

		clinical and radiological evidence of PVI.	sclerosant and coil.		follow-up.	VVCS from 8.4 at baseline to 3.6 at 3 months follow-up (P<0.001). No VV recurrence by 6 months.

Table S2a. Demographics details of the patients in the included studies of effectiveness of embolization (age)

Author (date)	Age (years)		
	Mean	SD	Range
Capasso 1997	35.2		24-59
Tarazov 1997	32.5	6.3	25-40
Cordts 1998	32.2	6.5	20-43
Scultetus 2002[£*]	34		24-48
Venbrux 2002	32.3		16-66
Chung 2003	40.1	4.9	
Pieri 2003	44.3		36-56
Kim 2006	34	12.5	
Leal Monedero 2006	NS		
Richardson	37.5	6.9	

2006[*]			
Creton 2007	41.5		31-50
Greiner 2007	41		32-65
Kwon 2007	39.1	9	25-64
Gandini 2008	36.9		22-44
Ratnam [#] 2008	46.3		28-70
Sukovatykh 2008	NS		
Tropeano 2008	36		19-50
Asciutto 2009	49	11	27-72
D'Archambeau 2010	40.3		20-66
Tinelli 2012	51		43-59
van der Vleuten 2012	41.7	9.6	30-71
Meneses	38		25-39

2013			

[*] Data for whole reported population, not solely those undergoing embolization

[#] Data recorded only for first 60 patients of 218 in study

[&] Described as mean parity and gravida in 15 parous women of the 19 in study

Table S2b. Demographics details of the patients in the included studies of effectiveness of embolization (parity)

Author (date)	Parity (Gravida)			
	Mean	**SD**	**Range**	**% Nulliparous**
Capasso 1997	2 (2)[&]		0(0) to 5(6)	22.2
Tarazov 1997	1.2 (6.5)		0(4) to 2(9)	16.6
Cordts 1998	>2 (>2)			0
Scultetus 2002[£*]	3.1		2 to 5	
Venbrux 2002	NS			
Chung 2003	2.1	1.1		7.7
Pieri 2003	NS			
Kim 2006	NS			

Leal Monedero 2006	NS			
Richardson 2006*	3.3	1.2		
Creton 2007	NS (2.5)		(1 to 4)	
Greiner 2007	4		2(2) to 8(8)	0
Kwon 2007	2.4			0
Gandini 2008				13.1
Ratnam # 2008				3.3
Sukovatykh 2008	NS			
Tropeano 2008	0.9(0.9)	0.9	0 to 2	46
Asciutto 2009	NS(2.5)		0 to 7	
D'Archambeau 2010	NS			
Tinelli 2012	2.1			

van der Vleuten 2012	2.9	1.1	2 to 6	
Meneses 2013	3.5		2 to 5	

* Data for whole reported population, not solely those undergoing embolization

Data recorded only for first 60 patients of 218 in study

& Described as mean parity and gravida in 15 parous women of the 19 in study

Table S3 Quality assessment of case series included in the systematic review of effectiveness of embolization for pelvic congestion syndrome

Study	**Aim**	**Prospective**	**Multi-center**	**Eligibility**	**Comparable pain at baseline**	**Technique**	**Other interventions**	**Outcomes described**	**Valid outcome**	**Statistics**	**Timepoints**	**Loss to follow-up**	**Variability**	**Adverse events**	**Conclusions**	**Conflicts**
Capasso 1997	Y	U	N	N	U	Y	Y	N	N	N/A	N	U	N/A	Y	Y	N
Tarazov 1997	Y	U	N	N	Y	Y	N	N	N	N/A	Y	U	N/A	Y	Y	N
Cordts 1998	Y	Y	N	N	Y	Y	Y	U	U	N/A	N	U	N/A	Y	Y	N
Scultetus 2002	Y	U	U	N	Y	Y	U	Y	U	N	N	Y	N/A	Y	U	N
Venbrux	Y	Y	U	N	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N

2002																
Pieri 2003	Y	U	N	N	U	Y	Y	N	N	N	Y	U	N/A	Y	U	N
Kim 2006	Y	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	None
Leal Monedero 2006	Y	U	N	Y	U	Y	Y	N	N	N	N	U	N/A	N	Y	N
Richardson 2006	Y	Y	N	N	U	Y	U	Y	Y	Y	N	U	Y	Y	Y	N
Creton 2007	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	N
Greiner 2007	Y	Y	N	N	U	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y	N
Kwon 2007	Y	U	N	N	N	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y	N

Gandini 2008	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	N
Ratnam 2008	Y	Y	N	N	U	Y	Y	N	N	N	Y	Y	N/A	Y	Y	N
Tropeano 2008	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Asciutto 2009	Y	Y	N	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	None
D'Archambeau 2010	Y	Y	U	U	U	Y	U	Y	Y	U	Y	Y	N/A	N	Y	N
Tinelli 2012	Y	U	Y	Y	Y	Y	Y	Y	U	U	Y	U	Y	Y	Y	N
Van der Vleurten 2012	Y	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	None

Meneses 2013	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	N

Table S4 Pain scores before and after embolization of pelvic vein incompetence

	Time-point (months)						
Study	**0**	**3**	**6**	**12**	**24**	**36**	**45**
Venbrux 2002	7.8	4.2[b]	3.8 [b]	2.7 [b]			
Chung 2003	7.8 (1.2)	4.5 (0.9)[a]	4.3(0.8) [a]	3.2 (0.9) [a]			
Kim 2006	7.6 (1.8)						2.9 (2.8)[d]
Richardson 2006	6.6 (1.9)				4.0 (2.8)[c]		
Creton 2007	5	1.0[c]		1.3 [c]	1.1 [c]	1.4 [c]	
Gandini 2008	7.8 (1.8)	4.2 (1.9)[a]	3.8 (0.9)[a]	2.7 (2.8)[a]			
Tropeano 2008	8*[b]	2* [b]	2.5* [b]	3* [b]			
Asciutto 2009	5.2 (3.5)			2.1	1.5	1.2 (0.9)[d]	
Meneses 2013	8.2 (0.9)	4.0 (1.7)[c]					

Key: *median

P values: a<0.05; b <0.01, c<0.001, d<0.0001, compared to baseline, as reported.

Supplementary appendix – Search strategies

Search strategy for population and treatment

All databases searched from inception to November 2013.

BIOSIS WEB OF KNOWLEDGE:

#1 TS=pelvic pain

#2 TS=chronic pelvic pain

#3 TS=CPP

#4 TS=pelvic congestion

#5 TS=PCS

#6 TS=congestion syndrome

#7 TS=pelvic congestion syndrome

#8 TS=pelvic venous incompetence

#9 TS=PVI

#10 TS=ovarian vein incompetence

#11 TS=((pelvic or pelvis or iliac or ovarian) adj (vein$ or varices))

#12 TS=(reflux& or incompetence)

#13 #12 AND #11

#14 #3 AND #2 AND #1

#15 #7 AND #6 AND #5 AND #4

#16 #9 AND #8

#17 #16 OR #15 OR #14 OR #13 OR #10

#18 TS=treatment

#19 TS=therap$

#20 TS=emboli*ation

#21 TS=sclerotherapy

#22 TS=sc*lerotherapy

#23 TS=ligation

#24 TS= interventional radiology

#25 TS=therapeutic emboli*ation

#26 TS=balloon occlusion

#27 TS=occulsion

#28 TS=dilatation

#29 TS=vasculari*ation

#30 TS=endovascular surgery

#31 TS=laparoscopic surgery

#32 TS=vascular surgical procedure

#33 TS=vascular surgery

#34 TS=embolotherapy

#35 #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18

#36 #35 AND #17

BRITISH NURSING INDEX:

Searched for: all (pelvic congestion)

CINAHL:

S1 TX=pelvic congestion

S2 TX=PCS

S3 TX=congestion syndrome

S4 TX=pelvic congestion syndrome

S5 TX=S1 OR S2 OR S3 OR S4

S6 TX=treatment

S7 TX=therapy

S8 TX=emboli*ation

S9 TX=embolisation

S10 TX=embolization

S11 TX=sclerotherapy

S12 TX=sc*lerotherapy

S13 TX=ligation

S14 TX=balloon occlusion

S15 TX=occlusion

S16 TX=dilatation

S17 TX=vasculari*ation

S18 TX=endovascular surgery

S19 TX=laparoscopic surgery

S20 TX=embolotherapy

S21 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20

S22 S5 AND S21

COCHRANE LIBRARY:

Pelvic congestion AND PCS search – HTAs

Pelvic congestion AND PCS search – trials

reflux AND vein search - Cochrane reviews

reflux AND vein search – HTAs

reflux AND vein search - Other reviews

reflux AND vein search – trials

DARE: pelvic congestion

reflux AND vein

EMBASE: *<1980 to 2013 Week 14>*

1 exp Pelvic pain/ or chronic pelvic pain.mp.

2 CPP.mp.

3 pelvic congestion.mp.

4 PCS.mp.

5 congestion syndrome.mp.

6 pelvic congestion syndrome.mp.

7 pelvic venous incompetence.mp.

8 PVI.mp.

9 ovarian vein incompetence.mp.

10 ((pelvic or pelvis or iliac or ovarian) adj (vein$ or varices)).mp.

11 (reflux$ or incompetence).mp.

12 10 and 11

13 1 and 2

14 3 and 4

15 3 and 4 and 5 and 6

16 7 and 8

17 9 or 12 or 13 or 15 or 16

18 treatment.mp.

19 therap$.mp.

20 emboli*ation.mp.

21 exp Sclerotherapy/ or sc*lerotherapy.mp.

22 ligation.mp. or exp ligation/

23 interventional radiology.mp. or exp Radiology, Interventional/

24 exp Embolization, therapeutic/ or balloon occulsion.mp.

25 occulsion.mp.

26 dilatation.mp. or exp Dilatation/

27 vasculari*ation.mp.

28 endovascular surgery.mp.

29 laparoscopic surgery.mp.

30 exp VascularSurgical Procedures/ or vascular surgery.mp.

31 embolotherapy.mp. or exp Embolization, therapeutic/

32 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31

33 17 and 32

IMEMR: pelvic congestion

reflux vein

IMSEAR: pelvic congestion syndrome

INDEX OF SCIENTIFIC AND TECHNICAL PROCEEDINGS:

Pelvic congestion syndrome AND vein

LILACS: pelvic AND congestion

reflux AND vein

MEDION: pelvic AND congestion

reflux AND vein

MEDLINE: *Ovid MEDLINE(R) <1946 to March Week 1 2013>*

1 exp Pelvic Pain/ or chronic pelvic pain.mp.

2 CPP.mp.

3 pelvic congestion.mp.

4 PCS.mp.

5 congestion syndrome.mp.

6 pelvic congestion syndrome.mp.

7 pelvic venous incompetence.mp.

8 PVI.mp.

9 ovarian vein incompetence.mp.

10 ((pelvic or pelvis or iliac or ovarian) adj (vein$ or varices)).mp.

11 (reflux$ or incompetence).mp.

12 10 and 11

13 1 and 2

14 3 and 4

15 3 and 4 and 5 and 6

16 7 and 8

17 9 or 12 or 13 or 15 or 16

18 treatment.mp.

19 therap$.mp.

20 emboli*ation.mp.

21 exp Sclerotherapy/ or sc*lerotherapy.mp.

22 ligation.mp. or exp Ligation/

23 interventional radiology.mp. or exp Radiology, Interventional/

24 exp Embolization, Therapeutic/ or balloon occulsion.mp.

25 occulsion.mp.

26 dilatation.mp. or exp Dilatation/

27 vasculari*ation.mp.

28 endovascular surgery.mp.

29 laparoscopic surgery.mp.

30 exp Vascular Surgical Procedures/ or vascular surgery.mp.

31 embolotherapy.mp. or exp Embolization, Therapeutic/

32 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31

33 17 and 32

PAHO: pelvic AND congestion

pelvic AND congestion AND syndrome

reflux AND vein

POPLINE: pelvic congestion syndrome

pelvic congestion

reflux vein

SciELO: pelvic AND congestion AND syndrome

reflux AND vein

pelvic congestion

WEB OF SCIENCE:

#1 TS=pelvic pain

#2 TS=chronic pelvic pain

#3 TS=CPP

#4 TS=pelvic congestion

#5 TS=PCS

#6 TS=congestion syndrome

#7 TS=pelvic congestion syndrome

#8 TS=pelvic venous incompetence

#9 TS=PVI

#10 TS=ovarian vein incompetence

#11 TS=((pelvic or pelvis or ovarian) adj (vein$ or varices))

#12 TS=(9reflux$ or incompetence)

#13 #12#AND #11

#14 #3 AND #2 AND #1

#15 #7 AND #6 AND #5 AND #4

#16 #9 AND #8

#17 #16 OR #15 OR #14 OR #13 OR #10

#18 TS=treatment

#19 TS=therap$

#20 TS=emboli*ation

#21 TS=sclerotherapy

#22 TS=sc*lerotherapy

#23 TS=ligation

#24 TS=interventional radiology

#25 TS=therapeutic emboli*ation

#26 TS=balloon occlusion

#27 TS=occlusion

#28 TS=dilatation

#29 TS=vasculari*ation

#30 TS=endovascular surgery

#31 TS=laparoscopic surgery

#32 TS=vascular surgical procedure

#33 TS=vascular surgery

#34 TS=embolotherapy

#35 #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18

#36 #35 AND #17

WPRIM: pelvic congestion

reflux vein