

AHRQ Comparative Effectiveness Review Surveillance Program

CER #41:

Noncyclic Chronic Pelvic Pain Therapies for Women: Comparative Effectiveness

Original release date:

January, 2012

Surveillance Report:

October, 2012

Key Findings:

- The conclusions for the key questions are still considered valid but there are a few additional studies available to inform KQ4 (non-surgical interventions)
- There were a number of label changes for non-surgical interventions (leuprolide, botulinum toxin, letrozole, conjugated estrogens / medroxyprogesterone acetate, estradiol gel, estradiol vaginal ring) but no new research studies were identified

Summary Decision

This CER's priority for updating is **Low**

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Noncyclic Chronic Pelvic Pain Therapies for Women: Comparative Effectiveness

1. Introduction

Comparative Effectiveness Review (CER) #41, Noncyclic Chronic Pelvic Pain Therapies for Women, was released in January 2012.¹ It was therefore due for a surveillance assessment in July, 2012. At that time, we contacted experts involved in the original CER and subject experts to get their opinions as to whether the conclusions had changed and need to be updated. We also conducted an update electronic literature search. Every month since the CER's original release, we received any FDA updates on the included treatments and tests.

2. Methods

2.1 Literature Searches

Using the search strategy employed for the original report, we conducted a limited literature search. We screened PubMed for the time period May 2011 to July 2012; the original report updated the search in May 2011. We removed the MEDLINE filter for human participants in order to capture all pertinent publications including those that have not yet been indexed by MEDLINE. Appendix A includes the search methodology for this topic.

2.2 Study selection

We used the same inclusion and exclusion criteria as the original CER. We screened the titles and abstracts and obtained full text copies of publications accordingly.

2.3 Expert Opinion

We shared the conclusions of the original report with 15 experts in the field (including the original project leader, all original technical expert panel (TEP) members, key informants, and peer reviewers for their assessment of the need to update the report and their recommendations of any relevant new studies; five subject matter experts responded. Appendix C shows the questionnaire matrix that was sent to the experts.

2.4 Check for qualitative and quantitative signals

After abstracting the study conditions and findings for each new included study into an evidence table, we assessed whether the new findings provided a signal according to the Ottawa Method and/or the RAND Method, suggesting the need for an update. The criteria are listed in the table below.^{2,3}

Ottawa Method	
Ottawa Qualitative Criteria for Signals of Potentially Invalidating Changes in Evidence	
A1	Opposing findings: A pivotal trial or systematic review (or guidelines) including at least one new trial that characterized the treatment in terms opposite to those used earlier.
A2	Substantial harm: A pivotal trial or systematic review (or guidelines) whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision making.
A3	A superior new treatment: A pivotal trial or systematic review (or guidelines) whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm.
Criteria for Signals of Major Changes in Evidence	
A4	Important changes in effectiveness short of “opposing findings”
A5	Clinically important expansion of treatment
A6	Clinically important caveat
A7	Opposing findings from discordant meta-analysis or nonpivotal trial
Quantitative Criteria for Signals of Potentially Invalidating Changes in Evidence	
B1	A change in statistical significance (from nonsignificant to significant)
B2	A change in relative effect size of at least 50 percent
RAND Method Indications for the Need for an Update	
1	Original conclusion is still valid and this portion of the original report does not need updating
2	Original conclusion is possibly out of date and this portion of the original report may need updating
3	Original conclusion is probably out of date and this portion of the original report may need updating
4	Original conclusion is out of date

2.5 Compilation of Findings and Conclusions

For this assessment we constructed a summary table that included the key questions, the original conclusions, and the findings of the new literature search, the expert assessments, and any FDA reports that pertained to each key question. To assess the conclusions in terms of the evidence that they might need updating, we used the 4-category scheme described in the table above for the RAND Method.

In making the decision to classify a CER conclusion into one category or another, we used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still valid.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.

- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

2.6 Determining Priority for Updating

We used the following two criteria in making our final conclusion for this CER:

- How much of the CER is possibly, probably, or certainly out of date?
- How out of date is that portion of the CER? For example, would the potential changes to the conclusions involve refinement of original estimates or do the potential changes mean some therapies are no longer favored or may not exist? Is the portion of the CER that is probably or certainly out of date an issue of safety (a drug withdrawn from the market, a black box warning) or the availability of a new drug within class (the latter being less of a signal to update than the former)?

3. Results

3.1 Search

The literature search identified 203 titles. After title and abstract review, we further reviewed the full text of 34 journal articles. The remaining titles were rejected because they clearly did not meet inclusion criteria for any of the review questions. In addition to the electronic database searches, we followed up suggestions from the topic experts for studies not already included in the original report. We reference-mined articles that met inclusion criteria as well as systematic reviews identified by the literature searches to identify additional articles that may have been published since the publication of the report.

Thus, 45 articles went on to full text review. Of these, 43 articles were rejected because they did not meet the inclusion criteria of the original report. The two remaining articles, both relevant to key question 4 (non-surgical interventions) were abstracted into an evidence table (Appendix B) for this assessment.^{4,5}

3.2 Expert Opinion

Key question 1: Four experts were in agreement that none of the conclusions changed based on new evidence. One expert noted though that there is emerging evidence regarding bladder pain / interstitial cystitis; one expert was unsure.

Key Question 4: Two experts indicated that there is new evidence, one thought the conclusions are still valid and one was unsure.

Key Question 2, 3, and 5: Four experts thought the conclusions are still valid, one was unsure.

3.3 Identifying qualitative and quantitative signals

Table 1 shows the original key questions, the conclusions of the original report, the results of the literature and drug database searches, the experts' assessments, the recommendations of the Southern California Evidence-based Practice Center (SCEPC) regarding the need for update, and qualitative signals.

Table 1: Summary Table

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
Key Question 1: Prevalence of Comorbidities				
Among women who have been diagnosed with noncyclic/mixed cyclic and noncyclic CPP, what is the prevalence of the following comorbidities: dysmenorrhea, major depressive disorder, anxiety disorder, temporomandibular joint pain disorder, fibromyalgia, IBS, interstitial cystitis (IC)/painful bladder syndrome (PBS), complex regional pain syndrome, vulvodynia, functional abdominal pain syndrome, low back pain, headache, and sexual dysfunction?				
Noncyclic CPP was variably defined, and diagnostic approaches were rarely reported. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Disproportionately few studies addressed noncyclic CPP, given the prevalence of the condition. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Comorbidities were similarly variably defined and frequently not diagnosed using standardized criteria. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Dysmenorrhea, dyspareunia, and IBS were the most frequently reported comorbidities in the literature meeting our criteria. [Key finding]	No new studies were identified.	None relevant	Four expert thought the conclusion is still valid but 1 noted that there is emerging new evidence and 1 was unsure.	The conclusions are still valid.
Understanding Comorbidity prevalence with CPP is difficult, as a condition may be considered part of the differential diagnosis or a concomitant condition. [Conclusion]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Key Question 2. Outcomes of Surgical Interventions for CPP				
Among women with noncyclic/mixed cyclic and noncyclic CPP, what is the effect of surgical interventions on pain status, functional status, satisfaction with care, and quality of life?				
Intervention studies overall included a limited number of participants and typically included only short-term followup. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Few studies of surgical approaches examined the same approach; none used a placebo control. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
No surgical approach was superior to a nonsurgical approach or comparative surgical approach. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
The strength of the evidence for surgical approaches overall was insufficient to low. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Among studies addressing treatment effects, little evidence demonstrates the effectiveness of surgical approaches. Despite numerous surgical techniques used extensively in treating CPP, few studies included more than 50 participants, and few were	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
considered high quality. All of the studies with comparison data failed to demonstrate that surgery in general or any specific surgical technique was more efficacious than either nonsurgical intervention or the comparator technique in improving pain status in patients. No surgical technique was superior, and the evidence to conclude that surgical intervention is either effective or ineffective for the treatment of CPP is insufficient. [Conclusion]				
Intervention studies overall included a limited number of participants and typically included only short-term followup. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Key Question 3: Evidence for Differences in Surgical Outcomes by Etiology What is the evidence that surgical outcomes differ if the etiology of noncyclic/mixed cyclic and noncyclic CPP is identified after surgery?				
No studies addressed evidence for differences in outcomes by etiology. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Key Question 4: Outcomes of Nonsurgical Interventions for CPP Among women with noncyclic/mixed cyclic and noncyclic CPP, what is the effect of nonsurgical interventions on pain status, functional status, satisfaction with care, quality of life, and harms?				
Most studies of nonsurgical approaches meeting our criteria addressed hormonal approaches and included women with endometriosis-associated CPP. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Few studies of nonsurgical interventions were placebo controlled, and few addressed nonpharmacologic approaches; strength of evidence was insufficient to low. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Hormonal studies reported equal effectiveness among the active agents investigated, with the exception of a placebo-controlled trial of raloxifene reporting more rapid return of pain in the raloxifene group. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Studies of nonhormonal and nonpharmacologic agents reported some positive effects on pain status. [Key finding]	Two new RCTs were identified: one RCT (N= 61) using micronized N-Palmitoylethanolamine transpolydatin or Celecoxib to treat CPP related to endometriosis after laparoscopic assessment	None relevant	1 expert indicated there is new evidence (see non-surgical approaches), 3 thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid but more studies are available.

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
	<p>reported a decrease in dysmenorrhea, dyspareunia, and pelvic pain with both agents compared to placebo, Celecoxib was most effective; the other RCT (N=59) concluded that the administration of antioxidants reduces chronic pelvic pain compared to placebo in women with endometriosis and chronic pelvic pain.</p>			
<p>Few nonsurgical studies reported harms. [Key finding]</p>	<p>One of the two new RCTs reported on side effects (no significant effects or alterations of laboratory data).</p>	<p>There were 5 label changes for leuprolide adding the adverse reactions convulsions; interstitial lung disease, thromboembolism, rarely reported serious liver injury, myocardial infarction, and diabetes.</p> <p>Dysmenorrhea/pelvic pain, exacerbation of chorea, ischemic colitis, growth potentiation of benign meningioma were added to the label of conjugated estrogens / medroxy-progesterone acetate. A label change for letrozole added angioedema and anaphylactic reactions. The post-marketing experiences toxic shock syndrome, ring adherence to the vaginal wall, and bowel obstruction were added to the label of estradiol vaginal rings. The contraindications known anaphylactic reaction, protein C, S, or antithrombin deficiency or thrombophilic disorders and a warning regarding hereditary angioedema were added to the</p>	<p>Four experts thought this conclusion was still valid, 1 was unsure.</p>	<p>The conclusions are still valid.</p>

Conclusions From CER Executive Summary	RAND Literature Search	FDA / Health Canada / MHRA (UK)	Expert Opinion EPC Investigator Other Experts	Conclusion from SCEPC
		label of estradiol gel. There is additional safety information and a new recommendation for botulinum toxin (possible muscle weakness association).		
Studies of nonsurgical approaches typically addressed hormonal management of endometriosis-related CPP and were not placebo controlled, thus limiting our ability to understand whether hormonal therapies would be beneficial for women with CPP without endometriosis and whether pain relief reported is due simply to the placebo effect. Some studies reported benefits of other nonsurgical approaches, but nonhormonal and nonpharmacologic management remains understudied. [Conclusions]	The two new RCTs addressed non-hormonal interventions and both were placebo-controlled but both were in endometriosis-related CPP.	None relevant	1 expert indicated there is new evidence, 3 thought this conclusion was still valid, 1 was unsure.	Overall, the conclusions are still valid but there are now two additional, small placebo-controlled RCTs available in the literature.
Key Question 5: Evidence for Selecting One Intervention Over Another				
What is the evidence for choosing one intervention over another to treat persistent or recurrent noncyclic/mixed cyclic and noncyclic CPP after an initial intervention fails to achieve target outcome(s)?				
No studies addressed [...] evidence for selecting one intervention over another if an intervention failed. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Overall				
Studies overall addressed a heterogeneous group of interventions and likely had significant variability across populations. [Key finding]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.
Improved characterization of the targeted condition, intervention, and population in CPP research is necessary to inform treatment choices for this commonly reported entity. A uniform definition of CPP and standardized evaluation of participants are lacking across the literature; study populations are likely to vary widely, and studies may be reporting effects from treating symptoms rather than a diagnosed condition. Thus, our understanding of potential treatment effects is diluted. [Conclusion]	No new studies were identified.	None relevant	Four experts thought this conclusion was still valid, 1 was unsure.	The conclusions are still valid.

Legend: CPP: chronic pelvic pain; RCT: randomized controlled trial; SCEPC: Southern California Evidence-based Practice Center

References

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5. Santanam N, Kavtaradze N, Murphy A, et al. Antioxidant supplementation reduces endometriosis-related pelvic pain in humans. *Transl Res.* 2012 May 31 PMID 22728166.

Appendices

Appendix A: Search Methodology

Appendix B: Evidence Tables

Appendix C: Questionnaire Matrix

Appendix A. Search Methodology

Search strategy

(Replication of search employed for original report but the filter for “human” was not used as it would exclude all new studies not yet tagged with MeSH headings)

#19- #16 NOT #17-

#17- #7 NOT (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) Filters: Publication date from 2011/05/01 to 2012/12/31; Humans; English

#16- #7 NOT (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15) Filters: Publication date from 2011/05/01 to 2012/12/31; English

#15- #7 AND practice guideline[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#14- #7 AND meta-analysis[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#13- #7 AND review[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#12- #7 AND editorial[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#11- #7 AND comment[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#10- #7 AND comment[pt]] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#9- #7 AND letter[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#8- #7 AND case reports[pt] Filters: Publication date from 2011/05/01 to 2012/12/31; English

#7- #1 OR (#2 AND (#3 OR #4)) Filters: Publication date from 2011/05/01 to 2012/12/31; English

#6- #1 OR (#2 AND (#3 OR #4)) Filters: Publication date from 2011/05/01 to 2012/12/31

#5- #1 OR (#2 AND (#3 OR #4))

#4- (musculoskeletal diseases[mh] OR myofascial[tiab]) AND (pelvic[tiab] OR pelvis[tiab] OR pelvis[mh] OR pelvic pain[tiab])

#3- “pelvic pain” OR pelvic pain[mh]

#2- chronic OR recurrent OR recurring OR chronic disease[mh] OR noncyclic OR non-cyclic OR mixed

#1- “chronic pelvic pain”

Latest search date: 7/12/2012

Retrieved citations: 203

Appendix B. Evidence Table

Evidence Table Key Question 4. Among women with noncyclic/mixed cyclic and noncyclic CPP, what is the effect of nonsurgical interventions on pain status, functional status, satisfaction with care, quality of life, and harms?

Study Description	Design	Intervention and Comparator	Population	Finding
Cobellis, 2011 ⁴	RCT	Association micronized N - Palmitoylethanolamine (PEA) -transpolydatin vs. Celecoxib vs. placebo	61 women between 24 and 41 years old with chronic pain related to endometriosis	A marked decrease in dysmenorrhea, dyspareunia and pelvic pain was observed in all groups; N-Palmitoylethanolamine-transpolydatin was more effective than placebo (p<.001); Celecoxib was more effective than both other arms for all 3 outcomes. 9/21, 4/20, and 8/20 patients in the treatment arms were very satisfied with the treatment. No significant side effect and alteration of laboratory data were found in the administration of N-Palmitoylethanolamine-transpolydatin.
Santanam, 2012 ⁵	RCT	Antioxidant vitamins E and C vs placebo	59 women between 19 and 41 years old with endometriosis-related pelvic pain	Everyday pain improved in 43%, dysmenorrhea in 37% and dyspareunia in 24% of patients in the treatment group, there was no change in the placebo group regarding chronic pain or dyspareunia and dysmenorrhea improved in 31% of patients

Appendix C. Questionnaire Matrix

Surveillance and Identification of Triggers for Updating Systematic Reviews for the EHC Program

Title: Noncyclic Chronic Pelvic Pain Therapies for Women: Comparative Effectiveness

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
<p>Key Question 1: Prevalence of Comorbidities Among women who have been diagnosed with noncyclic/mixed cyclic and noncyclic CPP, what is the prevalence of the following comorbidities: dysmenorrhea, major depressive disorder, anxiety disorder, temporomandibular joint pain disorder, fibromyalgia, IBS, interstitial cystitis (IC)/painful bladder syndrome (PBS), complex regional pain syndrome, vulvodynia, functional abdominal pain syndrome, low back pain, headache, and sexual dysfunction?</p>			
Noncyclic CPP was variably defined, and diagnostic approaches were rarely reported. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Disproportionately few studies addressed noncyclic CPP, given the prevalence of the condition. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Comorbidities were similarly variably defined and frequently not diagnosed using standardized criteria. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Dysmenorrhea, dyspareunia, and IBS were the most frequently reported comorbidities in the literature meeting our criteria. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Understanding Comorbidity prevalence with CPP is difficult, as a condition may be considered part of the differential diagnosis or a concomitant condition. [Conclusion]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Key Question 2. Outcomes of Surgical Interventions for CPP Among women with noncyclic/mixed cyclic and noncyclic CPP, what is the effect of surgical interventions on pain status, functional status, satisfaction with care, and quality of life?			
Intervention studies overall included a limited number of participants and typically included only short-term followup. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Few studies of surgical approaches examined the same approach; none used a placebo control. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
No surgical approach was superior to a nonsurgical approach or comparative surgical approach. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
The strength of the evidence for surgical approaches overall was insufficient to low. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Among studies addressing treatment effects, little evidence demonstrates the effectiveness of surgical approaches. Despite numerous surgical techniques used extensively in treating CPP, few studies included more than 50 participants,	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
and few were considered high quality. All of the studies with comparison data failed to demonstrate that surgery in general or any specific surgical technique was more efficacious than either nonsurgical intervention or the comparator technique in improving pain status in patients. No surgical technique was superior, and the evidence to conclude that surgical intervention is either effective or ineffective for the treatment of CPP is insufficient. [Conclusion]			
Key Question 3: Evidence for Differences in Surgical Outcomes by Etiology What is the evidence that surgical outcomes differ if the etiology of noncyclic/mixed cyclic and noncyclic CPP is identified after surgery?			
No studies addressed evidence for differences in outcomes by etiology. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Key Question 4: Outcomes of Nonsurgical Interventions for CPP Among women with noncyclic/mixed cyclic and noncyclic CPP, what is the effect of nonsurgical interventions on pain status, functional status, satisfaction with care, quality of life, and harms?			
Most studies of nonsurgical approaches meeting our criteria addressed hormonal approaches and included women with endometriosis-associated CPP. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Few studies of nonsurgical interventions were placebo controlled, and few addressed nonpharmacologic approaches; strength of evidence was insufficient to low. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Hormonal studies reported equal effectiveness among the active agents investigated, with the exception of a placebo-controlled trial of raloxifene reporting more rapid return of pain	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
in the raloxifene group. [Key finding]			
Studies of nonhormonal and nonpharmacologic agents reported some positive effects on pain status. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Few nonsurgical studies reported harms. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Studies of nonsurgical approaches typically addressed hormonal management of endometriosis-related CPP and were not placebo controlled, thus limiting our ability to understand whether hormonal therapies would be beneficial for women with CPP without endometriosis and whether pain relief reported is due simply to the placebo effect. Some studies reported benefits of other nonsurgical approaches, but nonhormonal and nonpharmacologic management remains understudied. [Conclusions]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Key Question 5: Evidence for Selecting One Intervention Over Another What is the evidence for choosing one intervention over another to treat persistent or recurrent noncyclic/mixed cyclic and noncyclic CPP after an initial intervention fails to achieve target outcome(s)?			
No studies addressed [...] evidence for selecting one intervention over another if an intervention failed. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Overall			

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Studies overall addressed a heterogeneous group of interventions and likely had significant variability across populations. [Key finding]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Improved characterization of the targeted condition, intervention, and population in CPP research is necessary to inform treatment choices for this commonly reported entity. A uniform definition of CPP and standardized evaluation of participants are lacking across the literature; study populations are likely to vary widely, and studies may be reporting effects from treating symptoms rather than a diagnosed condition. Thus, our understanding of potential treatment effects is diluted. [Conclusion]	<input type="checkbox"/>	New Evidence:	<input type="checkbox"/>
Are there new data that could inform the key questions that might not be addressed in the conclusions?			