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The Effectiveness of Herbal medicine on Hot Flashes in Post-menopausal Women: A Systematic Review and Bayesian Network Meta-analysis

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Abstract

This study conducted a network meta-analysis (NMA) to comprehensively evaluate the efficacy of herbal medicine in treating hot flashes among post-menopausal women. The research aimed to identify the most commonly used herbs in this context. Following PRISMA-NMA guidelines, a systematic search was performed on Persian and English databases, including SID, Magiran, Scopus, PubMed, Science Direct, Google Scholar, and Web of Science(ISI), until April 2023. Keywords were selected based on the PICO criteria. Bayesian network meta-analysis using the "BUGSnet" package in R software was employed for data synthesis.The effect estimates and credible intervals from the model indicated statistically significant differences at the 95% level between placebo and treatments involving Silybum marianum, Soy, and Valerian for the severity outcome. Silybum marianum and Soy ranked higher than other treatments, suggesting their superior efficacy in managing hot flashes.The hierarchical ranking of these herbal medicines provides insights that could inform the development of treatment algorithms, offering potential validation in prospective clinical trials.

KEYWORDS: Bayesian Network meta-analysis, post-menopausal women, hot flashes, herbal medicine.

Introduction

Menopause marks a natural phase in a woman's life characterized by the cessation of menstruation, officially acknowledged after 12 consecutive months without menstrual cycles. Ovarian aging leads to a decline in estrogen levels, reaching <25 pg/mL. During this transition, abnormal estradiol (E2) production persists until it stabilizes at lower levels in post-menopausal women. Hot flashes emerge as the predominant symptom during menopause, significantly impacting the quality of life for women. These hormonal shifts not only trigger hot flashes but also induce distressing symptoms and affect the vasomotor system [1].

Hot flashes in post-menopausal women manifest as transient spontaneous warmth or a sensation of heat on the face and neck, prompting medical attention [2]. Affecting over 75% of post-menopausal women, with more than 30% experiencing moderate to severe episodes for at least a decade [1], the frequency varies across cultures. For instance, hot flash prevalence ranges from 10 to 20 percent in Indonesian post-menopausal women, 10 to 25 percent in Chinese post-menopausal women, and 58 to 93 percent in Western women. Lifestyle and a diet rich in phytoestrogens from soy contribute to these variations [3].

Traditionally, hormone therapy, including estrogen therapy and combination therapies, has been the primary approach for managing hot flashes. However, concerns about long-term adverse effects such as thromboembolism, breast cancer, and stroke have led post-menopausal women to explore alternative therapies. In Switzerland, complementary medicine, particularly traditional Chinese medicine, has gained prominence. The United States, under the Food and Drug Administration Act of 1994, categorizes herbs as dietary supplements, exempting them from pre-sale safety or efficacy testing. Herbal medicine, a historical remedy embraced by post-menopausal women globally, has garnered attention in research studies [4].

This study employs network meta-analysis to assess the effectiveness of various treatments, comparing them based on direct and indirect evidence extracted from clinical trials [5]. The primary objective is to identify frequently used herbs by conducting a comprehensive network meta-analysis (NMA) evaluating the treatment effects of herbal medicine on hot flashes in post-menopausal women.

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Method

The methodology adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines [6]. The study involved a systematic search of databases, organization of documents for review, application of author-defined criteria for study selection, extraction of information, analysis, and ultimately, the presentation of the final report.

Data Resources and Search Strategies

In our quest for relevant articles, a systematic search encompassing both Persian and English databases was conducted. The databases included SID, Magiran, Scopus, PubMed, Science Direct, Google Scholar, and Web of Science(ISI), with the search extending until April 2023. Additionally, hand searches were performed in other resources listed in the references of identified manuscripts, and Google Scholar was consulted.

To identify appropriate keywords, a meticulous approach was taken, considering preliminary published studies, Medical Subject Headings (MESH Terms) in the PubMed database, and aligning with the study's questions based on PICO criteria [7]. The PICO criteria encompassed:

Participants: All women experiencing menopause without age restrictions. **Intervention:** Given the study's focus on identifying the most effective herbal medicine to alleviate hot flashes, articles were selected based on herbal medicines. **Control:** The evaluation of each treatment group compared to a placebo.

Outcome: Outcome measures included hot flush frequency and severity.
Primary studies meeting the eligibility criteria were sought in English electronic databases, utilizing search strings with four key English keywords, and their Persian equivalents were employed in Persian databases. The Boolean search method was applied to combine keywords. PubMed search strategy is used by the following terms: ("menopause"[MeSH Terms] OR menopausal [Text Word] OR "postmenopause"[MeSH Terms]) AND ("hot flashes"[MeSH Terms] OR "flushing"[MeSH Terms] OR flushing [Text Word]) AND (placebo [Text Word])

Inclusion and Exclusion Criteria

Inclusion Criteria: 1. Randomized Controlled Trial (RCT) studies. 2. Studies examining the impact of herbal medicine on hot flashes.

Exclusion Criteria: 1. Case-control studies. 2. Case reports. 3. Letters to the editor. 4. Cross-over studies. 5. Studies with unavailable full text. 6. Unrelated studies. 7. Studies with insufficient data. 8. Duplicated studies. 9. Systematic review and meta-analysis studies.

Data Extraction: For each selected study, socio-demographic and clinical variables were extracted. The risk of bias was evaluated using a checklist derived from the integration of quality assessment tools for quantitative studies [8]. Two authors independently assessed bias risk using the Cochrane Collaboration Tool [9]. Since the robustness of meta-analysis conclusions relies on the individual study findings' validity, assessing study quality is crucial. The checklist was employed to evaluate the following types of bias: 1. Bias in recruitment, evaluation, and randomization methods. 2. Blinding Outcome Assessment, examining assessors' knowledge of participants' intervention or exposure situation. 3. Incomplete data resulting from random cancellation and deletion assessment, evaluating the risk of accidental removal related to treatment. 4. Other sources of bias: A. Confounding variables assessed for significant differences between groups before intervening. B. Data collection methods evaluated the validity and reliability of instruments.

Search results were recorded in Excel 2013, and duplicates were eliminated. Two independent researchers assessed study eligibility, with the first screening focusing on titles and abstracts and the final screening involving full-text review. The first and second authors independently screened and rated each study, resolving disagreements through consensus discussion. The final score determined the study's risk of bias as low, moderate, or high. In cases of multiple follow-up periods in an article, the longest follow-up period was considered. The mean (SD) frequency and severity of hot flashes for experimental and control groups were extracted after the intervention in each study.

Measures of Treatment Effect

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The outcomes, encompassing both the frequency and severity of hot flashes, were treated as continuous variables. Mean values and standard deviation were computed for each group's responses. Additionally, 95% confidence intervals (CI) were provided for the mean difference between treatment groups.

Evaluation of Assumptions in Network Meta-Analysis

For the attainment of reliable NMA outcomes and enhanced interpretability, it is presupposed that certain conditions must be met. These conditions include the assurance of network transitivity (ensuring similar distribution of potential modifiers of treatment effects across trials), network consistency (ensuring that estimates of indirect effects align with direct effects), and homogeneity (ensuring uniform interpretation of treatment effects throughout the trial).

Statistical Analysis

The statistical analysis involved conducting a Bayesian network meta-analysis using the "BUGSnet" package in R software, relying on Bayesian inference with Gibbs Sampling. Prior to utilizing BUGSnet, installation of Just Another Gibbs Sampler (JAGS) on the computer was necessary [10]. Within this package, the initial step for meta-analysis network analysis, such as paired meta-analysis, was to define and process the data. This involved assigning variable names to the studies (I.D.) and their treatment arms, ensuring compatibility through the data.prep() function.

For visual representation and tabulation of meta-analysis networks, the Net.plot() and net.tab() functions were employed [11]. Assessing the heterogeneity of modifiers within an evidence network was achieved using the data.plot() function within BUGSnet. To explore inconsistency at both global and local levels, the inconsistency model's fit was compared against a consistency model using the nma.fit() function and examining the Deviance Information Criteria (DICs). Local inconsistency was further examined through leverage plots produced by nma.fit() and the nma.compare() function, which presented a comparison of the posterior mean deviance for the inconsistency and consistency models.

The choice to implement the inconsistency model in BUGSnet was based on its capability to handle diverse network structures and multi-arm trials, a feature not shared by other methods like the Bucher method [12]. Considering the continuous nature of the outcomes and the inclusion of multi-arm trials in the analysis, a normal probability model for multi-arm trials was applied. Random effects network meta-analyses were conducted, fitting a generalized linear model with an identity link function and normal likelihood function specified through the nma.model().

To align with the NICE-DSU technical support document, the analysis included a burn-in of 50,000 iterations followed by 100,000 iterations with 10,000 adaptations in the nma.run() function. The SUCRA plot graphically displayed the probability of the ranking of each treatment within a surface under the cumulative ranking curve (SUCRA).

Results

Table 1 provides a summary of the studies included in the network meta-analysis. The intervention treatments across the studies comprised various herbal medicines, such as Black cohosh, Danggui Buxue Tang (DBT), EstroG-100, evening primrose, fenugreek seed, flaxseed, herbal, hop, hypericum and vitex, labisia pumila and eurycoma longifolia, vitex, passion flower, lavender, hop, red clover, sage, soy, valerian, and licorice.

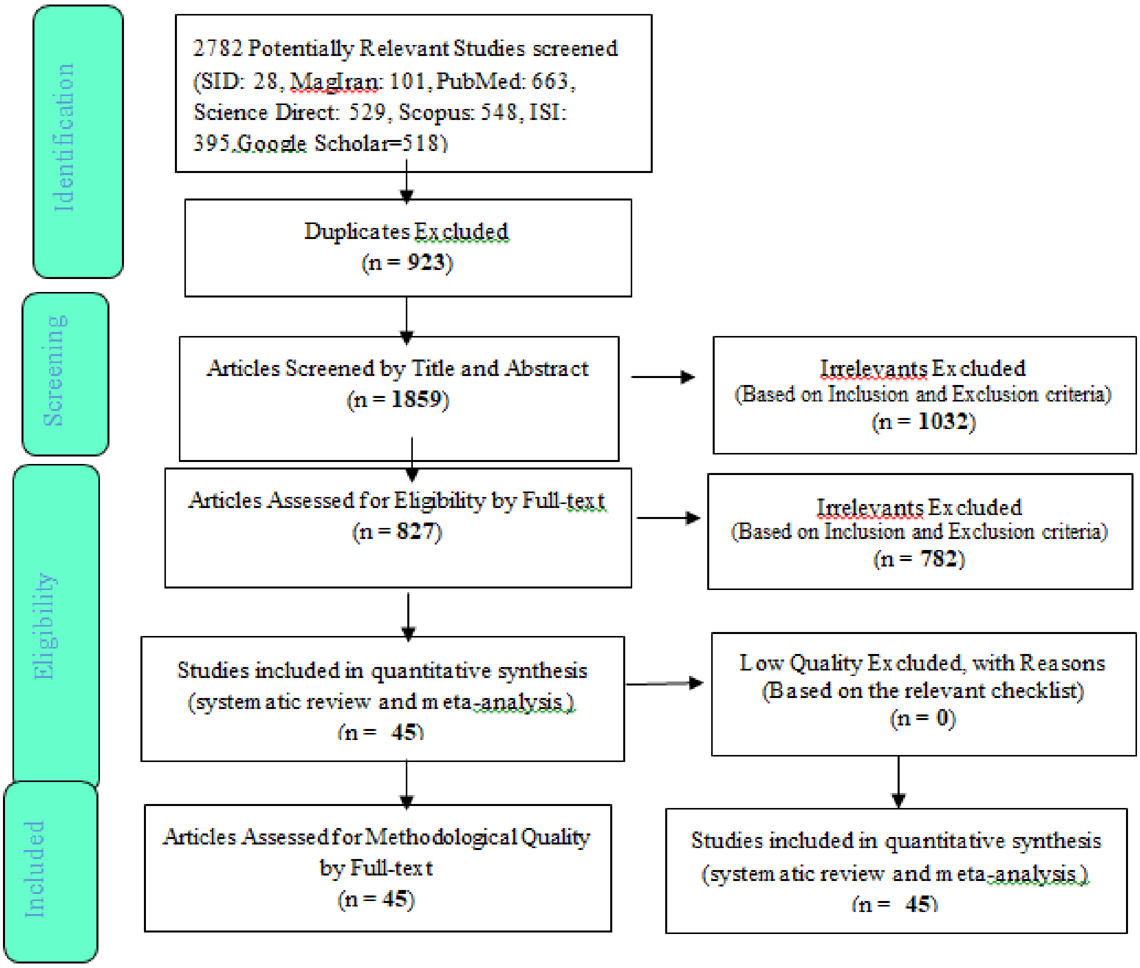

Figure 1: The flowchart on the stages of including the studies in the systematic review and meta-analysis (PRISMA-NMA)

The interventions focused on hot flash frequency and severity, resulting in a network comprising 231,120 pairwise comparisons. Figure 2 (A1 and A2) illustrates the net graph for hot flash frequency and severity. Node size corresponds to the number of participants per treatment, while line thickness indicates the number of randomized trials with direct treatment comparisons. St John's wort was utilized as herbal medicine in the intervention group in three studies [13-15], while Licorice was the treatment group in four studies [13, 16-18].

Table 1: Summary information of studies included in network meta-analysis.

First author	Publication year	Country	outcome	Treatment Number	Treatment	Sample size	Mean	SD	Treatment Duration(day)	Mean of age	S
Barnard, N. D.[19]	2021	America	Frequency hotflash	1	Soy	17	1.3	0.38	84	53.3	
				2	Placebo	17	2.5	0.58	84	55.5	
			Severity hotflash	1	Soy	17	0.8	0.33	84	53.3	
				2	Placebo	17	2.2	0.56	84	55.5	
Dastenaei,B [20]	2020	Iran	Severity hotflash	1	Evening Primrose	44	2.59	0.58	28	54.61	
				2	Placebo	46	1	0.78	28	54.71	
				3	Vitex	51	0.92	0.79	28	54.61	
Chinnappan, S. M.[21]	2020	Canada	Frequency hotflash	1	labisia pumila and eurycoma	38	5.06	4.51	168	51.53	

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					longifolia						
				2	Placebo	37	5.79	5.63	168	51.41	
Saberi, Z. [22]	2020	Iran	Frequency hotflash	1	Silybum marianum	38	1.34	0.17	84	52	
				2	Placebo	35	3.34	0.17	84	51	
			Severity hotflash	1	Silybum marianum	38	1.62	0.08	84	52	
				2	Placebo	35	5.6	0.09	84	51	
Dadfar,F.[23]	2019	Iran	Frequency hotflash	1	Sage	30	1.8	0.155	28	51.4	(
				2	Placebo	30	2.6	0.177	28	52.6	(
Eatemadnia, A. [24]	2019	Iran	Frequency hotflash	1	St John's wort	35	0.6	0.84	56	50.49	
				2	Placebo	35	3.97	0.96	56	50.63	
			Severity hotflash	1	St John's wort	35	0.37	0.49	56	50.49	
				2	Placebo	35	2.14	0.73	56	50.63	
Masoumi,sz[25]	2019	Iran	Frequency hotflash	1	Sage	40	1.98	0.733	56	52.25	
				2	Black cohosh	40	1.94	0.674	56	54.25	
Imhof, M.[26]	2018	Austria and Rumania and Germany	Frequency hotflash	1	Soy	54	2.65	2.19	168	45to <70	
				2	Placebo	80	2.7	2.11	168	45to <70	
Mehrpooya, M.[27]	2018	Iran	Frequency hotflash	1	Black cohosh	40	1.05	0.49	56	53.72	
				2	Evening Primrose	40	1.22	0.7	56	49.64	
			Severity hotflash	1	Black cohosh	40	1.5	0.55	56	53.72	
				2	evening primrose	40	1.92	0.61	56	49.64	
Dastenaei,M.B. [28]	2018	Iran	Frequency hotflash	1	evening primrose	46	7.89	0.37	28	54.6	
				2	Placebo	44	11.16	0.56	28	54.7	
			Severity hotflash	1	evening primrose	46	1	0.78	28	54.6	
				2	Placebo	44	2.59	0.58	28	54.7	
Motaghi,B. [29]	2018	Iran	Frequency hotflash	1	Vitex	50	0.8	0.65	28	54.17	
				2	Placebo	50	2.6	1.14	28	54.7	
Jenabi, E.[30]	2018	Iran	Frequency hotflash	1	Valerian	30	3.24	2.29	60	50.8	
				2	Placebo	30	6.81	4.32	60	51.2	
			Severity hotflash	1	Valerian	30	0.6	0.67	60	50.8	
				2	Placebo	30	1.9	0.71	60	51.2	
Motaghi,B. [31]	2017	Iran	Frequency hotflash	1	evening primrose	50	7.89	0.37	28	54.6	
				2	Placebo	50	11.16	0.56	28	54.7	
Aghamiri, V.[32]	2016	Iran	Frequency hotflash	1	hop	60	49.8	4.17	56	49.8	
				2	Placebo	60	50.5	5	56	50.5	
Rad, S.[33]	2016	Iran	Frequency hotflash	1	Sage	46	2.31	0.84	56	NA	
				2	Placebo	47	5.32	2.14	56	NA	
Kazemzadeh, R.[34]	2016	Iran	Frequency hotflash	1	lavender	50	10.58	7.34	84	51.5	
				2	Placebo	50	19.7	13.4	84	52.24	
Torkestani,A. [35]	2015	Iran	Frequency hotflash	1	Soy	30	0.5	0.63	56	50.2	
				2	fenugreek	30	0.7	0.76	56	51.4	

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					seed					
			Severity hotflash	1	Soy	30	1	0.64	56	50.2
				2	fenugreek seed	30	1.3	0.64	56	51.4
Asali,Z. [15]	2013	Iran	Severity hotflash	1	St John's wort	30	1.1	0.84	42	51.7
				2	Passion Flower	29	1	0.7	42	51.8
Farzaneh, F.[36]	2013	Iran	Frequency hotflash	1	evening primrose	28	3.2	1.8	42	51.9
				2	Placebo	28	3.7	2	42	51.9
			Severity hotflash	1	evening primrose	28	3.4	1.4	42	51.9
				2	Placebo	28	4.1	2	42	51.9
Sadeghi A.[37]	2013	Iran	Frequency hotflash	1	Sage	40	2.28	2.82	56	51.6
				2	Placebo	40	3.52	2.98	56	51.4
Sadeghi,A.H. [38]	2013	Iran	Frequency hotflash	1	Sage	42	2.28	2.82	56	51.6
				2	Placebo	42	3.52	2.98	56	51.4
Mirabi, P.[39]	2013	Iran	Frequency hotflash	1	Valerian	35	4.83	0.52	56	51.2
				2	Placebo	33	7.75	0.32	56	51.7
			Severity hotflash	1	Valerian	35	5.23	1.52	56	51.2
				2	Placebo	33	9.86	1.95	56	51.7
Colli, M. C. [40]	2012	Brazil	Severity hotflash	1	Flaxseed E	28	6.08	2.78	180	53.57
				2	Placebo	25	6.96	2.67	180	56.57
				3	Flaxseed M	22	4.54	3.14	180	54.16
Chang, A.[41]	2012	Korea	Frequency hotflash	1	EstroG-100	29	0.79	0.73	84	53.2
				2	Placebo	33	2.06	0.76	84	54.1
Nahidi, F. [18]	2012	Iran	Frequency hotflash	1	Licorice	45	6.43	0.94	56	53
				2	Placebo	45	7.75	0.55	56	52.69
			Severity hotflash	1	Licorice	45	2	0.7	56	53
				2	Placebo	45	1.7	0.7	56	52.69
Sekhavat,L. [42]	2012	Iran	Frequency hotflash	1	Soy	45	6.7	2.5	84	51.8
				2	Placebo	45	12.1	2.4	84	52.6
			Severity hotflash	1	Soy	45	4.3	0.6	84	51.8
				2	Placebo	45	7.1	2.4	84	52.6
Nahidi, F. [17]	2011	Iran	Frequency hotflash	1	Licorice	34	5.1	0.52	28	53.29
				2	Placebo	34	7.75	0.34	28	52.97
			Severity hotflash	1	Licorice	34	1.41	0.49	28	53.29
				2	Placebo	34	2.14	0.55	28	52.97
Enjezab.B[43]	2010	Iran	Frequency hotflash	1	Soy	31	2.16	1.48	90	50.34
				2	Placebo	31	5.88	2.61	90	50.34
Abdali, K.[13]	2010	Iran	Frequency hotflash	1	St John's wort	45	1.8	1.03	56	50.52
				2	Placebo	43	2.65	0.81	56	50.29
			Severity hotflash	1	St John's wort	45	0.93	0.44	56	50.52
				2	Placebo	43	1.7	0.62	56	50.29
Simbalista, R. L. [44]	2010	Brazil	Frequency hotflash	1	Flaxseed	20	5.2	3.9	84	52
				2	Placebo	18	4	2.4	84	52.7
van der Sluijs, C. P.[45]	2009	England	Frequency hotflash	1	Herbal	47	6.89	2.3	56	55.68
				2	Placebo	46	6.57	3.3	56	55.66
Al-Akoum, M.[14]	2009	canada	Frequency hotflash	1	St John's wort	20	4.6	4.1	90	53.4
				2	Placebo	20	6.7	4	90	54

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Van Die, M. D. [46]	2009	Australia	Frequency hotflash	1	Hypericum and Vitex	50	10.86	1.34	112	52.5
				2	Placebo	50	9.32	1.36	112	51.9
Haines, C. J . [47]	2008	China	Frequency hotflash	1	DBT	45	0.7	2.7	180	52.8
				2	Placebo	39	0.1	0.8	180	51.3
Ebrahimi, M. [48]	2008	Iran	Severity hotflash	1	Soy	40	2.8	0.1	84	51.67
				2	Placebo	40	7.6	0.1	84	49.37
Abdolahi,F[49]	2007	Iran	Frequency hotflash	1	Licorice	29	2.66	1.68	56	50.1
				2	Placebo	24	3.5	2.62	56	51.1
Nahas, E. A. P. [50]	2007	Brazil	Frequency hotflash	1	Soy	38	3.1	2.3	300	55.1
				2	Placebo	38	5.9	4.3	300	56.2
			Severity hotflash	1	Soy	38	2.8	2.4	300	55.1
				2	Placebo	38	5.3	3	300	56.2
Boroomandfar,KH. [51]	2007	Iran	Severity hotflash	1	Vitex	27	1.77	0.84	30	49.02
				2	Placebo	27	2.7	0.46	30	49.02
Lewis, J. E.[52]	2006	Canada	Frequency hotflash	1	Soy	33	3.37	2.55	112	53.3
				2	Placebo	33	3.79	3	112	52.9
				3	Flaxseed	33	2.6	2.42	112	53.2
			Severity hotflash	1	Soy	33	2.88	1.17	112	53.3
				2	Placebo	33	2.9	1.15	112	52.9
				3	Flaxseed	33	2.34	1.09	112	53.2
Kazemian,A.[53]	2006	Iran	Frequency hotflash	1	Valerian	29	2.75	3.68	60	52.76
				2	Placebo	20	5.88	5.02	60	52.76
			Severity hotflash	1	Valerian	29	1.1	0.72	60	52.76
				2	Placebo	20	1.75	0.71	60	52.76
Kazamian,A. [54]	2006	Iran	Severity hotflash	1	Passion Flower	23	1.78	0.95	30	50.48
				2	Placebo	27	2.29	0.82	30	49.52
Kazamian,A. [55]	2005	Iran	Severity hotflash	1	Vitex	27	1.77	0.84	30	NA
				2	Placebo	27	2.29	0.82	30	NA
				3	Passion flower	23	1.78	0.95	30	NA
Atkinson, C.[56]	2004	England	Frequency hotflash	1	Red clover	86	1.2	2.3	360	55.1
				2	Placebo	91	1.5	2	360	55.2
Abbaspoor, Z. [57]	2003	Iran	Frequency hotflash	1	Soy	30	5.45	1.74	28	49.9
				2	Placebo	31	9	2.54	28	50.3
Burke, G. L.[58]	2003	America	Frequency hotflash	1	Soy MI	70	1.7	0.27	365	51
				2	Placebo	76	1.4	0.23	365	50.9
				3	Soy HI	65	1.6	0.27	365	50.5
			Severity hotflash	1	Soy MI	70	1.7	1.13	365	51
				2	Placebo	76	1.4	1.003	365	50.9
				3	Soy HI	65	1.6	1.04	365	50.5

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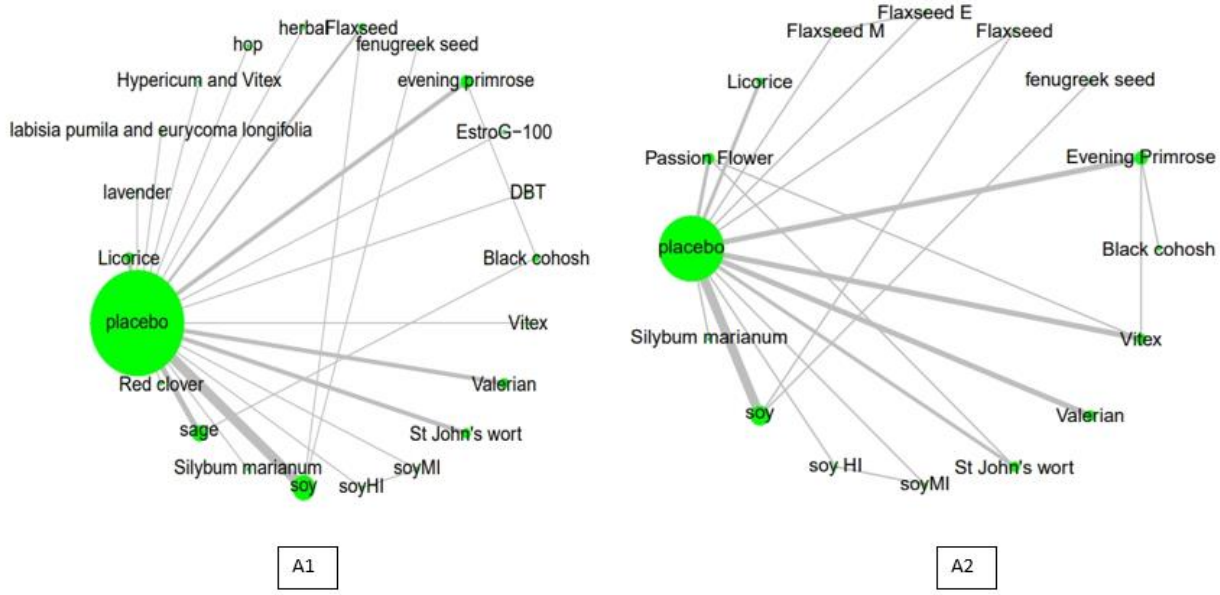

Figure. 2 Network plots produced by the net.plot() Function in BUGSnet for frequency (A1) and severity (A2) outcome

Figures 3 and 4 depict the mean age of participants within each treatment arm, with individual points reflecting similarity to the overall mean age of participants in the evidence base (red dotted line). Variability in ages within each treatment arm appears comparable based on standard deviation (+/− error bars), suggesting no meaningful heterogeneity in age distribution.

A comparison of fixed- and random-effects models favored the random effects model based on leverage plots and DIC values from nma.fit(). The random effects model exhibited a lower DIC value and fewer outliers in the leverage plot (Figures 5 and 6).

In the SUCRA plot, the hop and lavender curve consistently ranks above other treatments, indicating it as the most beneficial treatment for hot flash frequency (Higher rankings associated with smaller hot flash frequency). Similarly, the silybum marianum and soy curves consistently outperform other treatments in severity outcomes (Figure 7).

The silybum marianum and soy curves are consistently above the curves of the other treatments, suggesting that it is the most beneficial treatment concerning the treatment outcome included in the severity hot flash evidence network (Figure 8).

The league heat plot (Figure 9) show cases the effect estimates and credible intervals (CrI) generated by the earlier model for the frequency outcome. In this figure, the distinction between hop and other treatments is statistically significant at the 95% level. Similarly, for the severity outcome, the effect estimates and credible intervals from the previous model are presented in another league heat plot (Figure 10). In Figure 10, the disparities between placebo and the treatments involving silybum marianum, soy, and valerian are statistically significant at the 95% level (silybum marianum (MD = −4.00, 95% CrI −7.1 to −0.8), soy (MD = −2.3, 95% CrI −3.8 to −0.8) and valerian (MD = −2.1, 95% CrI −4 to −0.3)).

Figure 11 also illustrates the inconsistency plot of enrolled studies, suggesting a lack of evidence supporting inconsistency within the network.

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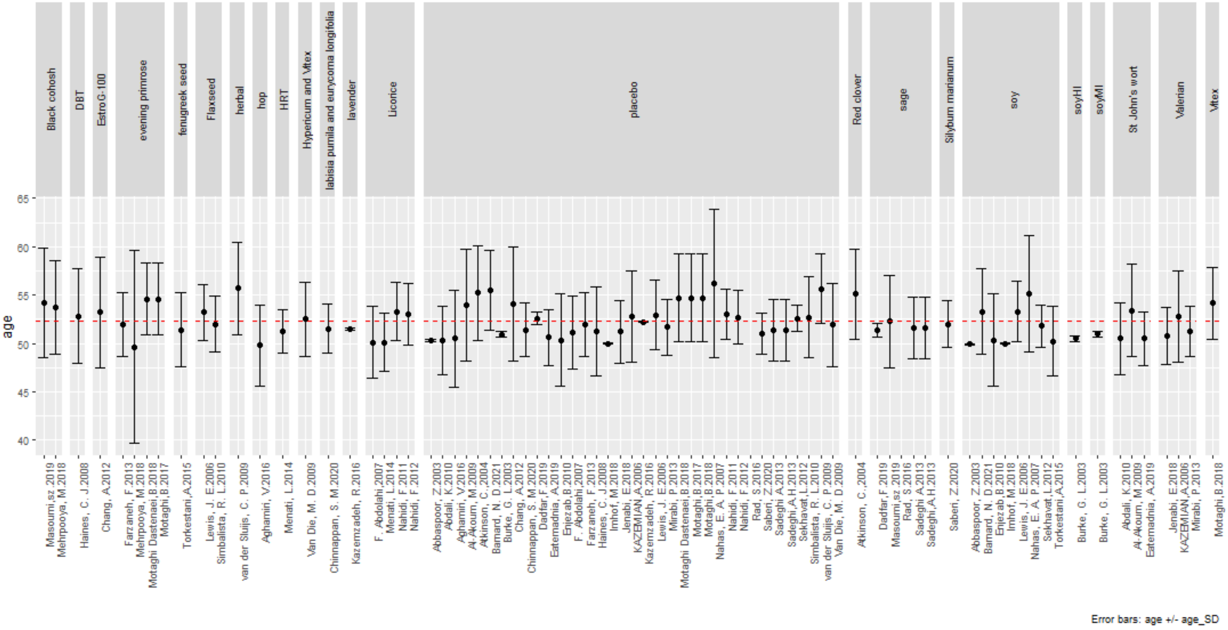

Figure. 3 Graph of patient age by treatment using the data.plot() function in BUGSnet for frequency

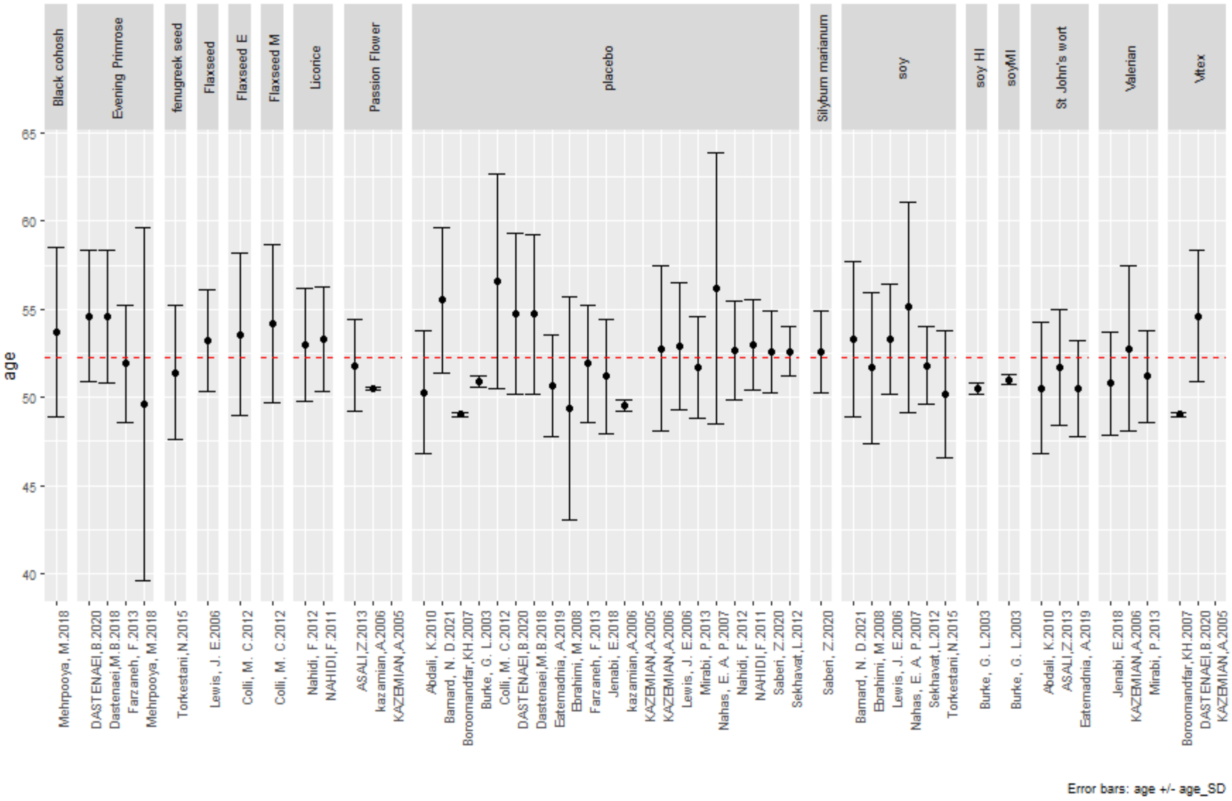

Figure. 4 Graph of patient age by treatment using the data.plot() function in BUGSnet for severity outcome

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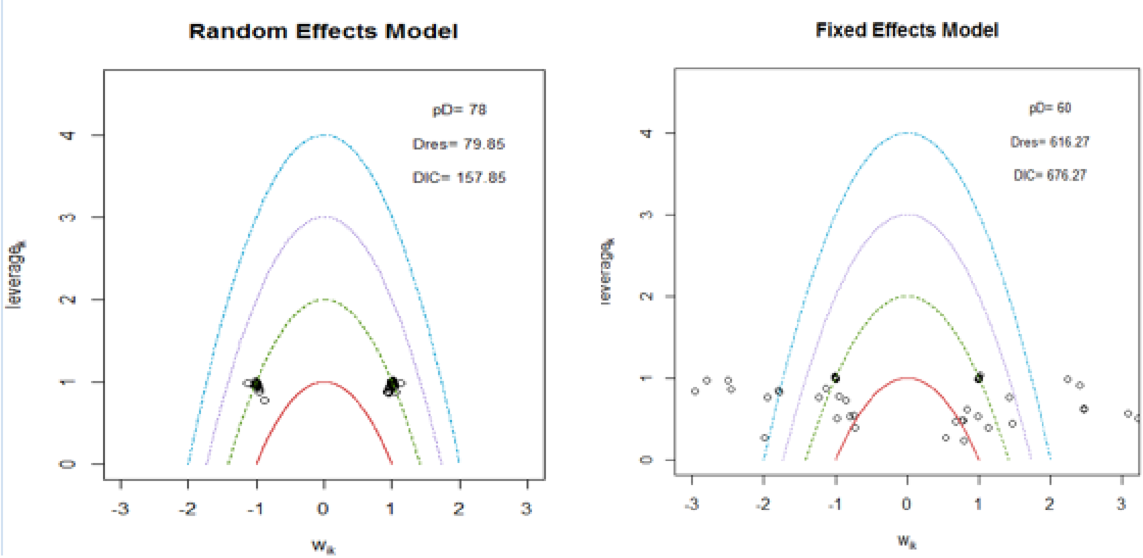

Figure. 5 Leverage plots and fit statistics produced by the nma.fit() Function in BUGSnet for frequency outcome

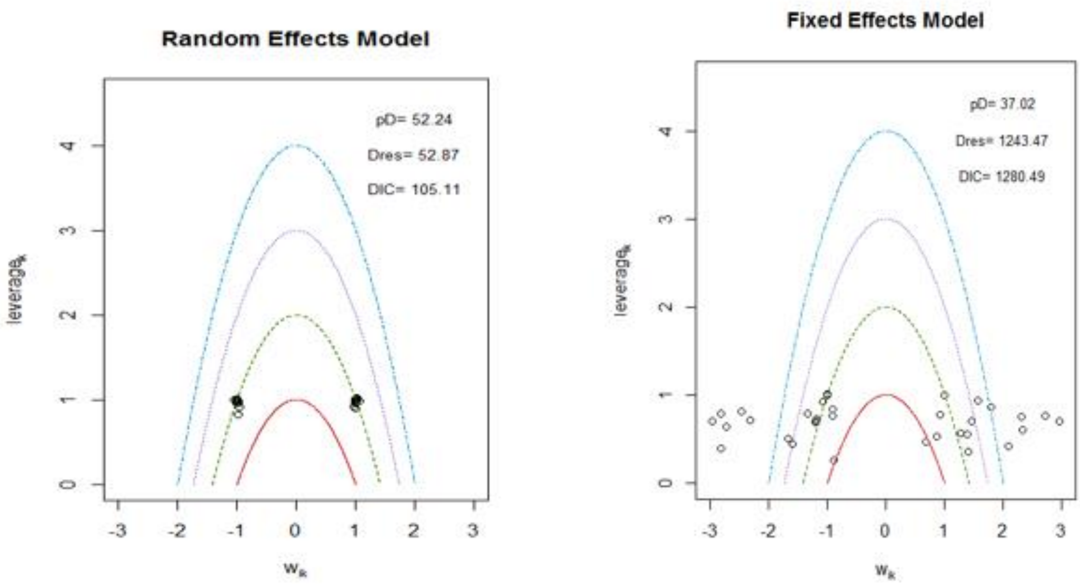

Figure. 6 Leverage plots and fit statistics produced by the nma.fit() Function in BUGSnet for severity outcome

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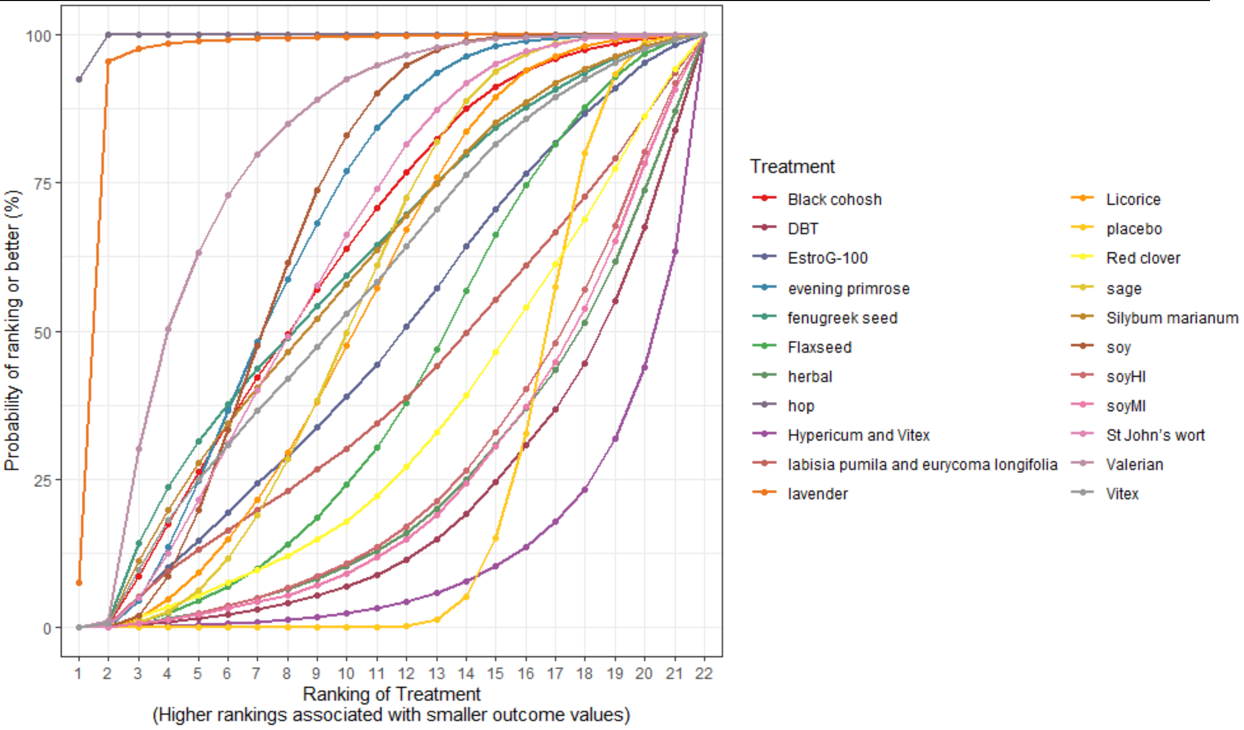

Figure. 7 SUCRA plot produced by the nma.rank() Function in BUGSnet for frequency outcome

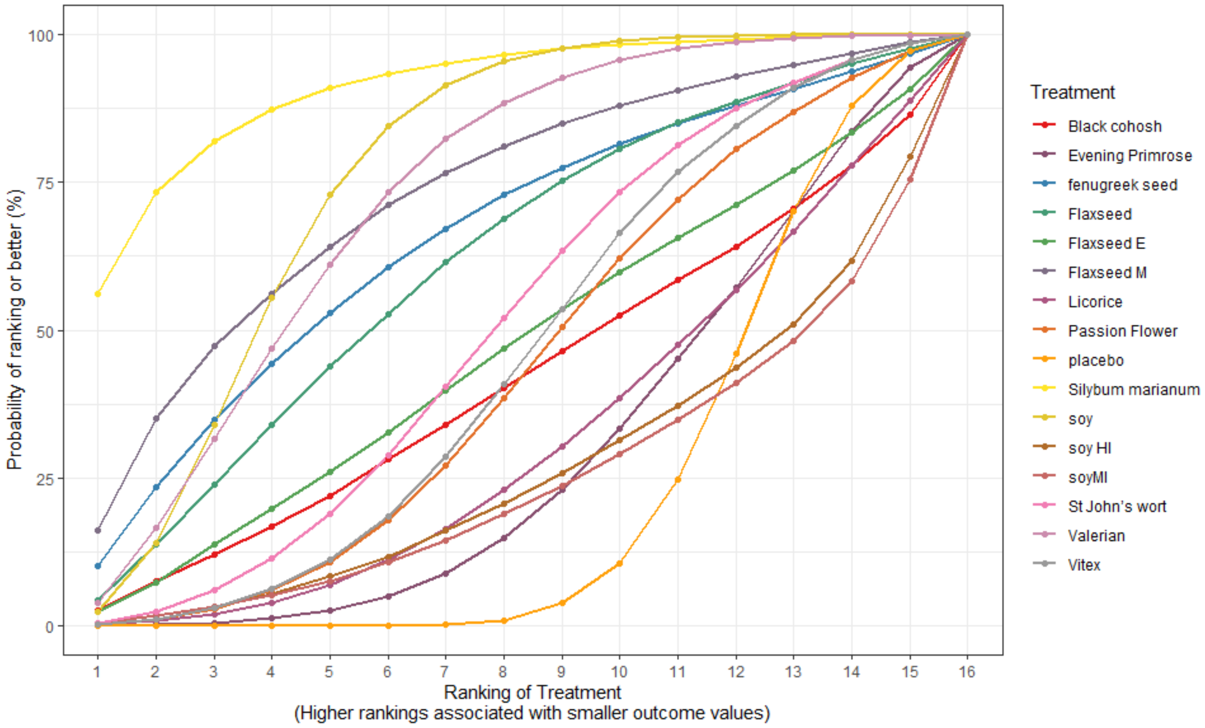

Figure. 8 SUCRA plot produced by the nma.rank() Function in BUGSnet for severity outcome

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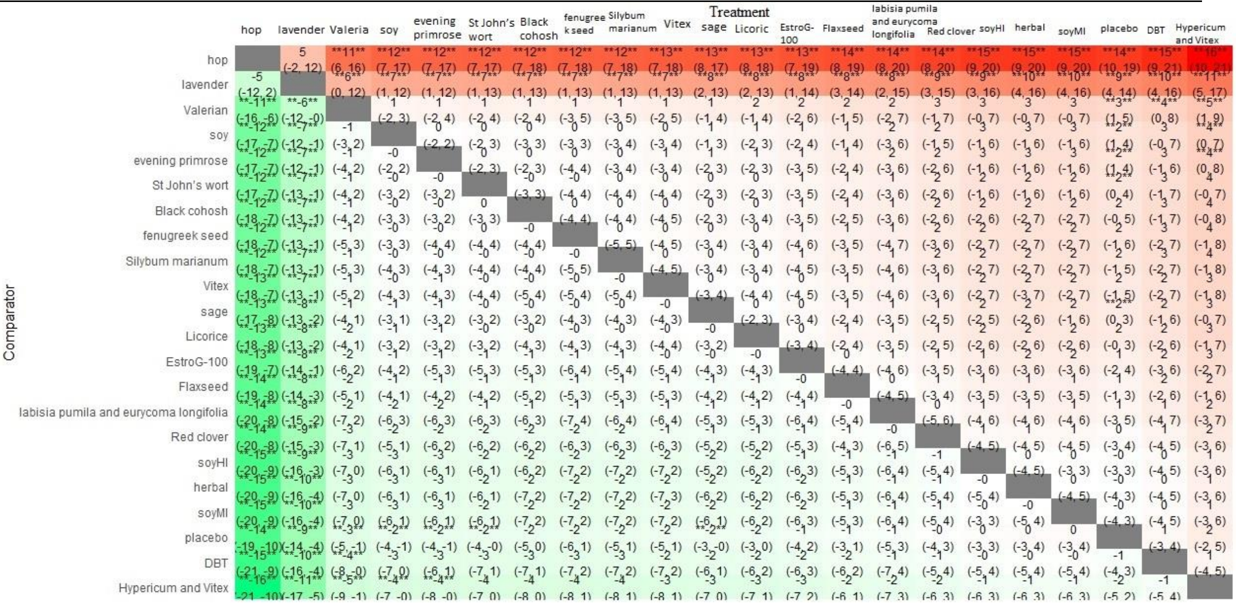

Figure. 9 League Table Heatmap for frequency outcome: The values in each cell represent the relative treatment effect (and 95% credible intervals) of the treatment on the top compared to the treatment on the left. A double asterisk indicates statistical significance.

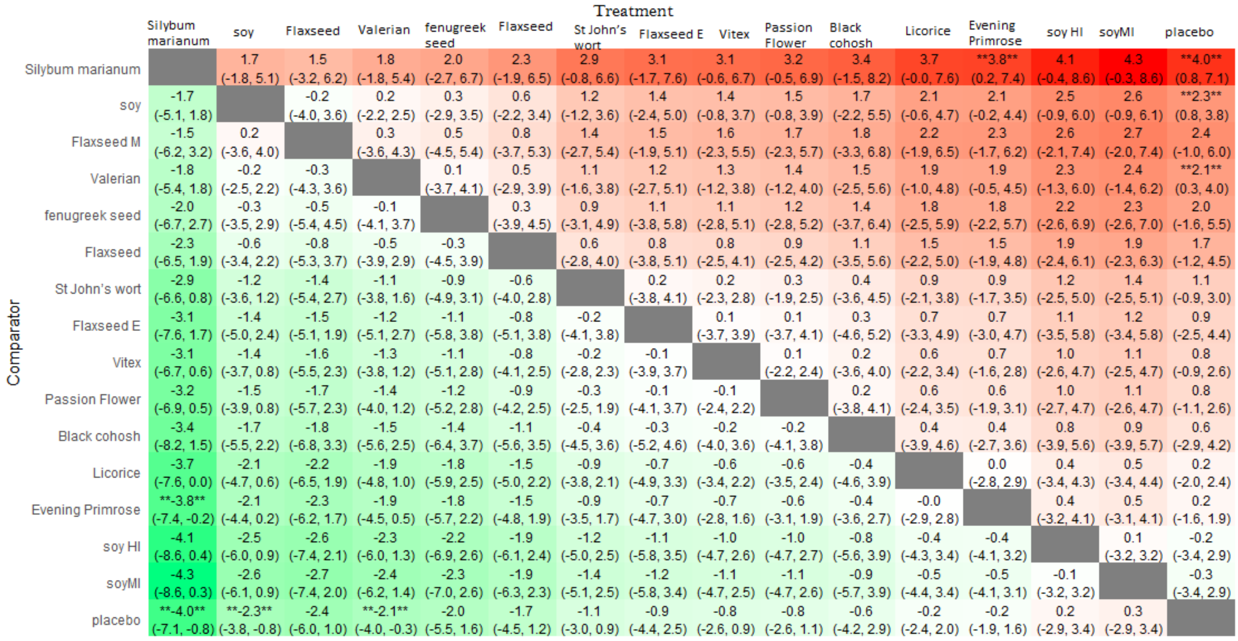

Figure. 10 League Table Heatmap for severity outcome: The values in each cell represent the relative treatment effect (and 95% credible intervals) of the treatment on the top compared to the treatment on the left. A double asterisk indicates statistical significance

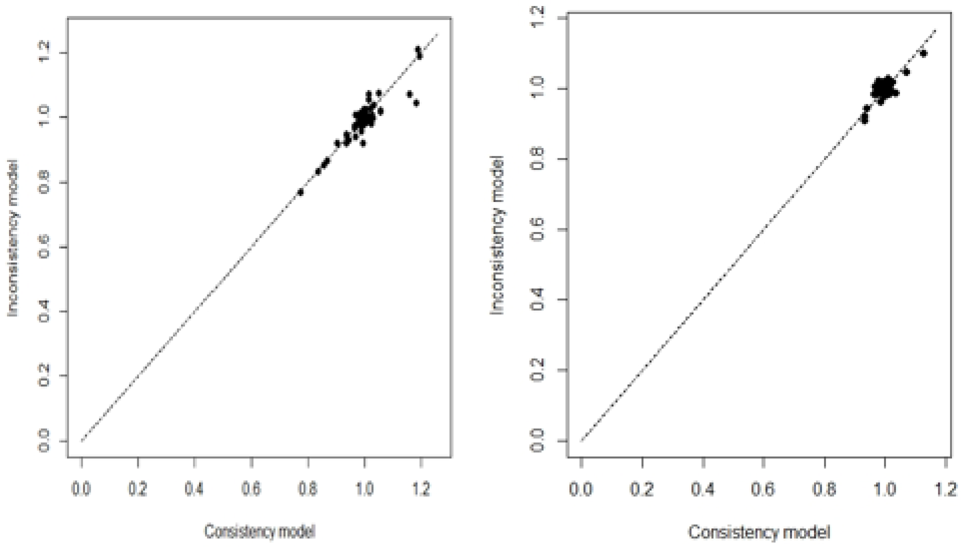

Figure. 11 Posterior mean deviance comparison plot produced by the nma.compare() Function in BUGSnet. Each data point represents a treatment arm's contribution to posterior mean deviance for the consistency model (horizontal axis) and the inconsistency model (vertical axis) for severity and frequency outcome from left to right, respectively.

Discussion

In conducting a systematic review and network meta-analysis, our aim was to synthesize comparative effectiveness evidence for herbal medicines in preventing the frequency and severity of hot flashes in post-menopausal women. Despite numerous randomized clinical trials, a definitive understanding of their relative efficacy remains elusive. Treatment decisions, lacking predictive biomarkers, rely solely on patient characteristics. Consequently, ranking the value of available options may facilitate the development of treatment algorithms, subject to validation in prospective clinical trials.

The choice of Bayesian network meta-analysis (NMA) was imperative, as it is the most suitable method for assessing the strength of evidence for treatments without direct comparisons. Our systematic review incorporated 45 randomized controlled trials (RCTs) involving 3,158 post-menopausal women for frequency outcomes, with a minimum follow-up period of 28 days for patients using herbal medicine.

While the overall study design quality was deemed satisfactory,Intention-to-treat (ITT) implementation was suboptimal across most studies, with more than half lacking a protocol for managing missing and incomplete data. Additionally, some studies did not comprehensively report the formulation and composition of investigated drugs. Despite these limitations, reporting bias was minimal, as most studies reported anticipated results, and no other discernible biases were identified.

To establish the efficacy of treatments for menopausal symptoms, clinical studies necessitate placebo-controlled trials or head-to-head comparisons with known effective treatments. Our study incorporated a placebo as the baseline treatment and included studies with comparisons against the placebo. This approach facilitated a comprehensive comparison of both direct and indirect treatment effects.

The findings of our study highlight that silybum marianum and soy emerge as more beneficial treatments than others for hot flash frequency. Furthermore, the statistical significance at the 95% level indicates that the difference between hop and other treatments is substantial for the frequency of hot flashes. Regarding the severity of hot flashes, silybum marianum, soy, and valerian treatments show statistically significant differences compared to placebo at the 95% level, while other treatments do not exhibit significant effect sizes when compared to each other.

Silybum marianum, a globally used medicinal plant, has been underexplored in clinical studies. While our results suggest its effectiveness in reducing menopausal symptoms, future research should focus on its metabolism, pharmacokinetics, and bioavailability. Soy, with varying consumption patterns across countries and races, has demonstrated inconsistent results in reducing hot flashes. Equol, a main isoflavonoid produced by intestinal bacteria, may play a role, necessitating further investigation. Valerian, a phytoestrogenic plant, has exhibited promise in reducing the frequency and severity of hot flashes, presenting a simple and non-invasive herbal treatment option for alleviating menopausal symptoms.

Conclusions

This study provides valuable evidence to identify the most effective herbal treatments for managing the frequency and severity of menopausal hot flashes. Notably, a significant difference was observed for most herbal medicines when compared to the placebo. The ranking of these herbal medicines presents opportunities for designing treatment algorithms that warrant validation in prospective clinical trials.

For optimal effectiveness, it is advisable to compare medicinal herbs with hormone therapy, which serves as a standard and routine treatment. Such comparative analyses can contribute to a more comprehensive understanding of the therapeutic landscape and guide informed decision-making in the management of menopausal symptoms.

Abbreviations

network meta-analysis: NMA
Preferred Reporting Items for Systematic Reviews and Meta-Analyses: PRISMA-NMA
Danggui Buxue Tang: DBT
Confidence interval: CI
Credible interval :CrI
Just Another Gibbs Sampler: JAGS
Bayesian inference Using Gibbs Sampling to conduct a Network meta-analysis: BUGSnet
Deviance Information Criterion: DIC

Declarations

Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

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Competing interests
The authors declare that they have no competing interests.

Authors' contributions
Shahsavari S, Keshavarzi F and Jambarsang S performed the analysis, and Shahsavari S, Salari N, and Jambarsang S interpreted the results. Shahsavari s, Keshavarzi F, Tahmasebi H, Setoodeh M and Rajabi Gomasai M drafted the paper. All authors read and approved the final manuscript.

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