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OREGON HEALTH AND SCIENCE UNIVERSITY
OFFICE OF CLINICAL INTEGRATION AND EVIDENCE-BASED PRACTICE

Evidence-Based Practice Summary

Benefits of Complementary and Alternative Medicine (CAM) Therapies for Menopausal Women with Low Libido

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BACKGROUND

Menopause is a transitional period during which a series of dynamic changes in physiology takes place, including hot flashes, night sweats, palpitations, insomnia, depression and vaginal dryness (Santoro 2004). Research suggests that postmenopausal women are 2.3 times more likely to experience sexual dysfunction when compared to premenopausal women (Garcia 2004). Currently, the treatment focus for women's sexual dysfunction has been nearly exclusively on pharmacotherapy, specifically thrandermal testosterone, bupropion, estrogen, and vaginal hormones (Basson 2007; Greendale 1996). Fewer women are advised to use hormone replacement therapy (HRT) because of the associated increased risk of breast cancer and cardiovascular disease (Shook 2011). Decreased confidence in HRT among menopausal women has highlighted the need for alternative treatment options (McPherson 2004). Therefore, the objective of this evidence brief is to evaluate the benefits of complementary and alternative medicine (CAM) therapies in menopausal women with low libido.

ASK THE QUESTION

Question 1: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.?

SEARCH FOR EVIDENCE

Databases included Ovid MEDLINE, MEDLINEinprocess, the Cochrane Central Register of Controlled Trials (CCRCT) & Cochrane Database of Systematic Reviews (CDSR).

1. exp Libido/ (4758)

2. exp Sexual Dysfunctions, Psychological/ (24675)
3. exp Sexual Dysfunction, Physiological/ (27985)
4. 1 or 2 or 3 (34837)
5. (libido* or ((sex* or coit* or intercours* or copulat*) adj3 (driv* or desir* or arous* or want* or need* or function* or dysfunction* or initia* or participa*))).mp. (45106)
6. ((reduc* or low* or decreas* or hypoactiv* or rais* or increas* or high* or elevat*) adj3 (driv* or desir* or arous* or function* or dysfunction* or want* or need* or function* or initia* or participa*)).mp. (364319)
7. exp sexual behavior/ (98928)
8. 5 or 6 (404317)
9. 7 and 8 (15626)
10. exp Neoplasms/ (3106401)
11. exp Antineoplastic Agents/ (1001490)
12. exp Radiotherapy/ (174126)
13. exp Antineoplastic Protocols/ (132555)
14. 10 or 11 or 12 or 13 (3676993)
15. 9 and 14 (1289)
16. limit 15 to humans (1284)
17. limit 16 to female (906)
18. limit 17 to (meta analysis or systematic reviews) (37)
19. limit 17 to (controlled clinical trial or guideline or randomized controlled trial) (69)
20. limit 17 to (comparative study or evaluation studies) (91)
21. exp Epidemiologic Studies/ (2177321)
22. 17 and 21 (297)
23. 18 or 19 or 20 or 22 (416)

Filters/limits included articles published in English in the last 10 years.

CRITICALLY ANALYZE THE EVIDENCE

The literature search resulted in various studies reporting on the benefits of CAM therapies for menopausal women with low libido. In order to simplify the review process, the evidence appraisal tables have been grouped between the following modalities reporting on benefits that were found in the literature (1) Polyacrylic Acid; (2) Genistein Supplements; (3) Lepidium mevenii (Maca); (4) Ginseng; (5) Lady Prelox; (6) Hypnotic Relaxation Therapy; and (7) Herbal Practice.

- **Polyacrylic Acid:** One RCT (Fernandes 2014) was found evaluating female sexual function comparing topic estrogen, testosterone and polyacrylic acid as vaginal lubricants with K-Y Jelly as a placebo lubricant. The study found that after 12 weeks of treatment, polyacrylic acid provided improvements for participants based on their female sexual function index score. Areas of improvement included sexual desire (*P* = 0.002), lubrication (*P* = 0.002), satisfaction (*P* = 0.003), reduced pain during intercourse (*P* = 0.033), and total score (*P* = 0.007), compared with lubricant alone.
  Quality of Evidence: Very Low

- **Genistein Supplements:** One Prospective Study (Battaglia 2009) was found evaluating the use of genistein in the treatment of vasomotor symptoms and its capacity to induce clitoral volumetric and vascular modifications. The genistein-treated patients did report improvements in vasomotor symptoms (*P* = 0.023), but did not show significant differences between the control group, nor influence any additional factors in the Italian McCoy Female Sexuality Questionnaire including desire, orgasm, arousal, pain, and satisfaction.
  Quality of Evidence: Very Low

- **Lepidium mevenii (Maca):** One systematic review (Shin 2010) was found examining Lepidium meyenii (Maca) for sexual dysfunction in menopausal women. The systematic review included three RCTs. One RCT reported positive effects of maca on sexual function in healthy menopausal women compared with the placebo control (MD, 0.70, 95% Cis, 0.08 to 1.32, *P* < 0.05). The other RCT tested both a high dosage of maca (3 g/d) and a low dosage of maca (1.5 g/d) on sexual desire compared to a placebo control and reported positive effects of both dosages of maca after 8 week (MD, 1.64, 95% CIs, 1.07 to 2.21, *P* < 0.01) and 12 weeks (MD, 1.64, 95% CIs, 1.07 to 2.21, *P* < 0.01). The last RCT included had a small sample size, and failed to show positive effects of maca in the improvement of sexual desire (MD, 6.38, 95% CIs, -11.32 to 24.08, NS).
  Quality of Evidence: Low

- **Ginseng:** One RCT (Oh 2010) was found that assessed whether Korean red ginseng (KRG) extracts would improve sexual function in menopausal women. The ginseng extract significantly improved scores on the FSFI (including domains for desire, arousal, lubrication, orgasm, global satisfaction and pain) from 3.10 + or - 0.87 to 3.50 + or - 0.72 in the sexual arousal domain (P = 0.006). The GAQ (consisting of simple sexual function questions) was more significantly affected by ginseng extracts than by placebo (P = 0.046). There were no severe adverse events in the KRG group, although two cases of vaginal bleeding occurred during KRG treatment.
  Quality of Evidence: Low

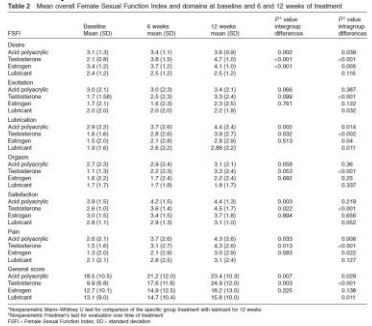
- **Lady Prelox:** One RCT (Bottari 2012) was found evaluating the efficacy of the dietary supplement, Lady Prelox, for improving sexual function in post-menopausal women. At baseline the women in the Lady Prelox group presented with a mean total FSFI score of 44.6 +/- 24.1 which increased significantly after four weeks treatment with Lady Prelox to 70.9 +/- 18.5 and further increased to 71.7 +/- 23.9 after completion of the eight-week trial period. In the control group the mean total FSFI was 44.1 +/- 22.8 at inclusion and non-significantly increased to 45 +/- 21.4 after four weeks and 47.4 +/- 21.8 after eight weeks, respectively. The treatment with Lady Prelox was comparatively significantly more effective than placebo after both four and eight weeks of treatment ($P<0.05$).
  Quality of Evidence: Very Low

- **Hypnotic Relaxation Therapy:** One RCT (Johnson 2016) was found examining the effect of hypnotic relaxation therapy on sexual dysfunction in postmenopausal women. Participants receiving hypnotic relaxation therapy (HRT) showed a significant improvement in sexual pleasure scores from a mean baseline score of 11.41–14.13 at the end of treatment (Week 6). Additionally, improvements in sexual discomfort were observed in the HRT condition, with a mean baseline score of 3.30 and a mean reduction of 3.08 after treatment.
  Quality of Evidence: Very Low

- **Herbal Practice:** One RCT (Green 2007) was found assessing the effectiveness of professional herbal practice in the treatment of menopausal symptoms. Participants in the treatment group received a course of individualized treatment from an herbal practitioner that demonstrated a statically and clinically signification reduction in menopausal symptoms compared to the control group. Total score for menopausal symptoms reduced for both groups. Reduction for the treated group was 9.05 points greater than that for the control group, CI 5.08-13.03, as were changes in vasomotor scores (mean 1.81, CI 1.00-2.62). Libido increased (mean 0.69, CI 0.38-0.99) in the group receiving herbal treatment.
  Quality of Evidence: Very Low

Conclusion: Overall, there is low to very low evidence demonstrating the benefits of various CAM therapies for menopausal women with low libido. The modalities were rated low due to inconsistency between studies and imprecision when studies included few patients and/or events.

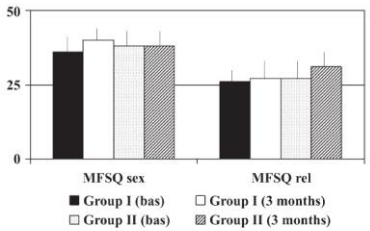
PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.						Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment*
Modality: Polyacrylic Acid						
Author/Dat	*Purpose*	*Study Design &*	*Sample*	*Outcomes*	*Design Limitations*	

e	*of Study*	*Methods*				
Total # of Studies: 1 # of RCTs: 1						
Fernandes, T., et al., 2014, *Journal of Sexual Medicine*	To evaluate female sexual function after using topic estrogen, testosterone, or polyacrylic acid as vaginal lubricants with K-Y jelly as a placebo lubricant	RCT; Postmenopausal women between 40 and 70 years of age were included with follow-up at the Menopause Clinic of the CAISM Unicamp. The women were randomized to treatment with topical vaginal estrogen, testosterone, polyacrylic acid, or oil lubricant alone, three times a week for a period of 12 weeks.	80 women; 20 allocated to polyacrylic acid intervention	After 12 weeks of treatment, polyacrylic acid produced improvements in the FSFI domains of sexual desire, lubrication, satisfaction, reduced pain during intercourse, and total score compared with lubricant alone. (P = 0.002) Table 2 Mean overall Female Sexual Function Index and domains at baseline and 6 and 12 weeks of treatment 	Study Limitations = ☒ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	*effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect

						Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.

Outcome: Genistein Supplements

Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*
Total # of Studies: 1 # of Non-Randomized Studie1					
Battaglia, C., et al., 2009, *Journal of Sexual Medicine*	To evaluate, in postmenopausal women who refused hormonal therapy, the role of genistein in the treatment of vasomotor symptoms and its capacity to induce clitoral volumetric and vascular modifications independently from sexual stimulation.	Prospective Study; Women who refused hormonal therapy were submitted to oral daily treatment with genistein 45; or no treatment The Group II patients served as controls. The patients were not randomly assigned to the two groups. The patients were studied before and after 3 months.	29 postmenopausal women; Genistein Group (Group I; N = 15); or no treatment (Group II; N = 14).	In the genistein-treated patients the vasomotor symptoms ameliorated at the end of the study (P = 0.023). The use of genistein did not influence any other parameter including desire, orgasm, arousal, pain, and satisfaction  **Figure 1** The two-factor Italian McCoy Female Sexuality Questionnaire (MFSQ), either for sexuality (sex) and partnership (rel), do not show significant differences between treated (Group I) and untreated (Group II) patients. bas = basal.	Study Limitations = ☒ None ***Non-Randomized Studies*** ☐ Failure to develop and apply appropriate eligibility criteria ☐ Flawed measurement of both exposure and outcome ☐ Failure to adequately control confounding ☐ Incomplete or inadequately short follow-up ☐ Differences in important prognostic factors at baseline

Lower Quality Rating if:
☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)*

☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*

☒ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)*

☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small,*

						positive studies found) Increase Quality Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.

Modality: Lepidium meyenii (Maca)

Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*
Total # of Studies: 2 # of Systematic Reviews: 1 # of RCTs: 1					
Shin, B.C., et al., 2010, *BMC Complementary & Alternative Medicine*	To assess the clinical evidence for or against the effectiveness of the maca plant as a treatment for sexual dysfunction	Systematic Review	3 RCTs	One RCT reported positive effects of maca on sexual function in healthy menopausal women compared with the placebo control (MD, 0.70, 95% Cis, 0.08 to 1.32, P < 0.05). The other RCT tested both a high dosage of maca (3 g/d) and a low dosage of maca (1.5 g/d) on sexual desire compared to a placebo control and reported positive effects of both dosages of maca after 8 week (MD, 1.64, 95% CIs, 1.07 to 2.21, P < 0.01) and 12 weeks (MD, 1.64, 95% CIs, 1.07 to 2.21, P < 0.01). The last RCT included had a small sample size, and failed to show positive effects	Study Limitations = ☐ None ***Systematic Review*** ☐ Review did not address focused clinical question ☐ Search was not detailed or exhaustive ☒ Quality of the studies was not appraised or studies were of low quality ☒ Methods and/or results were inconsistent across studies

Lower Quality Rating if:
☐ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)*

☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)*

☒ Studies are

				of maca in the improvement of sexual desire (MD, 6.38, 95% CIs, -11.32 to 24.08, NS).		imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☒ Low ☐ Very Low

PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.

Modality: Ginseng

Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	<u>Lower Quality Rating if:</u>
Total # of Studies: 1 # of RCTs: 1						☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)*
Oh, K.J., et al.,	To assess	RCT; Participants were	32 menopausal	The ginseng extract significantly	Study Limitations =	

2010, *Journal of Sexual Medicine*	whether Korean red ginseng (KRG) extracts would improve sexual function in menopausal women	randomized to either receive three capsules of ginseng (1 g per capsule) or placebo daily. After completing the KRG or placebo arm, the participants were crossed over to the other arm after a 2-week washout period. The efficacy and safety of the KRG extracts were measured by using questionnaires. Outcomes were measured using the Female Sexual Function Index (FSFI) and Global Assessment Questionnaire (GAQ). The FSFI consisted of six domains (desire, arousal, lubrication, orgasm, global satisfaction, and pain) assigned with 19 items. The GAQ consisted of a simple, single question asking whether sexual function had improved after each clinical trial arm.	women	improved scores on the FSFI from 3.10 + or - 0.87 to 3.50 + or - 0.72 in the sexual arousal domain (P = 0.006). The GAQ was more significantly affected by ginseng extracts than by placebo (P = 0.046). There were no severe adverse events in the KRG group, although two cases of vaginal bleeding occurred during KRG treatment.	☐ None ***RCTS*** ☐ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☒ Large losses to F/U ☐ Difference in important prognostic factors at baseline	☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High

						☐ Moderate ☒ Low ☐ Very Low

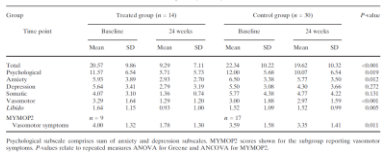
PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.						Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* Increase Quality
Modality: Lady Prelox						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 1 # of RCTs: 1						
Bottari, A., et al., 2012, Panminerva Medica	To evaluate the efficacy of a proprietary, dietary supplement Lady Prelox for supporting and improving sexual function in generally healthy, post-menopausal women	RCT; Women were randomized to Lady Prelox or control groups and were followed for eight weeks. Participants completed female sexual function index (FSFI) at baseline, four weeks, and weight weeks.	83 women; 40 in the Lady Prelox group and 43 in the control group	At baseline the women in the verum group presented with a mean total FSFI score of 44.6 +/- 24.1 which increased significantly after four weeks treatment with Lady Prelox to 70.9 +/- 18.5 and further increased to 71.7 +/- 23.9 after completion of the eight-week trial period. In the control group the mean total FSFI was 44.1 +/- 22.8 at inclusion and non-significantly increased to 45 +/- 21.4 after four weeks and 47.4 +/- 21.8 after eight weeks, respectively. The treatment with Lady Prelox was comparatively significantly more effective than placebo after both four and eight weeks of treatment (P<0.05). The individual six FSFI domains related to desire, arousal, lubrication, orgasm, satisfaction and pain did all respond favorably to treatment with Lady Prelox; however, with only marginable higher scores in the placebo group.	Study Limitations = ☐ None RCTS ☒ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	

						Rating if: ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.						Lower Quality Rating if: ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*When studies include few patients and few events and thus have*
Modality: Hypnotic Relaxation Therapy						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 1 # of RCTs: 1						
Johnson, A.K., et al., 2016, *International Journal of Clinical & Experimental Hypnosis*	To examine the effect of hypnotic relaxation therapy on sexual dysfunction in postmenopausal women	RCT; Sexual function was assessed using the Sexual Activity Questionnaire (SAQ). Intervention Participants attended 5 weekly sessions of hypnotic relaxation therapy, compared with control participants who received an attention control. Sexual function was assessed using the Sexual Activity Questionnaire (SAQ). Significant improvement in sexual pleasure and discomfort were reported following 5 weekly sessions of hypnotic relaxation therapy, compared with those receiving an attention control.	187 postmenopausal women	Participants receiving hypnotic relaxation therapy (HRT) showed a significant improvement in sexual pleasure scores from a mean baseline score of 11.41–14.13 at the end of treatment (Week 6). Improvements of sexual pleasure scores remained stable and showed a slight increase to 14.84 on the SAQ at the Week 12 follow-up. Additionally, improvements in sexual discomfort were observed in the HRT condition, with a mean baseline score of 3.30 and a mean reduction of 3.08 after treatment. Table 3 *Comparison of Means and Standard Deviations of SAQ Scores by Intervention* Week 0 / Week 5 / Week 12 SAQ Component — Hypnosis *M (SD)* — Control *M (SD)* — Hypnosis *M (SD)* — Control *M (SD)* — Hypnosis *M (SD)* — Control *M (SD)* Pleasure score — 11.41 (4.81) — 9.34 (4.12) — 14.13 (4.99) — 10.48 (4.14) — 14.84 (3.76) — 11.11 (4.37) Discomfort score — 3.30 (1.95) — 3.14 (2.23) — 2.38 (2.14) — 3.08 (1.93) — 2.43 (2.08) — 2.81 (2.11) Total score — 15.78 (5.45) — 13.70 (4.13) — 17.97 (5.84) — 14.97 (4.29) — 18.70 (4.65) — 15.29 (4.75)	Study Limitations = ☐ None ***RCTS*** ☒ Lack of blinding ☒ Lack of allocation concealment ☐ Stopped early for benefit ☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☒ Difference in important prognostic factors at baseline	

						wide confidence intervals and the results are uncertain) ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

PICO Question: In treatment of low libido in menopausal women, what are the benefits (and harms, if any) of CAM therapies such as acupuncture, chiropractic, massage, homeopathy, Ayurveda, supplements, herbs and botanicals, etc.						<u>Lower Quality Rating if:</u> ☒ Studies inconsistent (*wide variation of treatment effect across studies, populations, interventions, or outcomes varied)* ☐ Studies are indirect *(PICO question is*
Modality: Herbal Practice						
Author/Date	*Purpose of Study*	*Study Design & Methods*	*Sample*	*Outcomes*	*Design Limitations*	
Total # of Studies: 1 # of RCTs: 1						
Green, J., et al., 2007, *Family Practice*	To assess the effectiveness of professional herbal	RCT; Conducted in primary care in one urban UK practice. Women were invited to participant who were experiencing self-defined menopausal symptoms and no	45 women aged 46-59; Treatment group (n=15) and control group (n=30)	Forty-four participants completed the study. The treatment group demonstrated a statistically and clinically significant reduction in menopausal symptoms compared to the control group. Total scores for menopausal symptoms reduced for	Study Limitations = ☐ None ***RCTS*** ☒ Lack of blinding ☐ Lack of allocation concealment ☐ Stopped early for benefit	

	practice in the treatment of menopausal symptoms	menstrual bleeding for 3 months. Women were excluded who were using hormone replacement therapy. Participants were block randomized into a treatment group who received a course of individualized treatment from one of three herbal practitioners, and control group offered treatment after waiting 4 months. Treatment was six consultations over 5 months including discussion of nutrition, lifestyle and individualized herbal prescription. Change in menopausal symptoms was measured in both groups using the validated Greene Climacteric Scale. Measure Yourself Medical Outcome Profile recorded changes in self-defined most troublesome symptoms.		both groups. Reduction for the treated group was 9.05 points greater than that for the control group, CI 5.08-13.03, as were changes in vasomotor scores (mean 1.81, CI 1.00-2.62). Libido increased (mean 0.69, CI 0.38-0.99) in the group receiving herbal treatment. *TABLE 2 Greene Climacteric Scores expressed as mean and SD for those receiving herbal treatment and on waiting list (control group) at entry and time point 3 (24 weeks)*  Psychological subscale comprises sum of anxiety and depression subscales. MYMOP2 scores shown for the subgroup reporting vasomotor symptoms. *P*-values relate to repeated measures ANOVA for Greene and ANCOVA for MYMOP2.	☐ Incorrect analysis of ITT ☐ Selective reporting of measures (e.g., no effect outcome) ☐ Large losses to F/U ☐ Difference in important prognostic factors at baseline	*quite different from the available evidence in regard to population, intervention, comparison, or outcome)* ☒ Studies are imprecise (*When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)* ☐ Publication Bias *(e.g. pharmaceutical company sponsors study on effectiveness of drug, only small, positive studies found)* <u>Increase Quality Rating if:</u> ☐ Large Effect ☐ Dose-response gradient ☐ Plausible confounders or other biases increase certainty of effect Quality (certainty) of evidence for studies as a whole: ☐ High ☐ Moderate ☐ Low ☒ Very Low

Guideline Recommendations:

Three guidelines included recommendations on CAM therapies for menopausal women, which are outlined below.

The **American Family Physician** in 2016 stated mindfulness-based interventions have been shown to effectively treat low sexual desire and arousal, and acquired anorgasmia. (Evidence Rating – B)

The United Kingdom's National Institute for Health and Care Excellence (NICE)'s **National Collaborating Centre for Women's and Children's Health** in 2015 recommended the following for complementary therapies:

Complementary Therapies and Unregulated Preparations

Explain to women that the efficacy and safety of unregulated compounded bioidentical hormones are unknown.

Explain to women who wish to try complementary therapies that the quality, purity and constituents of products may be unknown.

Advise women with a history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may be of benefit in the relief of vasomotor symptoms, there is uncertainty about:

- Appropriate doses
- Persistence of effect
- Variation in the nature and potency of preparations
- Potential serious interactions with other drugs (including tamoxifen, anticoagulants and anticonvulsants)

The **Society of Obstetricians and Gynecologists of Canada in 2014** provided the following recommendation:

Health care providers may offer identified complementary and alternative medicine with demonstrated efficacy for mild menopausal symptoms (I-B).

Guideline Ratings

Guideline Issuer and Date	AFP 2016	NICE 2015	SOGC 2014

1. Transparency	C	A	B
2. Conflict of interest	NR	A	NR
3. Development group	C	A	NR
4. Systematic Review	B	A	B
5. Supporting evidence	A	A	A
6. Recommendations	A	B	B
7. External Review	NR	NR	NR
8. Currency and updates	B	B	B

See appendix B for full description of the Trustworthy Guideline grading system.

REFERENCES:

1. Basson, R. (2007). "Hormones and sexuality: Current complexities and future directions." Maturitas 57(1): 66-70.
2. Battaglia, C., et al. (2009). "Genistein supplements might not induce clitoral modifications in postmenopausal women: a prospective, pilot study." Journal of Sexual Medicine 6(11): 3132-3138.
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1. Appendix A. GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

Grades and interpretations:

High: Further research is very unlikely to change our confidence in the estimate of effect. Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low: Any estimate of effect is very uncertain.

Type of evidence and starting level

Randomized trial–high Observational study–low Any other evidence–very low

Criteria for increasing or decreasing level

Reductions Study quality has serious (–1) or very serious (–2) problems Important inconsistency in evidence (–1) Directness is somewhat (–1) or seriously (–2) uncertain Sparse or imprecise data (–1) Reporting bias highly probable (–1) **Increases** Evidence of association† strong (+1) or very strong (+2) †Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.

Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania's Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine's "Standards for Developing Trustworthy Clinical Practice Guidelines" (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guide-line does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

A	Guideline development methods are fully disclosed.
B	Guideline development methods are partially disclosed.
C	Guideline development methods are not disclosed.

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:
Who wrote the initial draft
How the committee voted on or otherwise approved recommendations
Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

A	Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).
B	Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.
C	Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.
NR	Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything,

this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

A	Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.
B	Guideline development group includes one of the above, but not both.
C	Guideline developers all from one specialty or organization, and no methodologists.
NR	Affiliations of guideline developers not reported

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A	Guideline includes a systematic review of the evidence or links to a current review.
B	Guideline is based on a review which may or may not meet systematic review criteria.
C	Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:
Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.
Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A	Specific supporting evidence (or lack thereof) for each recommendation is cited and graded
B	Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.
C	Recommendations are not supported by specific evidence.

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

A	Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.
B	Either one or the other of the above criteria is met.
C	Neither of the above criteria are met

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

A	Guideline was made available to external groups for review.
B	Guideline was reviewed by members of the sponsoring body only.
C	Guideline was not externally reviewed.
NR	No external review process is described.

8. Updating and currency of guideline

A	Guideline is current and an expiration date or update process is specified.
B	Guideline is current but no expiration date or update process is specified.
C	Guideline is outdated.

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.