# **APPENDIX A. SEARCH STRATEGY**

## **SYSTEMATIC REVIEWS**

PubMed: November 9, 2015

Search	Query	Items found
#1	Search "Menopause"[Mesh] OR menopaus*[tiab] OR "Climacteric"[Mesh:NoExp] OR "Hot Flashes"[Mesh] OR peri-menopaus*[tiab] OR perimenopaus*[tiab] OR postmenopaus*[tiab] OR post-menopaus*[tiab] OR climacteric*[tiab] OR hot-flash*[tiab] OR hot flash*[tiab] OR hot flush*[tiab] OR night sweat*[tiab] OR vasomotor symptom*[tiab]	91908
#2	Search systematic[sb] OR "Systematic Review"[tiab] OR "Umbrella Review"[tiab] OR meta-analysis[tiab] OR "meta analysis"[tiab]	280172
#3	Search #1 AND #2	2771
#4	Search "Acupuncture Therapy"[Mesh] OR "Acupuncture"[Mesh] OR "Acupressure"[Mesh] OR "acupuncture"[tiab] OR "acupressure"[tiab] OR "electroacupuncture"[tiab]	23260
#5	Search #3 AND #4	45
#6	Search "Mind-Body Therapies" [Mesh: NoExp] OR "Mind-Body Therapy" [tiab] OR "Mind Body Therapy" [tiab] OR "Mind-Body Therapies" [tiab] OR "Mind Body Therapies" [tiab] OR "Mind Body Medicine" [tiab] OR "Breathing Exercises" [Mesh] OR "Breathing Exercise" [tiab] OR "Respiratory Muscle Training" [tiab] OR "Imagery (Psychotherapy)" [Mesh] OR "Guided Imagery" [tiab] OR "Meditation" [Mesh] OR "Meditation" [tiab] OR "Relaxation Therapy" [Mesh] OR "Relaxation Techniques" [tiab] OR "Relaxation Technique" [tiab] OR "Relaxation Technique" [tiab] OR "Mind-Body Relations, Metaphysical" [Mesh] OR "Mindfulness" [Mesh] OR "Mindfulness-based Stress Reduction" [tiab] OR "MBSR" [tiab] OR "paced respiration" [tiab] OR "Hypnosis" [Mesh] OR Hypnoses [tiab] OR Hypnotherapies [tiab] OR Mesmerism [tiab]	
#7	Search #3 AND #6	16
#8	"Yoga"[Mesh] OR "Yoga"[tiab] OR "Tai Ji"[Mesh] OR "Tai Ji"[tiab] OR "Tai-ji"[tiab] OR "Tai Chi"[tiab] OR "T'ai Chi"[tiab] OR "Taiji"[tiab] OR "Taijiquan"[tiab] OR "Qi Gong"[tiab] OR "Qigong"[tiab] OR "Ch'I Kung"[tiab]	4440
#9	Search #3 AND #8	22
#10	Search "Exercise"[Mesh:NoExp] OR "Exercise"[Majr] OR "Circuit-Based Exercise"[Mesh] OR "Muscle Stretching Exercises"[Mesh] OR "Physical Conditioning, Human"[Mesh] OR "Resistance Training"[Mesh] OR "Resistance Training"[Itab] OR "Running"[Mesh] OR "Jogging"[Mesh] OR "Swimming"[Mesh] OR "Walking"[Mesh] OR "Exercise"[tiab] OR "Exercises"[tiab] OR "physical activity"[tiab] OR "aerobic activity"[tiab] OR "Exercise Movement Techniques"[Mesh] OR "Sports"[Mesh]	378950
#11	Search #3 AND #10	
#12	Search #5 OR #7 OR #9 OR #11	247
#13	Search (#12) AND ("2009/01/01"[Date – Publication]: "3000"[Date – Publication])	132
#14	Search #13 AND "English"[lang]	123



## EMBASE: November 9, 2015

Search	Ch Query	
#1	'menopause and climacterium'/exp OR 'menopause':ti,ab OR 'menopausal':ti,ab OR 'peri-menopause':ti,ab OR 'peri-menopause':ti,ab OR 'perimenopause':ti,ab OR 'perimenopause':ti,ab OR post-menopause:ti,ab OR post-menopause:ti,ab OR post-menopause:ti,ab OR 'hot flash':ti,ab OR 'hot flashes':ti,ab OR 'hot flush':ti,ab OR 'hot flushes':ti,ab OR 'night sweat':ti,ab OR 'night sweats':ti,ab OR 'vasomotor symptoms':ti,ab	140,141
#2	'SR'/exp OR 'meta analysis'/exp OR 'Systematic Review':ti,ab OR 'Umbrella Review':ti,ab OR 'meta analysis':ti,ab	200,849
#3	#1 AND #2	2,962
#4	'acupuncture'/exp OR 'acupuncture':ab,ti OR 'acupressure':ab,ti OR 'electroacupuncture':ab,ti	37,866
#5	#3 AND #4	55
#6	'alternative medicine'/exp OR 'Mind Body Therapy':ti,ab OR 'Mind Body Therapies':ti,ab OR 'Mind Body Medicine':ti,ab OR 'breathing exercise'/exp OR 'Breathing Exercise':ti,ab OR 'Breathing Exercises':ti,ab OR 'Respiratory Muscle Training':ti,ab OR 'guided imagery'/exp OR 'Guided Imagery':ti,ab OR 'meditation'/exp OR 'Meditation':ti,ab OR 'transcendental meditation'/exp OR 'relaxation training'/exp OR 'relaxation training':ti,ab OR 'Relaxation Therapy':ti,ab OR 'Relaxation Techniques':ti,ab OR 'Relaxation Technique':ti,ab OR 'Mindfulness-based Stress Reduction':ti,ab OR 'MBSR':ti,ab OR 'paced respiration':ti,ab OR 'hypnosis'/exp OR hypnogenesis:ti,ab OR hypnosis:ti,ab OR hypnosis:ti,ab OR mesmerism:ti	59,899
	#3 AND #6	65
#8	'Qi Gong':ti,ab OR 'Qigong':ti,ab OR 'Chi Kung':ti,ab OR 'Tai Chi'/exp OR 'Tai Ji':ti,ab OR 'Tai Chi':ti,ab OR 'Taiji':ti,ab OR 'Taijiquan':ti,ab OR 'Yoga':ti,ab OR 'kinesiotherapy'/exp	56,974
#9	#3 AND #8	60
#10	'exercise'/exp OR 'sport'/exp OR 'Resistance Training':ti,ab OR 'Exercise':ti,ab OR 'Exercises':ti,ab OR 'physical activity':ti,ab OR 'aerobic activity':ti,ab	510,515
#11	#3 AND #10	249
#12	#5 OR #7 OR #9 OR #11	319
#13	#12 AND [2009-2015]/py	180
#14	#13 AND [english]/lim	173

## Cochrane: November 9, 2015

Search	Query	Items found		
#1	menopause OR menopausal OR peri-menopause OR peri-menopausal OR perimenopause OR perimenopausal OR post-menopause OR post-menopausal OR climacteric OR hot flash OR hot flashes OR hot flush OR hot flushes OR night sweat OR night sweats OR vasomotor symptoms:ti,ab,kw (Word variations have been searched)			
#2	(MH "Acupuncture+") OR (MH "Alternative Therapies+") OR (MH "Mind Body Techniques+") OR (MH "Breathing Exercises+") OR (MH "Qigong") OR (MH "Guided Imagery") OR (MH "Meditation") OR (MH "Hypnosis+") OR (MH "Relaxation Techniques+") OR (MH "Alexander Technique") OR (MH "Tai Chi") OR (MH "Mindfulness") OR (MH "Resistance Training") OR (MH "Muscle Strengthening+") OR (MH "Therapeutic Exercise+") OR (MH "Exercise+") OR (MH "Sports+") OR (MH "Physical Activity") OR TI (acupuncture OR acupressure OR electroacupuncture OR "alternative medicine" OR "Mind Body Therapy" OR "Mind Body Therapies" OR "Qi Gong" OR "Guided Imagery" OR "Mind Body Medicine" OR "Breathing Exercises" OR "Breathing Exercises" OR "Guided Imagery" OR Meditation OR "relaxation training" OR "Relaxation Therapy" OR "Relaxation Techniques" OR "Relaxation Technique" OR hypnosis OR "Alexander Technique" OR "Tai Ji" OR "Tai Chi" OR Taiji OR Taijiquan OR Yoga OR "Mindfulness-based Stress Reduction" OR MBSR OR "paced respiration" OR sport OR "Resistance Training" OR Exercise OR Exercises OR "physical activity" OR "aerobic activity") OR AB (acupuncture OR acupressure OR electroacupuncture OR "alternative medicine" OR "Mind Body Therapy" OR "Mind Body Therapy" OR "Breathing Exercise" OR "Breathing Exercise" OR "Guided Imagery" OR Meditation OR "Breathing Exercise" OR "Breathing Exercise" OR "Qi Gong" OR Qigong OR "Chi Kung" OR "Respiratory Muscle Training" OR "Guided Imagery" OR Meditation OR "Resartion Technique" OR "Relaxation Technique" OR "Tai Ji" OR "Tai Chi" OR Taiji OR Taijiquan OR Yoga OR "Mindfulness-based Stress Reduction" OR "Relaxation Technique" OR "Relaxation Technique" OR "Tai Ji" OR "Tai Chi" OR Taiji OR Taijiquan OR Yoga OR "Mindfulness-based Stress Reduction" OR MBSR OR "paced respiration" OR sport OR "Resistance Training" OR Exercise OR Exercises OR "physical activity" OR "aerobic activity") (Word variations have been searched)	72084		
#3	#1 AND #2 Publication Year from 2009 to 2015	806		
#4	#3 Cochrane Reviews: 15 Other Reviews: 23	38		

## **RANDOMIZED CONTROLLED TRIALS**

## PubMed: February 12, 2016

Search	Query	Items found			
#1	Search "Menopause"[Mesh] OR menopaus*[tiab] OR "Climacteric"[Mesh:NoExp] OR "Hot Flashes"[Mesh] OR peri-menopaus*[tiab] OR perimenopaus*[tiab] OR postmenopaus*[tiab] OR post-menopaus*[tiab] OR climacteric*[tiab] OR hot-flash*[tiab] OR hot flash*[tiab] OR hot flush*[tiab] OR night sweat*[tiab] OR vasomotor symptom*[tiab]	92983			
#2	Search (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp])	2838660			
#3	Search #1 AND #2	33136			
#4	Search "Acupuncture Therapy"[Mesh] OR "Acupuncture"[Mesh] OR "Acupressure"[Mesh] OR "acupuncture"[tiab] OR "acupressure"[tiab] OR "electroacupuncture"[tiab]	23994			
#5	Search #3 AND #4	186			
#6	Search "Mind-Body Therapies" [Mesh: NoExp] OR "Mind-Body Therapy" [tiab] OR "Mind Body Therapy" [tiab] OR "Mind-Body Therapies" [tiab] OR "Mind Body Therapies" [tiab] OR "Mind Body Medicine" [tiab] OR "Breathing Exercises" [Mesh] OR "Breathing Exercises" [Mesh] OR "Breathing Exercises" [tiab] OR "Respiratory Muscle Training" [tiab] OR "Imagery (Psychotherapy)" [Mesh] OR "Guided Imagery" [tiab] OR "Meditation" [Mesh] OR "Meditation" [tiab] OR "Relaxation Therapy" [Mesh] OR "Relaxation Therapy" [tiab] OR "Relaxation Techniques" [tiab] OR "Relaxation Technique" [tiab] OR "Mind-Body Relations, Metaphysical" [Mesh] OR "Mindfulness" [Mesh] OR "Mindfulness-based Stress Reduction" [tiab] OR "MBSR" [tiab] OR "paced respiration" [tiab] OR "Hypnosis" [Mesh] OR Hypnoses [tiab] OR Hypnotherapy [tiab] OR Hypnotherapies [tiab] OR Mesmerism [tiab]	28100			
#7	Search #3 AND #6	79			
#8	Search "Yoga"[Mesh] OR "Yoga"[tiab] OR "Tai Ji"[Mesh] OR "Tai Ji"[tiab] OR "Tai- ji"[tiab] OR "Tai Chi"[tiab] OR "T'ai Chi"[tiab] OR "Taiji"[tiab] OR "Taijiquan"[tiab] OR "Qi Gong"[tiab] OR "Qigong"[tiab] OR "Ch'I Kung"[tiab]	4576			
#9	Search #3 AND #8	84			
#10	Search "Exercise" [Mesh:NoExp] OR "Exercise" [Majr] OR "Circuit-Based Exercise" [Mesh] OR "Muscle Stretching Exercises" [Mesh] OR "Physical Conditioning, Human" [Mesh] OR "Resistance Training" [Mesh] OR "Running" [Mesh] OR "Jogging" [Mesh] OR "Swimming" [Mesh] OR "Walking" [Mesh] OR "Exercise" [tiab] OR "Exercises" [tiab] OR "physical activity" [tiab] OR "aerobic activity" [tiab] OR "Exercise Movement Techniques" [Mesh] OR "Sports" [Mesh]	387613			
#11	Search #3 AND #10	2129			
#12	Search #5 OR #7 OR #9 OR #11	2338			
#13	Search #12 AND ("2012/01/01"[Date - Publication] : "3000"[Date - Publication])	653			
#14	Search #13 AND "English"[lang] Sort by: Author	612			

# EMBASE: February 12, 2016

Search	Query	Items found
	'menopause and climacterium'/exp OR 'menopause':ti,ab OR 'menopausal':ti,ab OR 'peri-menopause':ti,ab OR 'peri-menopause':ti,ab OR 'perimenopause':ti,ab OR 'perimenopausal':ti,ab OR post-menopausal:ti,ab OR post-menopause:ti,ab OR climacteric:ti,ab OR 'hot flash':ti,ab OR 'hot flashes':ti,ab OR 'hot flush':ti,ab OR 'night sweat':ti,ab OR 'menopause':ti,ab OR 'perimenopause':ti,ab OR post-menopause:ti,ab OR climacteric:ti,ab OR 'hot flashes':ti,ab OR 'night sweat':ti,ab OR 'nigh	
	(('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR random* OR factorial* OR crossover* OR cross NEAR/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*) NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp OR 'conference paper'/exp)) AND ([humans]/lim AND [english]/lim AND [2012-2016]/py)	428,259
#3	#1 AND #2	6,358
	'acupuncture'/exp OR 'acupuncture':ab,ti OR 'acupressure':ab,ti OR 'electroacupuncture':ab,ti OR 'alternative medicine'/exp OR 'Mind Body Therapy':ti,ab OR 'Mind Body Therapies':ti,ab OR 'Mind Body Medicine':ti,ab OR 'breathing exercise'/exp OR 'Breathing Exercise':ti,ab OR 'Breathing Exercises':ti,ab OR 'Respiratory Muscle Training':ti,ab OR 'guided imagery'/exp OR 'Guided Imagery':ti,ab OR 'meditation'/exp OR 'Meditation':ti,ab OR 'transcendental meditation'/exp OR 'relaxation training':ti,ab OR 'Relaxation Therapy':ti,ab OR 'Relaxation Techniques':ti,ab OR 'Relaxation Techniques':ti,ab OR 'Relaxation Technique':ti,ab OR 'Alexander Technique':ti,ab OR 'mindfulness'/exp OR 'Mindfulness-based Stress Reduction':ti,ab OR 'MBSR':ti,ab OR 'paced respiration':ti,ab OR 'hypnosis'/exp OR hypnogenesis:ti,ab OR hypnosis:ti,ab OR hypnosis:ti,ab OR mesmerism:ti,ab OR 'Qi Gong':ti,ab OR 'Qigong':ti,ab OR 'Chi Kung':ti,ab OR 'Tai Chi'/exp OR 'Tai Ji':ti,ab OR 'Tai Chi':ti,ab OR 'Taiji':ti,ab OR 'Taijiquan':ti,ab OR 'Yoga':ti,ab OR 'Resistance Training':ti,ab OR 'Exercise':ti,ab OR 'Exercises':ti,ab OR 'physical activity':ti,ab OR 'aerobic activity':ti,ab	630,791
	#3 AND #4	849

## CINAHL: February 12, 2016

Search	Query	
	(MH "Menopause+") OR TI (menopause OR menopausal OR "peri-menopause" OR "peri-menopausal" OR perimenopause OR perimenopausal OR postmenopause OR postmenopausal OR "post-menopause" OR "post-menopausal" OR climacteric OR "hot flash" OR "hot flashes" OR "hot flush" OR "hot flushes" OR "night sweat" OR "night sweats" OR "vasomotor symptoms") OR AB (menopause OR menopausal OR "peri-menopause" OR "peri-menopausal" OR perimenopause OR perimenopausal OR postmenopause OR postmenopausal OR "post-menopause" OR "post-menopausal" OR climacteric OR "hot flash" OR "hot flashes" OR "hot flush" OR "hot flushes" OR "night sweat" OR "night sweats" OR "vasomotor symptoms")	22,202
	(MH "Acupuncture+") OR (MH "Alternative Therapies+") OR (MH "Mind Body Techniques+") OR (MH "Breathing Exercises+") OR (MH "Qigong") OR (MH "Guided Imagery") OR (MH "Meditation") OR (MH "Hypnosis+") OR (MH "Relaxation Techniques+") OR (MH "Alexander Technique") OR (MH "Tai Chi") OR (MH "Mindfulness") OR (MH "Resistance Training") OR (MH "Muscle Strengthening+") OR (MH "Therapeutic Exercise+") OR (MH "Exercise+") OR (MH "Sports+") OR (MH	341,974



Search	Query	Items found
	"Physical Activity") OR TI (acupuncture OR acupressure OR electroacupuncture OR "alternative medicine" OR "Mind Body Therapy" OR "Mind Body Therapies" OR "Mind Body Medicine" OR "Breathing Exercise" OR "Breathing Exercises" OR "Qi Gong" OR Qigong OR "Chi Kung" OR "Respiratory Muscle Training" OR "Guided Imagery" OR Meditation OR "relaxation training" OR "Relaxation Therapy" OR "Relaxation Techniques" OR "Relaxation Technique" OR hypnosis OR "Alexander Technique" OR "Tai Ji" OR "Tai Chi" OR Taiji OR Taijiquan OR Yoga OR "Mindfulness-based Stress Reduction" OR MBSR OR "paced respiration" OR sport OR "Resistance Training" OR Exercise OR Exercises OR "physical activity" OR "aerobic activity") OR AB (acupuncture OR acupressure OR electroacupuncture OR "alternative medicine" OR "Mind Body Therapy" OR "Mind Body Therapies" OR "Mind Body Medicine" OR "Breathing Exercise" OR "Breathing Exercises" OR "Qi Gong" OR Qigong OR "Chi Kung" OR "Respiratory Muscle Training" OR "Guided Imagery" OR Meditation OR "relaxation training" OR "Relaxation Therapy" OR "Relaxation Techniques" OR "Relaxation Technique" OR "Tai Ji" OR "Tai Chi" OR Taiji OR Taijiquan OR Yoga OR "Mindfulness-based Stress Reduction" OR MBSR OR "paced respiration" OR sport OR "Resistance Training" OR Exercise OR Exercise OR "physical activity" OR "aerobic activity")	
S3	S1 AND S2 Published Date: 20120101-20160231	1,029
S4	TI ("randomized controlled trial" OR "controlled clinical trial" OR "randomized" OR "randomized" OR "randomization" OR "randomization" OR "placebo" OR "randomly" OR "trial" OR "groups" OR AB ("randomized controlled trial" OR "controlled clinical trial" OR "randomized" OR "randomized" OR "randomization" OR "placebo" OR "randomly" OR "trial" OR "groups") OR (MH "Randomized Controlled Trials")	391,791
<b>S</b> 5	S3 AND S4	345
S6	S5 NOT PT (Book OR Book Chapter OR Book Review OR Case Study OR Commentary OR Doctoral Dissertation OR Editorial OR Letter OR Masters Thesis OR Pamphlet OR Pamphlet Chapter OR Poetry)	339

### APPENDIX B. CRITERIA USED IN QUALITY ASSESSMENT

#### SYSTEMATIC REVIEWS

General instructions: The purpose of this rating tool is to evaluate the scientific quality of SRs. It is not intended to measure the literary quality, importance, relevance, originality, or other attributes of SRs.

Step 1: First determine whether it is a SR (SR). Systematic reviews are studies that: 1) include an explicit and adequate search, 2) apply prespecified eligibility criteria, and 3) consider quality of included studies or risk of bias assessment, and/or describe plans to synthesize or attempt to synthesize findings quantitatively and/or qualitatively.

Step 2: For SRs, grade each of the criteria listed below as "Yes," "No," "Can't tell," or "Not Applicable." Factors to consider when making an assessment are listed under each criterion. For each domain, summarize key methods, level of concern overall (low, high, unclear), and rationale for concerns.

ST	STUDY ELIGIBILITY CRITERIA				
1.	Was an 'a priori' design provided?  The research question and inclusion criteria should be established before the conduct of the review and the review should adhere to pre-defined objectives and eligibility criteria.				
	Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."				
	[] Yes [] No [] Can't tell [] N/A Comment: No published protocol; however, their approach is reasonable				
2.	Were study eligibility criteria clearly specified?  Note: Criteria should be sufficiently detailed to allow replication of study  [] Yes [] No [] Can't tell [] N/A  Comment:				

3. Were restrictions in eligibility criteria appropriate? Restrictions based on study characteristics (eg, date, sample size, study quality, outcomes measured) and based on sources of information (eg, publication status or format, language) should be appropriate?

[] Yes

[] No

[] Can't tell

[] N/A

Comment: No language or country restrictions given

Summarize key methods related to Eligibility:

Summarize <u>concerns</u> (low/high/unclear) and your <u>rationale</u> regarding specification of study eligibility criteria:

#### IDENTIFICATION AND SELECTION OF STUDIES

#### 4. Was a comprehensive literature search performed?

At least 2 electronic sources should be searched and electronic searches should be supplemented by consulting: reference lists from prior reviews, textbooks, or included studies; specialized registries (eg, Cochrane registries); or queries to experts in the field.

Note: If at least 2 sources + one supplementary strategy used, select "yes"; grey literature search counts as supplementary



v a	Somotor Sym	iptoms		
	[] Yes Comment:	[] No	[] Can't tell	[] N/A
5.	Were the te		d structure of t	the search strategy likely to retrieve as many eligible studies
				ribe: search date, databases used, and search terms (Key words and where feasible the search strategy should be provided).
	[] Yes Comment:	[] No	[] Can't tell	[] N/A
6.		ctions I [] No		publication format, or language appropriate? [] N/A
7.	gives appro	reports priate re	the number of st	tudies identified through searches, the numbers excluded, and ding – based on explicit inclusion/exclusion criteria. Two or more cisions.
	[] Yes Comment:	[] No	[] Can't tell	[] N/A
Su	mmarize <u>key</u>	method	s related to Stud	dy Selection:
Su	mmarize <u>con</u>	cerns (lo	ow, high, unclea	r) and rationale regarding Study Selection
D/	ATA COLLI	ECTIO	N AND STUD	Y APPRAISAL
8.	Did two or none rater ov Was an app [] Yes	nore inv ver-read propriate [] No	estigators abstra	resolve disagreements ( <i>eg</i> , a consensus procedure)? [] N/A
9.	In an aggreg participants (eg, age, rad	gated fo , interve ce, sex,	rm such as a tal ntions and outco relevant socioe	ble, data from the original studies should be provided on the omes. The ranges of characteristics in all the studies analyzed conomic data, disease status, duration, severity or other diseases) ail to allow the review authors and readers to interpret the results.
	Note: Accep	otable if	not in table form	nat as long as they are described as above.
	[] Yes Comment:	[] No	[] Can't tell	[] N/A

#### 10. Was the scientific quality of the included studies assessed and documented?

<u>A priori</u> methods of assessment should be provided and criteria used to assess study quality specified in enough detail to permit replication.

Note: Can include use of a quality scoring tool or checklist, eg, Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or



	"high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).	
	[] Yes [] No [] Can't tell [] N/A Comment:	
	nmarize <u>key methods</u> related to data collection/ROB: nmarize <u>concerns</u> regarding data collection/ROB:	
SY	NTHESIS AND FINDINGS	
11.	Was the scientific quality of the included studies used appropriately in formulating conclusions?  The results of the methodological rigor and scientific quality should be considered in the analysis (eg subgroup analyses) and the conclusions of the review, and explicitly stated in formulating recommendations.	,
	Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 10.	/
	[] Yes [] No [] Can't tell [] N/A Comment:	
12.	Were the methods used to combine the findings of studies appropriate?  For pooled results, the synthesis should be appropriate given the nature and similarity of included studies (conceptual homogeneity), and an accepted quantitative method of pooling should be used (ie, more than simple addition; eg, random-effects or fixed-effect model). If only qualitative analyses are completed, the study should describe the reasons that quantitative analyses were not completed. [] Yes [] No [] Can't tell [] N/A@ Comment:.	
13.	<b>Was between-study variation (heterogeneity) minimal or addressed in the synthesis?</b> For pooled results, a qualitative and quantitative assessment of homogeneity (Cochran's Q and/or I <sup>2</sup> ) should be performed.	١
	Note: Indicate "yes" if they explain that they cannot pool because of heterogeneity/variability between interventions.	1
	[] Yes [] No [] Can't tell [] N/A@ Comment:	
14.	Was the likelihood of publication bias assessed? Publication bias tested using funnel plots, test statistics ( <i>eg,</i> Egger's regression test), and/or search of trials registry for unpublished studies.	of
	Note: If no test values, clinical trials.gov search, or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.	
	[] Yes [] No [] Can't tell [] N/A Comment:	

15. Are the stated conclusions supported by the data presented?

Were the conclusions made by the author(s) supported by the data and/or analyses reported in the SR? Conclusions should address limitations of the SR and limitations of the primary studies.





Nonpharmacologic Treatments for Menopause-Associated Vasomotor Symptoms	Evidence-based Synthesis Prograr
Conclusions should consider relevance of the included studie [] Yes [] No [] Can't tell [] N/A	s to the research question.
Summarize key methods related to synthesis: Summarize concerns regarding synthesis:	
OTHER	
16. Was the conflict of interest stated?  Potential sources of support should be clearly acknowledged Note: To get a "yes," must indicate source of funding or support included studies  [] Yes [] No [] Can't tell [] N/A  Comment: Competing interest for SR authors given (none) but	ort for the SR AND for each of the
Step 3: Rate the overall quality of the SR as "Good," "Fair," or and summarize major reasons for rating in the comments bo	

and summarize major reasons for rating in the comments box.

**Good** = After considering items 1-15, item 15 is rated "Yes" with no important limitations. This means that few of the items 1-14 are rated "No," and none of the limitations are thought to decrease the validity of the conclusions. If items 3, 4, 7, 9, 10, 11 or 12 are rated "no", then the review is likely to have major flaws

**Fair** = After considering items 1-15, item 15 is rated "Yes," but with at least some important limitations. This means that enough of the items 1-15 are rated "No" to introduce some uncertainty about the validity of the conclusions.

**Poor** = After considering items 1-15, item 15 is rated "No." This means that several of items 1-15 are rated "No," introducing serious uncertainty about the validity of the conclusions.

Overall rating comments:		



### Concerns regarding specifications of eligibility criteria

Low concern	Considerable effort has been made to clearly specify the review question and objectives, and to pre-specify and justify appropriate and detailed eligibility criteria that have been adhered to during the review
High concern	Studies that would have been important and relevant to answering the review question are likely to have been excluded from the review, either due to the lack of pre-specified objectives and eligibility criteria, or because inappropriate restrictions were imposed or studies that are not appropriate for addressing the review question have been included.
Unclear concern	Insufficient information is reported to make a judgement about risk of bias.

### Concerns regarding methods used to identify and/or select studies

Low concern	Given the review question and eligibility criteria as assessed in Domain 1, a substantial effort has been made to identify as many relevant studies as possible through a variety of search methods using a sensitive and appropriate search strategy and steps were taken to minimise bias and errors when selecting studies for inclusion.
High concern	Some eligible studies are likely to be missing from the review.
Unclear concern	There is insufficient information reported to make a judgement on risk of bias.

### Concerns regarding methods used to collect data and appraise studies

Low concern	Given the studies included in the review as assessed in domain 2, risk of bias was assessed using appropriate criteria, data extraction and risk of bias assessment involved two reviewers, and relevant study characteristics and results were extracted
High concern	Some bias may have been introduced through the data collection or risk of bias assessment processes.
Unclear concerns	There is insufficient information reported to inform a judgement on risk of bias.



#### Concerns regarding methods used to synthesize results

Low concern	The synthesis is unlikely to produce biased results, because any limitations in the data were overcome, or the findings were so convincing that the limitations would have little impact
High concern	The synthesis is likely to produce biased results, because (i) potential biases were ignored (within and/or across studies), (ii) important between-study variation was not accounted for; (iii) there were important inadequacies in the methodology; or (iv) findings are incompletely reported in a way that raises concerns.
Unclear concerns	There is insufficient information reported to make a judgement on risk of bias.

#### References

Marinopoulos SS, Dorman T, Ratanawongsa N, et al. Effectiveness of continuing medical education. Evid Rep Technol Assess (Full Rep). 2007(149):1-69.

Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. Lancet. 1999;354(9193):1896-1900.

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#### RANDOMIZED CONTROLLED TRIALS

General instructions: Rate each risk of bias item listed below as "Low," "High," or "Unclear."

#### Rating of individual items:

1.Selection bias:

#### Domain: Random sequence generation

(<u>Support for judgement:</u> Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.)

#### Was the allocation sequence adequately generated?

Low risk High risk Unclear risk

Comment			



#### **Domain: Allocation concealment?**

(Support for judgement: Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment)

Was allocation adequately concealed?	
Low risk High risk Unclear risk	
Comment	
2. Performance bias	
Domain: Blinding of participants and "treating" personnel (ie, the person(s) delivering the intervention).	
(Support for judgement: Describe all measures used, if any, to blind study participants and persifrom knowledge of which intervention a participant received. Provide any information relating to with the intended blinding was effective.)	
Was knowledge of the allocated intervention adequately prevented during the study?	
Low risk High risk Unclear risk Outcome NR	
Comment	
3a. Detection bias (VMS symptoms):	
Domain: Blinding of outcome assessment	
(Support for judgement: Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whethe intended blinding was effective.)	r the
Was knowledge of the allocated intervention adequately prevented from outcome assesso	rs?
Low risk High risk Unclear risk Outcome NR	
Comment	



#### 3b. Detection bias (outcomes measured by self-report, ie, depression, anxiety, sleep, QoL, etc):

#### **Domain: Blinding of outcome assessment**

(Support for judgement: Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.)

	olinding was	,		
Low risk	High risk	e allocated inte	ervention adequately prevented from outcome a Outcome NR	ssessors?
Comm	ent			
3c. Detec	tion bias (A	dverse effects)	:	J
Domain:	Blinding of	outcome asses	sment	
knowledge		tervention a part	ll measures used, if any, to blind outcome assessor ticipant received. Provide any information relating to	
Was kno	wledge of th	ne allocated into	ervention adequately prevented from outcome a	ssessors?
Low risk	High risk	Unclear risk	Outcome NR	
Comm	ent			
4. Attritio	n bias:			
<u>Domain:</u>	Incomplete	outcome data		
attrition ar numbers i	nd exclusions in each interv	s from the analys vention group (co	ne completeness of outcome data for each main out sis. State whether attrition and exclusions were repo compared with total randomized participants), reason d any re-inclusions in analyses performed by the re	orted, the ns for
Were inc	omplete out	come data ade	equately addressed?	
Low risk	High risk	Unclear risk		
Comm	ent			



Unclear risk

#### 5. Reporting bias:

Low risk

#### **Domain: Selective outcomes reporting**

High risk

(**Support for judgement:** State how the possibility of selective outcome reporting was examined by the review authors, and what was found.)

Are reports of the study free of suggestion of selective outcome reporting? (i.e., the author states they will measure an outcome but do not report it)

Comment
6. Other
Domain: Other sources of bias
(Support for judgement: State any important concerns about bias not addressed in the other domains in the tool.  If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.)
Are reports of the study free from other bias due to problems not covered above?  Low risk High risk Unclear risk
Comment
Overall risk of bias rating
_ow Unclear High Narrative:



Risk of Bias	Interpretation	Criteria
Low risk of bias	Bias, if present, is unlikely to alter the results seriously.	Adequacy of random sequence generation, allocation concealment, and blinding scored as "low risk of bias" and no important concerns related to the other domains.
Unclear risk of bias	A risk of bias that raises some doubts about the results	One or two domains are scored "not clear" or not done.
High risk of bias	Bias may alter the results seriously	More than 2 domains are scored as "not clear" or not done

<sup>\*</sup> Items contained in Cochrane Risk of Bias Tool

# **APPENDIX C. QUALITY ASSESSMENT RATINGS**

References cited in this appendix appear in the reference list of the main report.

### **SYSTEMATIC REVIEWS**

Publication	Eligibility Criteria	ID/Select Studies	Data Collection	Synthesis	Overall
Acupuncture					
Dodin 2013 <sup>40</sup>	Low	Low	Low	Low	Good
Garcia 2015 <sup>41</sup>	Low	High	Low	Low	Fair
Garcia 2013 <sup>64</sup>	Low	High	Low	Low	Fair
Yoga					
Cramer 2012 <sup>43</sup>	Low	Low	Low	Low	Good
Exercise					
Daley 2014 <sup>44</sup>	Low	Low	Low	Low	Good
Meditation/Mindfulness/ Hypnosis/ Relaxation/Mixed					
Saensak 2014 <sup>45</sup>	Low	Low	Low	Low	Good
Woods 2014 <sup>46</sup>	Low	Low	High	High	Fair
Cramer 2015 <sup>49</sup>	Low	Low	Low	High	Fair
Innes 2010 <sup>47</sup>	Low	Low	Low	High	Fair
Rada 2010 <sup>48</sup>	Low	Low	Low	Low	Good



### **RANDOMIZED CONTROLLED TRIALS**

Publication	1	2	3	4	5	6	7	8	9	Overall
Acupuncture										
Avis 2016 <sup>52</sup>	LR	LR	HR	LR	LR	Outcome NR	LR	LR	UR	Low
Ee 2016 <sup>50</sup>	LR	LR	LR	LR	LR	LR	LR	LR	LR	Low
Mao 2015 <sup>51</sup>	LR	LR	LR	LR	LR	LR	LR	LR	LR	Low
Nedeljkovic 2014 <sup>53</sup>	LR	LR	LR	LR	LR	UR	LR	LR	UR	Low
Yoga										
Avis 2014 <sup>54</sup>	UR	UR	HR	LR	UR	UR	LR	LR	HR	High
Ngowsiri 2014 <sup>55</sup>	HR	HR	HR	HR	HR	HR	HR	HR	UR	High
Exercise										_
Daley 2015 <sup>62</sup>	LR	LR	UR	UR	UR	Outcome NR	LR	LR	HR	Unclear
Duijts 2012 <sup>63</sup>	LR	UR	HR	LR	LR	Outcome NR	LR	LR	LR	Low
Meditation/Mindfulness/										
Hypnosis/Relaxation/Mixed										
Carpenter 2013 <sup>56</sup>	LR	LR	HR	LR	LR	LR	UR	LR	LR	Low
Huang 2015 <sup>57</sup>	LR	LR	LR	LR	UR	UR	LR	LR	LR	Low
Lindh-Astrand 2013 <sup>58</sup>	LR	LR	HR	UR	UR	UR	LR	LR	LR	Unclear
Lindh-Astrand 2015 <sup>61</sup>	LR	LR	HR	LR	Outcome NR	Outcome NR	HR	LR	HR	High
Saensak 2013 <sup>59</sup>	LR	LR	LR	LR	Outcome NR	Outcome NR	LR	LR	HR	Low
Sood 2013 <sup>60</sup>	HR	HR	UR	LR	LR	LR	UR	LR	UR	Unclear

Risk of bias abbreviations: HR = High risk; LR = Low risk; UR = Unclear risk

Column headings:

- 1. Randomization adequate
- 2. Allocation concealment
- 3. Performance bias4. Detection bias: VMS
- 5. Detection bias: Health-related quality of life
- 6. Detection bias: Adverse effects
- 7. Incomplete outcome
- 8. Selective outcomes reporting
- 9. Other bias



# **Risk of Bias Summary for New RCTs**

Sood, 2013	Saensak, 2013	Ngowsiri, 2014	Nedeljkovic, 2014	Mao, 2015	Lindh-Astrand, 2015	Lindh-Astrand, 2013	Huang, 2015	Elkins, 2013	Ee, 2016	Duijts, 2012	Daley, 2015	Carpenter, 2013	Avis, 2016	Avis, 2014	
•	•	•	•	•	•	•	•	•	•	•	•	•	•	?	Random sequence generation (selection bias)
•	•	•	•	•	•	•	•	•	•	?	•	•	•	?	Allocation concealment (selection bias)
?	•	•	•	•	•	•	•	•	•	•	•	•	•	•	Blinding of participants and personnel (performance bias)
•	•	•	•	•	•	~	•	•	•	•	•	•	•	•	Blinding of outcome assessment (detection bias-VMS)
•		•	•	•		•	?	•	•	•	•	•	•	•	Blinding of outcome assessment (detection bias- HRQoL)
•		•	?	•		•	?	•	•			•		•	Blinding of outcomes assessment (detection bias- AE)
?	•	•	•	•	•	•	•	•	•	•	•	?	•	•	Incomplete outcome data (attrition bias)
•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	Selective reporting (reporting bias)
?	•	?	?	•	•	•	•	•	•	•	•	•	•	•	Other bias
?	•	•	•	•	•	?	•	•	•	•	?	•	•	•	Overall

# APPENDIX D. MEASUREMENT SCALES FOR MENOPAUSE

### **VASOMOTOR SYMPTOMS (VMS)**

- Daily Hot Flash Diary (Sloan et al, 2001). A measure of self-reported hot flashes, night sweats and/or severity of hot flashes typically using a dairy to record the frequency and severity of hot flashes using a 4-point scale: mild, moderate, severe, very severe to provide a hot flash index (sum of the number of hot flashes multiplied by severity).
- Hot Flush Rating Scale (Hunter et al, 1995). Yields a hot flush frequency score (2 items that each have times/day and days/week summed to give number of hot flushes and night sweats that have caused waking in the past week) and a hot flush problem rating (3 items, each scored 1 to 10).
- Vasomotor subscales. From instruments such as the Green Climacteric Scale, the Kupperman Menopausal Index, the Women's Health Questionnaire (WHQ), and the Menopause-specific Quality of Life (MENQOL), Health-related Quality of Life (HRQOL) Specific to Perimenopausal Symptoms (*ie*, measures used to report menopause-related HRQOL).
- Greene Climacteric Scale. 21 questions covering 5 domains: anxiety, depression, somatic symptoms, vasomotor symptoms, and sexual function. Each question is answered on a 4-point Likert scale. The answers to all 21 questions are summed to give a total quality-of-life measure; a higher score indicates a worse quality of life.
- Global quality of life. Not a specific measure but a term used for single-item visual analogue scales designed to measure overall quality of life when 0 is the lowest possible and 100 is the highest possible quality of life.
- Hot Flush Behavior Scale (or Hunter menopause scale). A measure of behavioral reactions to VMS.
- Hot Flash Related Daily Interference Scale. A 10-item measure for assessing the impact of vasomotor symptoms on daily activities in nine specific domains within the past week (work, social activities, leisure activities, sleep, mood, concentration, relation with others, sexuality, and enjoyment of life) and overall quality of life.
- Kupperman Menopausal Index. A numerical index that scores 11 menopausal symptoms: hot flushes, paresthesia, insomnia, nervousness, melancholia, vertigo, weakness, arthralgia or myalgia, headache, palpitations, and formication. Each symptom is rated from 0 to 3 according to severity. The scores are weighted and a total sum is calculated with a higher score indicating a worse quality of life.
- Menopause-specific quality of life (MENQOL) (Lewis et al, 2005). 29 questions covering 4 domains: vasomotor, psychosocial, physical, and sexual. The scoring for each question is 1–"No", 2–"Yes, but not at all bothered" through 8–"Yes, extremely



bothered." The scores for each question are summed for a total quality-of-life score where a higher score indicates a worse quality of life.

- Menopause Rating Scale. Scores 11 menopausal symptoms: hot flushes, heart discomfort, sleep problems, depressive mood, irritability, anxiety, physical and mental exhaustion, sexual problems, bladder problems, vaginal dryness, and joint and muscular discomfort. Each item is scored from 0-4. The scores are summed for a total quality-of-life score, in which a higher score indicates a worse quality of life.
- Women's Health Questionnaire (WHQ). Contains menopause-specific quality of life subscales enabling a detailed assessment of dimensions of emotional and physical health, such as depression, anxiety, sleep problems, somatic symptoms, with optional subscales for menstrual problems and sexual difficulties.
- Utian Quality of Life Scale (UQOL). 23 items scored 1 to 5; 4 subscales (occupational, health, emotional, sexual) and total score.

### **GENERAL HEALTH-RELATED QUALITY OF LIFE (HRQOL)**

- SF-36 or Rand-36. Consists of 36 questions covering 8 domains: physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, energy/fatigue, pain, and general health perceptions. This questionnaire produces outcomes on total quality of life, subscores for each of the domains, a physical health sub-score, or a mental health sub-score. For this scale, the higher the score, the better the quality of life.
- Functional Assessment of Cancer Therapy-Endocrine Subscale (FACT-ES). An 18-item instrument designed to measure the side effects and benefits of hormonal treatments used in women with breast cancer.
- EQ-5D-3L. Evaluates function in 5 domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, extreme problems.
- EQ-5D-5L. Like the EQ-5D-3L but each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems.
- EQ VAS. Records the respondent's self-rated health on a 20 cm vertical, visual analogue scale with endpoints labelled "the best health you can imagine" and "the worst health you can imagine."
- Functional Assessment of Cancer Therapy-Breast (FACT-B). Measures overall quality of life and has 5 subscales including physical, social, emotional, functional well-being, and breast concerns.

# APPENDIX E. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Reviewer	Comment	Response		
Question 1. Are the objectives, scope, and methods for this review clearly described?				
1	Yes	Acknowledged		
2	Yes	Acknowledged		
3	No: I had difficulty with statements like "judged to be of high quality" (p 7, line 48) and "poor quality" (p 7, line 57) that came before the detailed Methods explanation and discussion of how "quality" was judged. This may just be the ESP format but I found it hard to read statements like these w/o knowing more. This is a minor point, but may be best to avoid the statement HT "only for short-term use" as this doesn't encompass newer recommendations to individualize care. These alternative/integrative methods are really a move toward individualization or personalization of health.	We added a statement in the abstract that briefly defines good- and fair-quality reviews.  We clarified the statement about current recommendations for duration of HT use to encompass guidance around individualization of care as recommended.		
4	Yes	Acknowledged		
Question 2.	Are there any <u>published</u> or <u>unpublished</u> studies that we may h	ave overlooked?		
1	No	Acknowledged		
2	No	Acknowledged		
3	No	Acknowledged		
4	No	Acknowledged		
Question 3. Is there any indication of bias in our synthesis of the evidence?				
1	No	Acknowledged		
2	No	Acknowledged		
3	No	Acknowledged		
4	<b>Yes</b> : Lesi et al. J. Clin Onc, 2016 studied acupuncture vs. usual care (included 190 women with breast cancer)	This study was published after our search date and including it in the analysis without completing an updated search for other recently published studies could introduce bias. However, we added a citation to this study in the discussion and note that results were consistent with our review findings.		

Reviewer	Comment	Response		
Question 4: Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.				
1	This is an incredibly extensive and thorough review. It would be helpful to indicate if at all possible if the results from the meta-analysis that were statistically significant translated to clinically meaningful changes in the outcomes (e.g. frequency of VMS). Some of these look quite small and it is difficult to determine whether these changes would make a meaningful difference to women struggling with VMS.	Thank you for this comment. For daily hot flash frequency, which was measured in a consistent manner, we were able to make this transformation. For hot flash severity and health-related quality-of-life, there was too much variability in measurement to make a reliable transformation back to natural units. Although we wanted to add information on the minimum clinically important difference for hot flash frequency, there is no consensus on this value.		
2	Very thorough review of existing SR's and RCTs on topics related to nonpharmacological therapies for VMS. This review was well-written, clear, and described each area very well. Two suggestions: 1. Please add information on the inclusion/exclusion criteria for the SR's and RCTs that were reviewed for this synthesis. 2. Please provide information on the strength of evidence guidelines that were used by the authorsthere is a reference to AHRQ's Methods, however, even a short description of what good, fair, etc entails would be helpful for the reader. Otherwise, well done, comprehensive review.	Eligibility criteria and definitions of the strength of evidence are presented in detail in the Methods section		
3	See above, well written, difficult topic to take on. This provides important contributions to Women's Health.	Thank you.		

Reviewer	Comment	Response
4	I had the pleasure reviewing the Non-pharmacological treatment of menopause associated vasomotor symptoms prepared for the Department of Veterans Affairs (Lead author: John Williams). This review is thorough, well-written, with appropriately stated conclusions. I think this will have important implications for improving VM symptom management.  A few aspects should be addressed to enhance the quality of this	Thank you
	manuscript	
	One new paper just published is highly relevant to this review. Lesi et al. J. Clin Onc, 2016 studied acupuncture vs. usual care (included 190 women with breast cancer)	See response to this comment above.
	I am not sure whether there would be enough trials to do a meaningful comparison for acupuncture against non-hormonal based drugs (Gabapentin, Venlafaxine) for effect size, adverse events, and treatment durability. I am aware of at least two such studies. This may be a particularly useful comparison given that for those women who do not want hormones, these are viable options. The authors advocated for comparative effectiveness trials so these analyses (even a qualitative review) may help the authors to be more explicit on what these comparisons should focus on, main effects on hot flashes, adverse effects, durability.	We considered but did not think it appropriate to compare acupuncture with any drug therapy (i.e., drugs from differing classes with differing mechanisms of effect). Our <i>a priori</i> threshold for meta-analysis was 3 trials and comparisons of acupuncture to differing drug classes, and so this did not meet that threshold.
	Another aspect is the durability of treatment effect. Currently, this is buried in the text. For women, they want to know if they choose a therapy (acupuncture, yoga, or drugs), if the reduction of their symptoms are durable or they need to get continued treatments. It will be great to summarize these findings as it will have impact on patient quality of life and health care utilization (getting a defined course of acupuncture/drugs will have very different cost implications for VA than getting continued treatment for a long period of time	Thank you for this comment. We have revised the text to more clearly identify timing of outcome assessments and whether the durability of treatment effect was addressed.

Reviewer	Comment	Response
4 continued	Other minor edits	
	Introduction:	
	P11line10: change "2" to "two"	Per VA report editorial style, all numbers below 10 (except "one") are to use numerals.
	P11line 22: please add "severity"	This line of the report is in the Data Analysis section of the Methods, which is not concerned with frequency or severity of VMS. Perhaps the reviewer meant a different line. We have carefully reviewed the manuscript to ensure that frequency and severity are used properly and are present where necessary.
	In third paragraph of the introduction, please discuss that hormonal treatment is contraindicated for breast cancer survivors or those with high risk for breast cancer	Text was added to note that HT is contraindicated in women with a history of breast cancer or those at high risk for breast cancer.
	Page 45: "though it found no difference due to hypnosis when compared to treatment with gabapentin". I would assume gabapentin is an active control since it has been shown to be more beneficial than placebo for hot flashes	This sentence was adjusted to clarify that gabapentin is an active comparator.