Supplementary Online Content

Locher C, Kossowsky J, Koechlin H, et al. Efficacy, safety and acceptability of pharmacologic treatments for pediatric migraine prophylaxis: a systematic review and network meta-analysis. *JAMA Pediatr.* Published online February 10, 2020. doi:10.1001/jamapediatrics.2019.5856

eAppendix 1. Search Terms

Medline Search Strategy (Adapted for other databases)

# ▲	**Searches**
1	randomi* controlled trial.pt.
2	placebo.ab.
3	drug therapy.fs.
4	random*.ab.
5	trial.ab.
6	groups.ab.
7	1 or 2 or 3 or 4 or 5 or 6
8	exp animals/ not humans.sh.
9	7 not 8
10	exp migraine disorders/dh, dt, pc, su, th
11	migrain*.mp.
12	vascular headaches/dt, pc, su, th
13	(vascular adj3 headache*).mp.
14	10 or 11 or 12 or 13
15	exp adolescent/ or exp child/ or exp infant/
16	(child* or adolescen* or infant* or juvenile* or pediatric* or paediatric* or developmental age).mp.
17	15 or 16
18	9 and 14 and 17

eAppendix 2. GRADE Ratings for each network

Using the Grading of Recommendations Assessment, Development, and Evaluation ratings (GRADE)[3] as well as the recently developed web application to apply this framework[4], we estimated the certainty of evidence for each network estimate according to the following criteria:

Study limitations (Within study bias): We categorized the overall risk of bias of each study. According to the Cochrane Risk of Bias tool[5], we rated five risk of bias items (i.e., allocation sequence concealment, adequate blinding, incomplete outcome data, selective outcome reporting, and other potential threats to validity). We calculated the average risk of bias by building the mean of all risk of bias items. For example: a study would be judged as *medium* risk of bias [some concerns] when the individual items would be once *high risk* [major concerns], three times *low risk* [no concerns], and twice *medium OR unclear risk* [some concerns]. We then used the contribution matrix to calculate the percentage of contribution from each study, and finally assessed the study limitation for each network estimate based on the weighted average risk of bias of the contributing studies. We selected the rule "Average Risk of Bias" in order to calculate the within study bias.

Publication bias (Across studies bias): Since there is so far a lack of a concrete methodology of assessing across-studies bias (publication bias) in NMA, a comparison-adjusted funnel plot with accompanying Egger test for asymmetry was conducted.

Indirectness: We judged that there was no concern in this domain as the included studies matched our inclusion criteria and study questions.

Imprecision: In line with previous analyses[6], we considered a clinically meaningful threshold for standardized mean difference (SMD) to be 0.20.

Heterogeneity: We evaluated the degree of concerns through comparing the clinical inference based on the 95% confidence intervals (CI) and that based on the 95% prediction interval (PI), the latter reflecting the degree of heterogeneity. Appling the same clinical inference framework as for imprecision, we saw no concerns in heterogeneity when the two judgements matched (e.g. no concern based on 95% CI and no concern based on 95% PI), some concerns when they differed by one degree (e.g. no concern based on 95% CI but some concerns based on 95% PI), and major concerns when they differed by two degrees (e.g. no concern based on 95% CI but major concerns based on 95% PI).

Incoherence (Inconsistency): For inconsistency, we looked at the results of side splitting and we saw major concerns when $p<0.05$ but no concern otherwise.

Efficacy

We found some concerns for *within-study bias* (i.e., study limitations) for several pair-wise comparisons. In terms of the *across-study bias* (i.e., publication bias), the Egger test for funnel plot asymmetry was non-significant (p=0.93) indicating that selection bias is not a big threat to the network meta-analysis. There was no concern for *indirectness*, since the included studies all matched our study questions. Evaluating *imprecision*, we found that the two statistically significant comparisons (i.e., propranolol vs placebo; topiramate vs. placebo) revealed a clinically significant effect size. Furthermore, we examine *heterogeneity*, which is represented by the 95% prediction interval for each individual comparison. For both, propranolol vs. placebo and topiramate vs. placebo, the 95% prediction interval was non-significant. Furthermore, we found evidence for substantial and statistically significant heterogeneity in the network (within design Q=26.13, p<.001, tau^2=0.18; I^2=75.1%). Finally, there was no evidence of *inconsistency* between the direct and indirect evidence, i.e., all p-values were above 5%. Also, we identified no evidence of inconsistency in the NMA when calculating the global design-by-treatment interaction test (between designs Q=2.08, p=.556).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence								
Butterbur root extract vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Placebo	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Propranolol	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Placebo	1	Some concerns	--	No concerns	Some concerns	Some concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Propranolol	1	Some concerns	--	No concerns	No concerns	Major concerns	No concerns	Low
Placebo vs Riboflavin	3	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Sodium Valproate	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Topiramate	2	Some concerns	--	No concerns	No concerns	Major concerns	No concerns	Low
Pregabalin vs Propranolol	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Sodium Valproate	2	Some concerns	--	No concerns	Some concerns	Some concerns	No concerns	Low
Propranolol vs Topiramate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

		Indirect evidence						
Butterbur root extract vs Cinnarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs CoEnzyme Q10	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs L-5-Hydroxytryptophan (L-5HTP)	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Butterbur root extract vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs CoEnzyme Q10	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs L-5-Hydroxytryptophan (L-5HTP)	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs L-5-Hydroxytryptophan (L-5HTP)	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

CoEnzyme Q10 vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
CoEnzyme Q10 vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs L-5-Hydroxytryptophan (L-5HTP)	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Flunarizine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
L-5-Hydroxytryptophan (L-5HTP) vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
L-5-Hydroxytryptophan (L-5HTP) vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Nimodipine vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Nimodipine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Topiramate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Sodium Valproate vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Acceptability

We did not find evidence for heterogeneity (within design Q=1.99, p=.851, tau^2=0.00; I^2=0%). There was no evidence of inconsistency between the direct and indirect evidence, i.e., all p-values were above 5%. Also, we found no evidence of inconsistency in the NMA when calculating the global design-by-treatment interaction test (between designs Q=3.14, p=.208).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
			Mixed evidence					
Amitriptylin vs Melatonin	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Butterbur root extract vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Placebo	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Propranolol	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Melatonin vs Placebo	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Nimodipine vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Riboflavin	3	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Sodium Valproate	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Topiramate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Propranolol	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Sodium Valproate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Topiramate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

		Indirect evidence						
Amitriptylin vs Butterbur root extract	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Cinnarizine	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs CoEnzyme Q10	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Flunarizine	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Nimodipine	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Placebo	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Pregabalin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Propranolol	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Amitriptylin vs Topiramate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Butterbur root extract vs Cinnarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs CoEnzyme Q10	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Melatonin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Butterbur root extract vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs CoEnzyme Q10	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Melatonin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Cinnarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Melatonin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Melatonin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Flunarizine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Melatonin vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Melatonin vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Melatonin vs Propranolol	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Melatonin vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Melatonin vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Melatonin vs Topiramate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Nimodipine vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Pregabalin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Pregabalin vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Propranolol vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Topiramate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Sodium Valproate vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Safety

Studies showed no significant heterogeneity (within design Q=0.21, p=.900, tau2=0.00; I^2=0%). In terms of inconsistency, we found no differences between the direct and indirect evidence. Finally, there was no evidence of inconsistency in the NMA according to the global design-by-treatment interaction test (between designs Q=0.12, p=.732).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
			Mixed evidence					
Butterbur root extract vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Propranolol	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Placebo	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Riboflavin	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Sodium Valproate	1	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Placebo vs Topiramate	1	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Sodium Valproate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Topiramate	2	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

			Indirect evidence					
Butterbur root extract vs Cinnarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Butterbur root extract vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Flunarizine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Placebo	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Cinnarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Nimodipine	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Flunarizine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

Nimodipine vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Riboflavin	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Sodium Valproate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Nimodipine vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Propranolol	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low
Propranolol vs Riboflavin	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Sodium Valproate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Riboflavin vs Topiramate	--	No concerns	--	No concerns	Major concerns	No concerns	No concerns	Moderate
Sodium Valproate vs Topiramate	--	Some concerns	--	No concerns	Major concerns	No concerns	No concerns	Low

eAppendix 3. Details on Inconsistency

Efficacy – Local approach

```
Back-calculation method to split direct and indirect evidence

Random effects model:

                                      comparison k prop     nma  direct  indir.    Diff     z p-value
                  Butterbur root extract:Cinnarizine 0    0 -0.5185       . -0.5185       .     .       .
                 Butterbur root extract:CoEnzyme Q10 0    0 -0.2984       . -0.2984       .     .       .
                  Butterbur root extract:Flunarizine 0    0 -0.9319       . -0.9319       .     .       .
 Butterbur root extract:L-5-Hydroxytryptophan (L-5HTP) 0    0  0.2068       .  0.2068       .     .       .
                   Butterbur root extract:Nimodipine 0    0 -0.0000       . -0.0000       .     .       .
                      Butterbur root extract:Placebo 1 1.00 -0.0000  0.0000       .       .     .       .
                   Butterbur root extract:Pregabalin 0    0 -0.8139       . -0.8139       .     .       .
                  Butterbur root extract:Propranolol 0    0 -0.6018       . -0.6018       .     .       .
                   Butterbur root extract:Riboflavin 0    0 -0.1947       . -0.1947       .     .       .
              Butterbur root extract:Sodium Valproate 0    0 -0.2175       . -0.2175       .     .       .
                   Butterbur root extract:Topiramate 0    0 -0.5906       . -0.5906       .     .       .
                             Cinnarizine:CoEnzyme Q10 0    0  0.2200       .  0.2200       .     .       .
                              Cinnarizine:Flunarizine 0    0 -0.4134       . -0.4134       .     .       .
           Cinnarizine:L-5-Hydroxytryptophan (L-5HTP) 0    0  0.7253       .  0.7253       .     .       .
                              Cinnarizine:Nimodipine 0    0  0.5185       .  0.5185       .     .       .
                                 Cinnarizine:Placebo 1 0.57  0.5185  0.2318  0.8918 -0.6600 -0.88  0.3798
                              Cinnarizine:Pregabalin 0    0 -0.2954       . -0.2954       .     .       .
                             Cinnarizine:Propranolol 1 0.62 -0.0833  0.1688 -0.4911  0.6600  0.88  0.3798
                              Cinnarizine:Riboflavin 0    0  0.3238       .  0.3238       .     .       .
                          Cinnarizine:Sodium Valproate 0    0  0.3010       .  0.3010       .     .       .
                              Cinnarizine:Topiramate 0    0 -0.0721       . -0.0721       .     .       .
                            CoEnzyme Q10:Flunarizine 0    0 -0.6335       . -0.6335       .     .       .
          CoEnzyme Q10:L-5-Hydroxytryptophan (L-5HTP) 0    0  0.5053       .  0.5053       .     .       .
                             CoEnzyme Q10:Nimodipine 0    0  0.2984       .  0.2984       .     .       .
                                CoEnzyme Q10:Placebo 1 1.00  0.2984  0.2984       .       .     .       .
                             CoEnzyme Q10:Pregabalin 0    0 -0.5155       . -0.5155       .     .       .
                            CoEnzyme Q10:Propranolol 0    0 -0.3034       . -0.3034       .     .       .
                             CoEnzyme Q10:Riboflavin 0    0  0.1037       .  0.1037       .     .       .
                         CoEnzyme Q10:Sodium Valproate 0    0  0.0810       .  0.0810       .     .       .
                             CoEnzyme Q10:Topiramate 0    0 -0.2922       . -0.2922       .     .       .
           Flunarizine:L-5-Hydroxytryptophan (L-5HTP) 0    0  1.1387       .  1.1387       .     .       .
                              Flunarizine:Nimodipine 0    0  0.9319       .  0.9319       .     .       .
                                 Flunarizine:Placebo 1 1.00  0.9319  0.9319       .       .     .       .
                              Flunarizine:Pregabalin 0    0  0.1180       .  0.1180       .     .       .

                             Flunarizine:Propranolol 0    0  0.3301       .  0.3301       .     .       .
                              Flunarizine:Riboflavin 0    0  0.7372       .  0.7372       .     .       .
                          Flunarizine:Sodium Valproate 0    0  0.7144       .  0.7144       .     .       .
                              Flunarizine:Topiramate 0    0  0.3413       .  0.3413       .     .       .
            L-5-Hydroxytryptophan (L-5HTP):Nimodipine 0    0 -0.2068       . -0.2068       .     .       .
               L-5-Hydroxytryptophan (L-5HTP):Placebo 1 1.00 -0.2068 -0.2068       .       .     .       .
            L-5-Hydroxytryptophan (L-5HTP):Pregabalin 0    0 -1.0208       . -1.0208       .     .       .
           L-5-Hydroxytryptophan (L-5HTP):Propranolol 0    0 -0.8087       . -0.8087       .     .       .
            L-5-Hydroxytryptophan (L-5HTP):Riboflavin 0    0 -0.4016       . -0.4016       .     .       .
        L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate 0    0 -0.4243       . -0.4243       .     .       .
            L-5-Hydroxytryptophan (L-5HTP):Topiramate 0    0 -0.7974       . -0.7974       .     .       .
                               Nimodipine:Placebo 1 1.00 -0.0000  0.0000       .       .     .       .
                            Nimodipine:Pregabalin 0    0 -0.8139       . -0.8139       .     .       .
                           Nimodipine:Propranolol 0    0 -0.6018       . -0.6018       .     .       .
                            Nimodipine:Riboflavin 0    0 -0.1947       . -0.1947       .     .       .
                        Nimodipine:Sodium Valproate 0    0 -0.2175       . -0.2175       .     .       .
                            Nimodipine:Topiramate 0    0 -0.5906       . -0.5906       .     .       .
                               Pregabalin:Placebo 0    0  0.8139       .  0.8139       .     .       .
                             Propranolol:Placebo 1 0.19  0.6018  1.5075  0.3876  1.1199  1.51  0.1300
                              Riboflavin:Placebo 3 1.00  0.1947  0.1947       .       .     .       .
                         Sodium Valproate:Placebo 1 0.54  0.2175  0.1019  0.3522 -0.2504 -0.38  0.7027
                              Topiramate:Placebo 2 0.66  0.5906  0.5533  0.6629 -0.1095 -0.18  0.8569
                          Pregabalin:Propranolol 1 1.00  0.2121  0.2121       .       .     .       .
                           Pregabalin:Riboflavin 0    0  0.6192       .  0.6192       .     .       .
                       Pregabalin:Sodium Valproate 0    0  0.5964       .  0.5964       .     .       .
                           Pregabalin:Topiramate 0    0  0.2233       .  0.2233       .     .       .
                          Propranolol:Riboflavin 0    0  0.4071       .  0.4071       .     .       .
                      Propranolol:Sodium Valproate 2 0.73  0.3844  0.3170  0.5673 -0.2504 -0.38  0.7027
                           Propranolol:Topiramate 2 0.70  0.0112 -0.0220  0.0875 -0.1095 -0.18  0.8569
                       Riboflavin:Sodium Valproate 0    0 -0.0227       . -0.0227       .     .       .
                            Riboflavin:Topiramate 0    0 -0.3959       . -0.3959       .     .       .
                        Sodium Valproate:Topiramate 0    0 -0.3731       . -0.3731       .     .       .
```

```
Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Efficacy – Global approach

```
Q statistics to assess homogeneity / consistency

                    Q df  p-value
Total           32.13  8 < 0.0001
Within designs  26.13  5 < 0.0001
Between designs  6.01  3   0.1113

Design-specific decomposition of within-designs Q statistic

                       Design     Q df p-value
           Placebo:Riboflavin 15.98  2  0.0003
           Placebo:Topiramate  0.83  1  0.3626
 Propranolol:Sodium Valproate  4.47  1  0.0345
       Propranolol:Topiramate  4.85  1  0.0276

Between-designs Q statistic after detaching of single designs

              Detached design    Q df p-value
      Cinnarizine:Propranolol 4.58  2  0.1010
          Placebo:Cinnarizine 4.58  2  0.1010
          Placebo:Propranolol 1.04  2  0.5932
     Placebo:Sodium Valproate 5.75  2  0.0563
           Placebo:Topiramate 5.91  2  0.0520
 Propranolol:Sodium Valproate 5.75  2  0.0563
       Propranolol:Topiramate 5.91  2  0.0520

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                  Q df p-value tau.within tau2.within
Between designs 2.08  3  0.5561     0.5172      0.2675
```

Acceptability – Local approach

```
Back-calculation method to split direct and indirect evidence

Random effects model:

                             comparison k prop    nma direct indir.    RoR     z p-value
     Amitriptylin:Butterbur root extract 0    0 0.6178      . 0.6178      .     .       .
                Amitriptylin:Cinnarizine 0    0 0.5162      . 0.5162      .     .       .
              Amitriptylin:CoEnzyme Q10 0    0 0.6957      . 0.6957      .     .       .
                Amitriptylin:Flunarizine 0    0 0.5870      . 0.5870      .     .       .
                  Amitriptylin:Melatonin 1 1.00 1.1739 1.1739      .      .     .       .
                 Amitriptylin:Nimodipine 0    0 0.7414      . 0.7414      .     .       .
                    Amitriptylin:Placebo 0    0 0.5870      . 0.5870      .     .       .
                 Amitriptylin:Pregabalin 0    0 0.6204      . 0.6204      .     .       .
                Amitriptylin:Propranolol 0    0 0.6069      . 0.6069      .     .       .
                 Amitriptylin:Riboflavin 0    0 1.1922      . 1.1922      .     .       .
           Amitriptylin:Sodium Valproate 0    0 0.3917      . 0.3917      .     .       .
                 Amitriptylin:Topiramate 0    0 0.5833      . 0.5833      .     .       .
      Butterbur root extract:Cinnarizine 0    0 0.8356      . 0.8356      .     .       .
     Butterbur root extract:CoEnzyme Q10 0    0 1.1259      . 1.1259      .     .       .
      Butterbur root extract:Flunarizine 0    0 0.9500      . 0.9500      .     .       .
        Butterbur root extract:Melatonin 0    0 1.9000      . 1.9000      .     .       .
       Butterbur root extract:Nimodipine 0    0 1.2000      . 1.2000      .     .       .
          Butterbur root extract:Placebo 1 1.00 0.9500 0.9500      .      .     .       .
       Butterbur root extract:Pregabalin 0    0 1.0041      . 1.0041      .     .       .
      Butterbur root extract:Propranolol 0    0 0.9822      . 0.9822      .     .       .
       Butterbur root extract:Riboflavin 0    0 1.9297      . 1.9297      .     .       .
 Butterbur root extract:Sodium Valproate 0    0 0.6341      . 0.6341      .     .       .
       Butterbur root extract:Topiramate 0    0 0.9440      . 0.9440      .     .       .
                 Cinnarizine:CoEnzyme Q10 0    0 1.3475      . 1.3475      .     .       .
                  Cinnarizine:Flunarizine 0    0 1.1370      . 1.1370      .     .       .
                    Cinnarizine:Melatonin 0    0 2.2739      . 2.2739      .     .       .
                   Cinnarizine:Nimodipine 0    0 1.4362      . 1.4362      .     .       .
                      Cinnarizine:Placebo 1 0.57 1.1370 2.0000 0.5449 3.6707  1.03  0.3026
                   Cinnarizine:Pregabalin 0    0 1.2017      . 1.2017      .     .       .
                  Cinnarizine:Propranolol 1 0.65 1.1756 0.7500 2.7530 0.2724 -1.03  0.3026
                   Cinnarizine:Riboflavin 0    0 2.3095      . 2.3095      .     .       .
             Cinnarizine:Sodium Valproate 0    0 0.7588      . 0.7588      .     .       .
                   Cinnarizine:Topiramate 0    0 1.1298      . 1.1298      .     .       .
```

```
           CoEnzyme Q10:Flunarizine 0    0 0.8438      . 0.8438      .     .       .
             CoEnzyme Q10:Melatonin 0    0 1.6875      . 1.6875      .     .       .
            CoEnzyme Q10:Nimodipine 0    0 1.0658      . 1.0658      .     .       .
               CoEnzyme Q10:Placebo 1 1.00 0.8438 0.8438      .      .     .       .
            CoEnzyme Q10:Pregabalin 0    0 0.8918      . 0.8918      .     .       .
          CoEnzyme Q10:Propranolol 0    0 0.8724      . 0.8724      .     .       .
           CoEnzyme Q10:Riboflavin 0    0 1.7139      . 1.7139      .     .       .
      CoEnzyme Q10:Sodium Valproate 0    0 0.5631      . 0.5631      .     .       .
         CoEnzyme Q10:Topiramate 0    0 0.8384      . 0.8384      .     .       .
             Flunarizine:Melatonin 0    0 2.0000      . 2.0000      .     .       .
            Flunarizine:Nimodipine 0    0 1.2632      . 1.2632      .     .       .
               Flunarizine:Placebo 1 1.00 1.0000 1.0000      .      .     .       .
            Flunarizine:Pregabalin 0    0 1.0569      . 1.0569      .     .       .
          Flunarizine:Propranolol 0    0 1.0339      . 1.0339      .     .       .
           Flunarizine:Riboflavin 0    0 2.0312      . 2.0312      .     .       .
      Flunarizine:Sodium Valproate 0    0 0.6674      . 0.6674      .     .       .
         Flunarizine:Topiramate 0    0 0.9937      . 0.9937      .     .       .
             Melatonin:Nimodipine 0    0 0.6316      . 0.6316      .     .       .
                Melatonin:Placebo 1 1.00 0.5000 0.5000      .      .     .       .
             Melatonin:Pregabalin 0    0 0.5285      . 0.5285      .     .       .
           Melatonin:Propranolol 0    0 0.5170      . 0.5170      .     .       .
            Melatonin:Riboflavin 0    0 1.0156      . 1.0156      .     .       .
       Melatonin:Sodium Valproate 0    0 0.3337      . 0.3337      .     .       .
            Melatonin:Topiramate 0    0 0.4968      . 0.4968      .     .       .
              Nimodipine:Placebo 1 1.00 0.7917 0.7917      .      .     .       .
           Nimodipine:Pregabalin 0    0 0.8367      . 0.8367      .     .       .
         Nimodipine:Propranolol 0    0 0.8185      . 0.8185      .     .       .
          Nimodipine:Riboflavin 0    0 1.6081      . 1.6081      .     .       .
     Nimodipine:Sodium Valproate 0    0 0.5284      . 0.5284      .     .       .
           Nimodipine:Topiramate 0    0 0.7867      . 0.7867      .     .       .
              Pregabalin:Placebo 0    0 0.9462      . 0.9462      .     .       .
            Propranolol:Placebo 0    0 0.9672      . 0.9672      .     .       .
             Riboflavin:Placebo 3 1.00 0.4923 0.4923      .      .     .       .
        Sodium Valproate:Placebo 1 0.84 1.4983 1.7306 0.6889 2.5123  0.86  0.3890
             Topiramate:Placebo 2 0.85 1.0063 0.7611 4.9417 0.1540 -1.74  0.0815
          Pregabalin:Propranolol 1 1.00 0.9783 0.9783      .      .     .       .
           Pregabalin:Riboflavin 0    0 1.9219      . 1.9219      .     .       .
     Pregabalin:Sodium Valproate 0    0 0.6315      . 0.6315      .     .       .
              Pregabalin:Topiramate 0    0 0.9402      . 0.9402      .     .       .
             Propranolol:Riboflavin 0    0 1.9646      . 1.9646      .     .       .
        Propranolol:Sodium Valproate 2 0.55 0.6455 0.9764 0.3887 2.5123  0.86  0.3890
             Propranolol:Topiramate 2 0.53 0.9611 0.4027 2.6143 0.1540 -1.74  0.0815
          Riboflavin:Sodium Valproate 0    0 0.3286      . 0.3286      .     .       .
           Riboflavin:Topiramate 0    0 0.4892      . 0.4892      .     .       .
        Sodium Valproate:Topiramate 0    0 1.4889      . 1.4889      .     .       .

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (RR) in network meta-analysis
 direct     - Estimated treatment effect (RR) derived from direct evidence
 indir.     - Estimated treatment effect (RR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Acceptability – Global approach

```
Q statistics to assess homogeneity / consistency

                  Q df p-value
Total          5.13  7  0.6439
Within designs 1.99  5  0.8507
Between designs 3.14  2  0.2077

Design-specific decomposition of within-designs Q statistic

                       Design    Q df p-value
          Placebo:Riboflavin 1.20  2  0.5500
          Placebo:Topiramate 0.04  1  0.8359
 Propranolol:Sodium Valproate 0.51  1  0.4756
       Propranolol:Topiramate 0.24  1  0.6230

Between-designs Q statistic after detaching of single designs

              Detached design    Q df p-value
     Cinnarizine:Propranolol 2.08  1  0.1492
         Placebo:Cinnarizine 2.08  1  0.1492
     Placebo:Sodium Valproate 2.40  1  0.1213
          Placebo:Topiramate 0.11  1  0.7429
 Propranolol:Sodium Valproate 2.40  1  0.1213
       Propranolol:Topiramate 0.11  1  0.7429

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                  Q df p-value tau.within tau2.within
Between designs 3.14  2  0.2077          0           0
```

Safety – Local approach

```
Back-calculation method to split direct and indirect evidence

Random effects model:

                            comparison k prop    nma direct indir.    RoR     z p-value
      Butterbur root extract:Cinnarizine 0    0 0.5424      . 0.5424      .     .       .
      Butterbur root extract:Flunarizine 0    0 0.1359      . 0.1359      .     .       .
       Butterbur root extract:Nimodipine 0    0 0.9024      . 0.9024      .     .       .
          Butterbur root extract:Placebo 1 1.00 0.9512 0.9512      .      .     .       .
      Butterbur root extract:Propranolol 0    0 0.5424      . 0.5424      .     .       .
       Butterbur root extract:Riboflavin 0    0 1.2167      . 1.2167      .     .       .
 Butterbur root extract:Sodium Valproate 0    0 0.3962      . 0.3962      .     .       .
       Butterbur root extract:Topiramate 0    0 0.2839      . 0.2839      .     .       .
                 Cinnarizine:Flunarizine 0    0 0.2505      . 0.2505      .     .       .
                  Cinnarizine:Nimodipine 0    0 1.6639      . 1.6639      .     .       .
                     Cinnarizine:Placebo 0    0 1.7538      . 1.7538      .     .       .
                 Cinnarizine:Propranolol 1 1.00 1.0000 1.0000      .      .     .       .
                  Cinnarizine:Riboflavin 0    0 2.2433      . 2.2433      .     .       .
               Cinnarizine:Sodium Valproate 0    0 0.7305      . 0.7305      .     .       .
                  Cinnarizine:Topiramate 0    0 0.5234      . 0.5234      .     .       .
                  Flunarizine:Nimodipine 0    0 6.6410      . 6.6410      .     .       .
                     Flunarizine:Placebo 1 1.00 7.0000 7.0000      .      .     .       .
                 Flunarizine:Propranolol 0    0 3.9913      . 3.9913      .     .       .
                  Flunarizine:Riboflavin 0    0 8.9535      . 8.9535      .     .       .
               Flunarizine:Sodium Valproate 0    0 2.9155      . 2.9155      .     .       .
                  Flunarizine:Topiramate 0    0 2.0890      . 2.0890      .     .       .
                      Nimodipine:Placebo 1 1.00 1.0541 1.0541      .      .     .       .
                  Nimodipine:Propranolol 0    0 0.6010      . 0.6010      .     .       .
                   Nimodipine:Riboflavin 0    0 1.3482      . 1.3482      .     .       .
                Nimodipine:Sodium Valproate 0    0 0.4390      . 0.4390      .     .       .
                   Nimodipine:Topiramate 0    0 0.3146      . 0.3146      .     .       .
                     Propranolol:Placebo 0    0 1.7538      . 1.7538      .     .       .
                      Riboflavin:Placebo 1 1.00 0.7818 0.7818      .      .     .       .
                  Sodium Valproate:Placebo 1 0.79 2.4010 2.8319 1.2987 2.1805  0.34  0.7315
                       Topiramate:Placebo 1 0.78 3.3508 2.8286 6.1678 0.4586 -0.34  0.7315
                   Propranolol:Riboflavin 0    0 2.2433      . 2.2433      .     .       .
               Propranolol:Sodium Valproate 2 0.62 0.7305 0.9844 0.4515 2.1805  0.34  0.7315
                   Propranolol:Topiramate 2 0.81 0.5234 0.4520 0.9856 0.4586 -0.34  0.7315
                Riboflavin:Sodium Valproate 0    0 0.3256      . 0.3256      .     .       .
                     Riboflavin:Topiramate 0    0 0.2333      . 0.2333      .     .       .
                Sodium Valproate:Topiramate 0    0 0.7165      . 0.7165      .     .       .
```

```
Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (RR) in network meta-analysis
 direct     - Estimated treatment effect (RR) derived from direct evidence
 indir.     - Estimated treatment effect (RR) derived from indirect evidence
 RoR        - Ratio of Ratios (direct versus indirect)
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Safety – Global approach

```
Q statistics to assess homogeneity / consistency

                   Q df p-value
Total           0.33  3  0.9545
Within designs  0.21  2  0.8998
Between designs 0.12  1  0.7315

Design-specific decomposition of within-designs Q statistic

                       Design    Q df p-value
 Propranolol:Sodium Valproate 0.00  1  0.9911
       Propranolol:Topiramate 0.21  1  0.6460

Between-designs Q statistic after detaching of single designs

              Detached design    Q df p-value
     Placebo:Sodium Valproate 0.00  0      --
           Placebo:Topiramate 0.00  0      --
 Propranolol:Sodium Valproate 0.00  0      --
       Propranolol:Topiramate 0.00  0      --

Q statistic to assess consistency under the assumption of
a full design-by-treatment interaction random effects model

                   Q df p-value tau.within tau2.within
Between designs 0.12  1  0.7315          0           0
```

eAppendix 4. Details on Publication Bias

Currently, there is a lack of a concrete methodology of assessing across-studies bias (publication bias) for a network meta-analytic approach. Therefore, a comparison-adjusted funnel plot with accompanying Egger test for asymmetry was conducted[2]. See eFigures 2, 3, and 4 for results.

eAppendix 5. Details on Prediction Intervals

Prediction intervals help in the clinical interpretation of the *heterogeneity* by providing a region within which a given percentage of true treatment effects are expected, were calculated.[1] For example, a 95% prediction interval estimates where the true effects are to be expected for 95% of similar (exchangeable) studies that might be conducted in the future. Reporting a prediction interval in addition to the standardized mean differences and confidence intervals can help estimate the range of true effects that can be expected in future settings.

70% Prediction Interval

```
Number of studies: k = 19
Number of treatments: n = 12
Number of pairwise comparisons: m = 19
Number of designs: d = 14

Random effects model

Treatment estimate (sm = 'SMD', comparison: other treatments vs 'Placebo'):
                                   SMD            95%-CI            70%-PI
Butterbur root extract         -0.0000 [-1.1517; 1.1517] [-0.8113; 0.8113]
Cinnarizine                     0.5185 [-0.2116; 1.2486] [-0.1136; 1.1506]
CoEnzyme Q10                    0.2984 [-0.6082; 1.2051] [-0.4042; 1.0011]
Flunarizine                     0.9319 [-0.1179; 1.9817] [ 0.1670; 1.6968]
L-5-Hydroxytryptophan (L-5HTP) -0.2068 [-1.4029; 0.9893] [-1.0388; 0.6252]
Nimodipine                     -0.0000 [-1.0526; 1.0526] [-0.7662; 0.7662]
Placebo                              .                 .                 .
Pregabalin                      0.8139 [-0.2757; 1.9036] [ 0.0310; 1.5968]
Propranolol                     0.6018 [ 0.0317; 1.1720] [ 0.0259; 1.1778]
Riboflavin                      0.1947 [-0.3883; 0.7778] [-0.3855; 0.7749]
Sodium Valproate                0.2175 [-0.4235; 0.8585] [-0.3823; 0.8173]
Topiramate                      0.5906 [ 0.0266; 1.1547] [ 0.0166; 1.1646]

Quantifying heterogeneity / inconsistency:
tau^2 = 0.1803; I^2 = 75.1%

Tests of heterogeneity (within designs) and inconsistency (between designs):
                    Q d.f.  p-value
Total           32.13    8 < 0.0001
Within designs  26.13    5 < 0.0001
Between designs  6.01    3   0.1113
```

75% Prediction Interval

```
Number of studies: k = 19
Number of treatments: n = 12
Number of pairwise comparisons: m = 19
Number of designs: d = 14

Random effects model

Treatment estimate (sm = 'SMD', comparison: other treatments vs 'Placebo'):
                                  SMD            95%-CI            75%-PI
Butterbur root extract        -0.0000 [-1.1517; 1.1517] [-0.9093; 0.9093]
Cinnarizine                    0.5185 [-0.2116; 1.2486] [-0.1899; 1.2269]
CoEnzyme Q10                   0.2984 [-0.6082; 1.2051] [-0.4891; 1.0860]
Flunarizine                    0.9319 [-0.1179; 1.9817] [ 0.0746; 1.7892]
L-5-Hydroxytryptophan (L-5HTP) -0.2068 [-1.4029; 0.9893] [-1.1393; 0.7256]
Nimodipine                    -0.0000 [-1.0526; 1.0526] [-0.8587; 0.8587]
Placebo                             .                 .                 .
Pregabalin                     0.8139 [-0.2757; 1.9036] [-0.0635; 1.6913]
Propranolol                    0.6018 [ 0.0317; 1.1720] [-0.0437; 1.2474]
Riboflavin                     0.1947 [-0.3883; 0.7778] [-0.4555; 0.8450]
Sodium Valproate               0.2175 [-0.4235; 0.8585] [-0.4547; 0.8897]
Topiramate                     0.5906 [ 0.0266; 1.1547] [-0.0527; 1.2339]

Quantifying heterogeneity / inconsistency:
tau^2 = 0.1803; I^2 = 75.1%

Tests of heterogeneity (within designs) and inconsistency (between designs):
                   Q d.f.  p-value
Total          32.13    8 < 0.0001
Within designs 26.13    5 < 0.0001
Between designs  6.01    3   0.1113
```

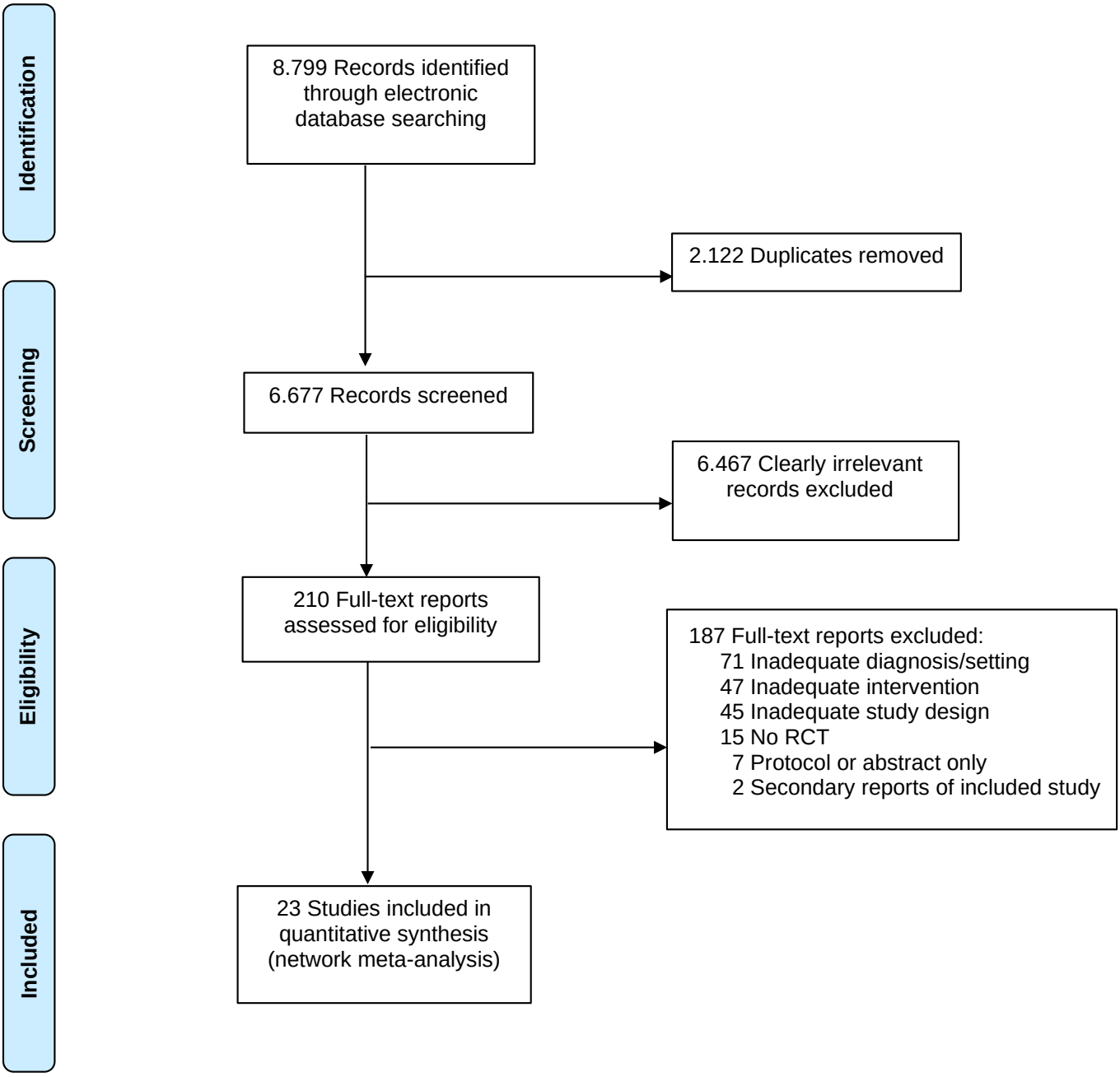
95% Prediction Interval

```
Number of studies: k = 19
Number of treatments: n = 12
Number of pairwise comparisons: m = 19
Number of designs: d = 14

Random effects model

Treatment estimate (sm = 'SMD', comparison: other treatments vs 'Placebo'):
                                  SMD            95%-CI            95%-PI
Butterbur root extract        -0.0000 [-1.1517; 1.1517] [-1.7142; 1.7142]
Cinnarizine                    0.5185 [-0.2116; 1.2486] [-0.8171; 1.8540]
CoEnzyme Q10                   0.2984 [-0.6082; 1.2051] [-1.1862; 1.7831]
Flunarizine                    0.9319 [-0.1179; 1.9817] [-0.6843; 2.5481]
L-5-Hydroxytryptophan (L-5HTP) -0.2068 [-1.4029; 0.9893] [-1.9647; 1.5511]
Nimodipine                    -0.0000 [-1.0526; 1.0526] [-1.6189; 1.6189]
Placebo                             .                 .                 .
Pregabalin                     0.8139 [-0.2757; 1.9036] [-0.8402; 2.4681]
Propranolol                    0.6018 [ 0.0317; 1.1720] [-0.6151; 1.8188]
Riboflavin                     0.1947 [-0.3883; 0.7778] [-1.0311; 1.4206]
Sodium Valproate               0.2175 [-0.4235; 0.8585] [-1.0498; 1.4847]
Topiramate                     0.5906 [ 0.0266; 1.1547] [-0.6222; 1.8034]

Quantifying heterogeneity / inconsistency:
tau^2 = 0.1803; I^2 = 75.1%

Tests of heterogeneity (within designs) and inconsistency (between designs):
                   Q d.f.  p-value
Total          32.13    8 < 0.0001
Within designs 26.13    5 < 0.0001
Between designs  6.01    3   0.1113
```

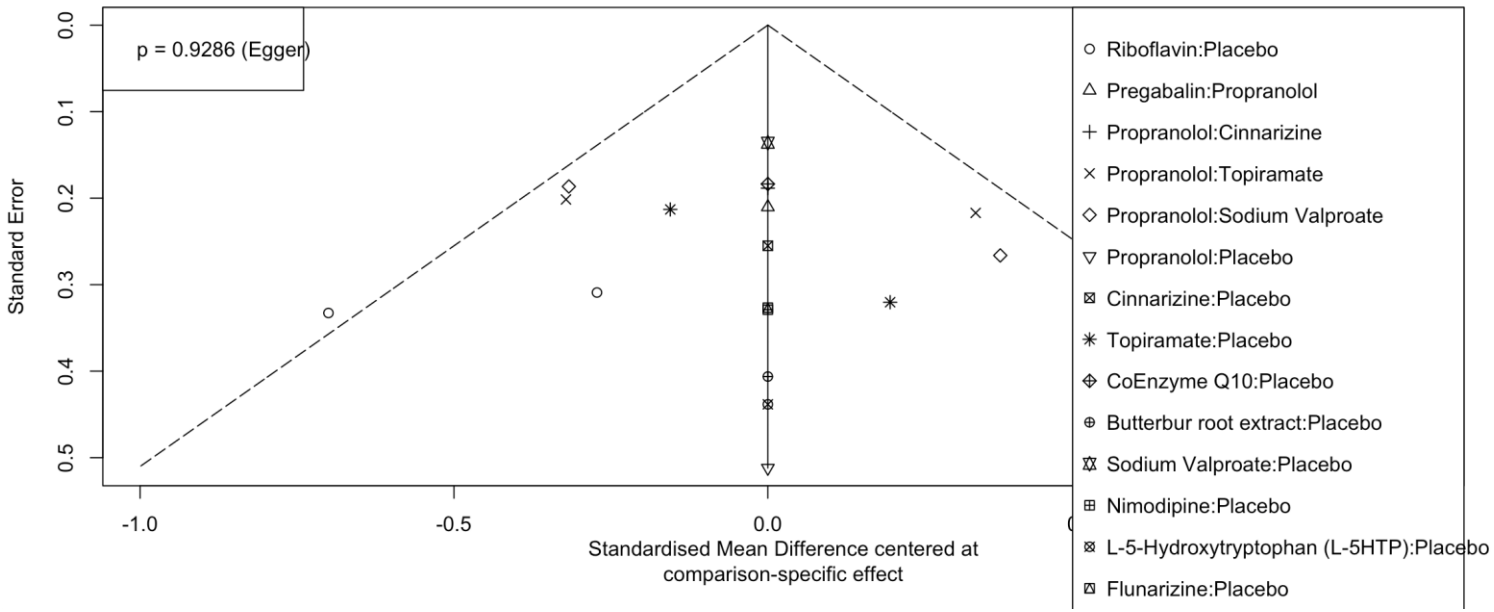
eAppendix 6. Results of Long-term Analysis

For the analysis of long-term effects, we added the measurements with 5-6 months as well as more than 6 months to the data-set. We preferably considered the data with the longest time window after randomization. Two additional studies were considered in the long-term analysis which were not included in the main analysis[7,8]. See eFigures 5, 6, and 7 and eTables 3a, 3b, and 3c for results.

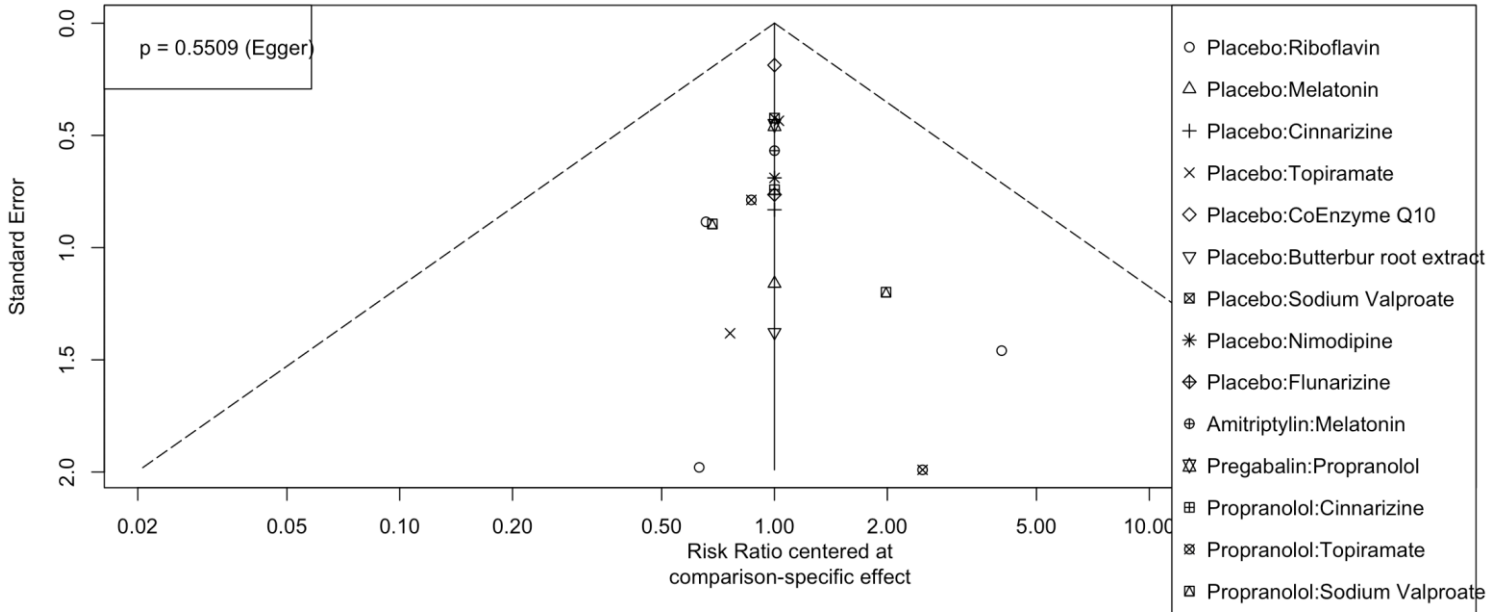
eFigure 1. Flow Chart



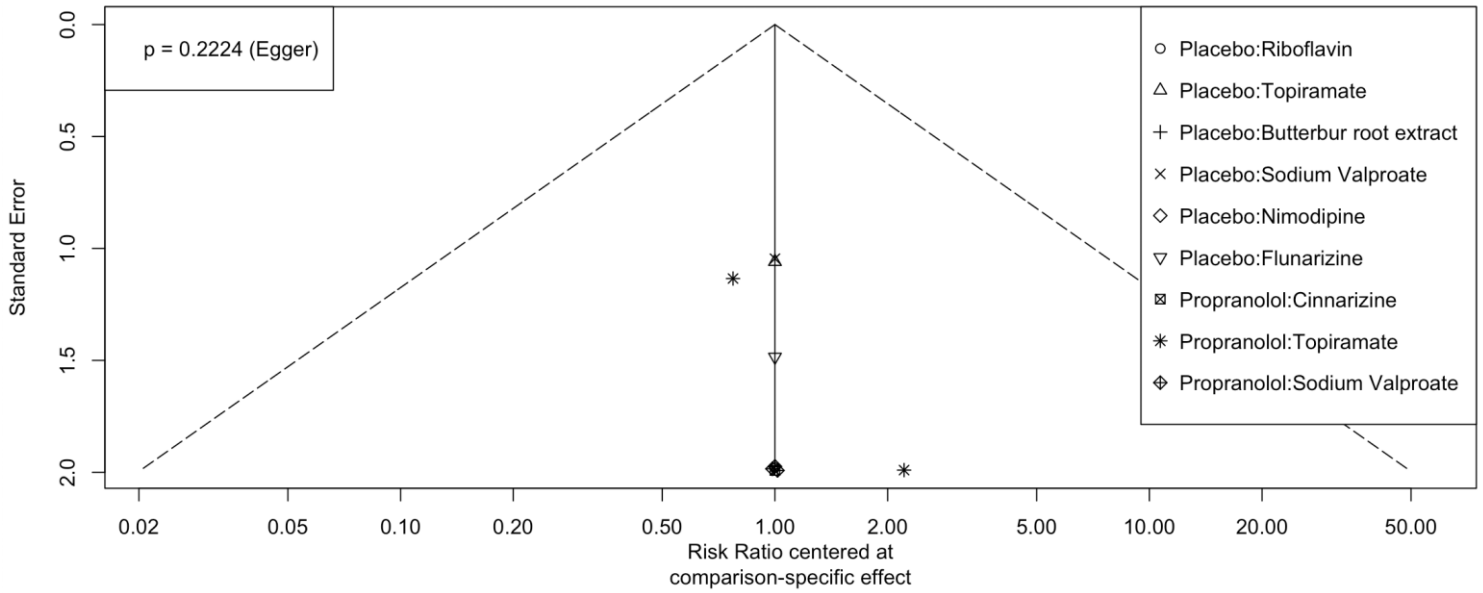
eFigure 2. Funnel plot with accompanying Egger test: Efficacy



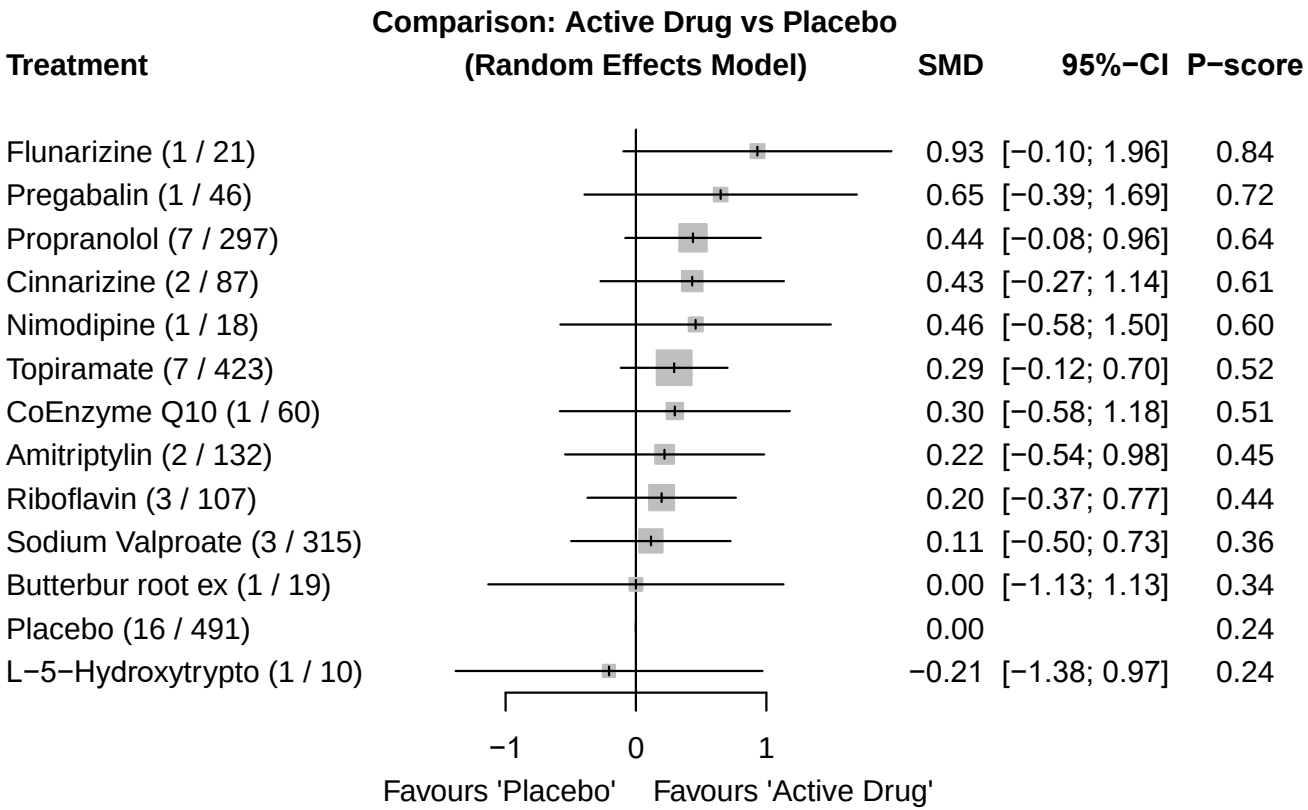
eFigure 3. Funnel plot with accompanying Egger test: Acceptability



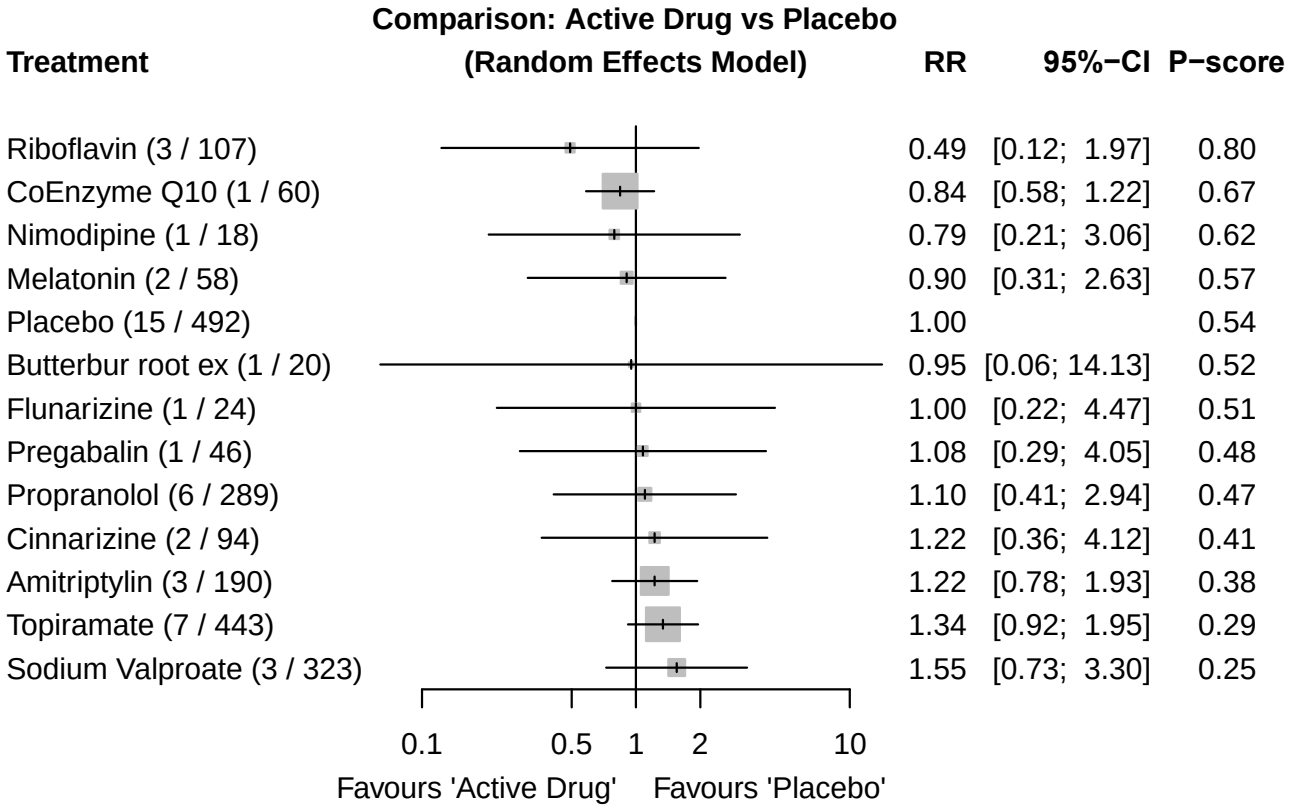
eFigure 4. Funnel plot with accompanying Egger test: Safety



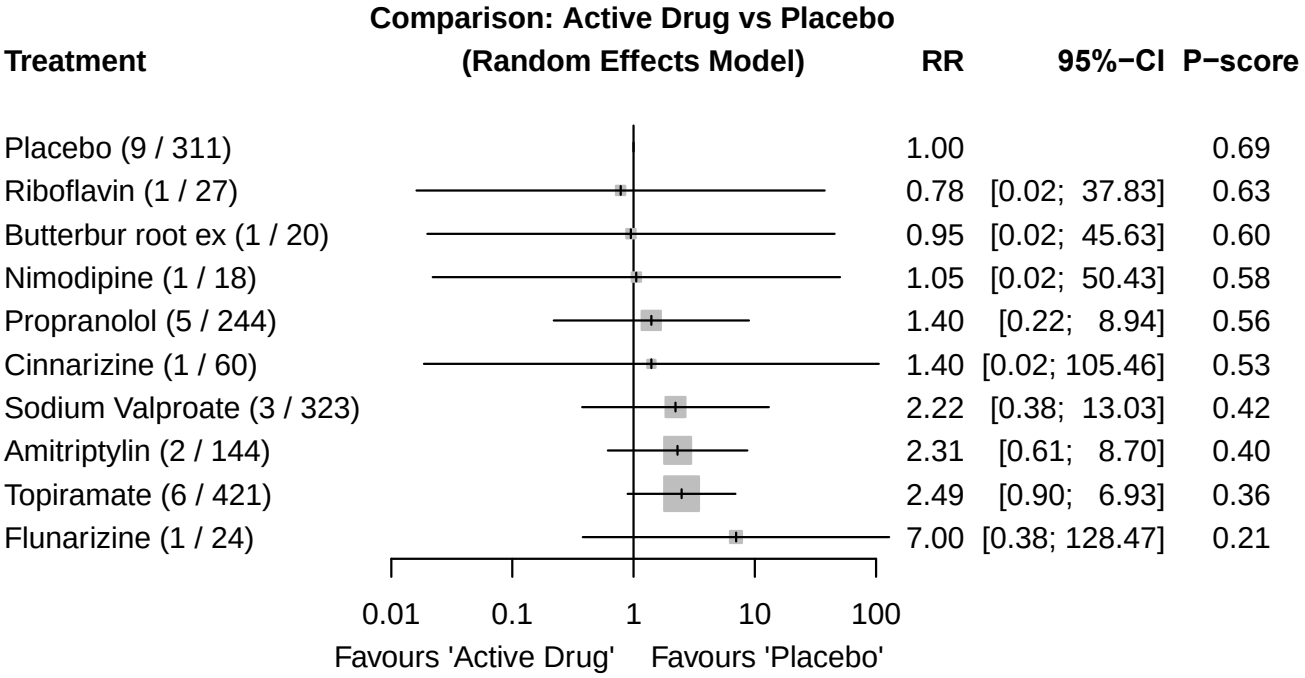
eFigure 5. Long-Term Efficacy – Forest Plot



eFigure 6. Long-Term Acceptability – Forest Plot



eFigure 7. Long-Term Safety – Forest Plot



eTable 1a. Demographics and Study Characteristics

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Apostol 2008	Efficacy Acceptability Safety	250 mg/day Divalproex sodium extended release	500 mg/day Divalproex sodium extended release	1000 mg/day Divalproex sodium extended release	Placebo Identical tablets	migraine	ICHD second edition	250 mg: 14.2 (1.69) 500 mg: 14.1 (1.56) 1000 mg: 14.3 (1.66) Placebo: 14.2 (1.50)	250 mg: 64.2 500 mg: 54 1000 mg: 46.6 Placebo: 52	USA	Low
Ashrafi 2005	Efficacy Acceptability Safety	Sodium Valproate (up to 40 mg/kg/day in 2 doses)	Propranolol (1–3 mg/kg/day in two doses)	-	-	migraine without aura	ICHD first edition	Sodium Valporate: 10.0 (2.30) Propranolol: 10.0 (2.70)	Sodium Valporate: 36.8 Propranolol: 31	not reported	Moderate
Ashrafi 2014	Efficacy Acceptability	Cinnarizine (1.5 mg/kg/day for <30kg, if >30kg: 50mg)		-	Placebo Pill	migraine with and without aura	ICHD second edition	Cinnarizine: 16.7 (2.4) Placebo: 8.9 (1.9)	Cinnarizine: 46.6 Placebo: 65.6	Iran	Low
Bakhshandeh Bali 2015	Efficacy Acceptability	Pregabalin (50-75 mg/day)	Propanolol (10-20 mg/day, in 2 doses)	-	-	migraine with and without aura	ICHD second edition	Pregabalin: 9.95 (n.r.) Propranolol:9.81 (n.r.)	Pregabalin: 26 Propranolol: 31.1	Iran	Moderate
Battistella 1990	Efficacy Acceptability Safety	Nimodipine (10-20 mg/day in 3 doses)	-	-	Placebo Drops	migraine with and without aura	ICHD first edition	Nimodipine: 12.0 (3.4) Placebo:12.4 (3.3)	Nimodipine: 50 Placebo 52.6	Italy	Moderate

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Bidabadi 2010	Efficacy Acceptability Safety	Propranolol (3 mg/kg/day in 2 doses; after one month: 2 mg/kg/day)	Sodium Valproate (30 mg/kg/day in 2 doses; after one month: 15 mg/kg/day)	-	-	migraine without aura	ICHD second edition	Propranolol: 9.8 (2.8) Sodium Valproate: 9.9 (2.57)	Propranolol: 37 Sodium Valproate 30	Iran	Moderate
Bruijn 2010	Efficacy Acceptability	Riboflavin (50 mg/day)	-	-	Placebo Carotene capsules	migraine with and without aura	ICHD second edition	Riboflavin: 9.9 (1.89) Placebo: 9.5 (1.63)	Riboflavin: 40 Placebo: 45.5	Netherlands	Low
Fallah 2013	Efficacy Acceptability Safety	Topiramate (3 mg/kg/day)	Propranolol (1 mg/kg/day)	-	-	migraine with and without aura	n.r.	Topiramate: 10.1 (2.24) Propranolol: 10.7 (2.35)	Topiramate: 58 Propranolol: 46	Iran	Low
Fallah 2018[b]	Acceptability	Amitriptylin (1 mg/kg/day; max. 50 mg/day)	Melatonin (0.3 mg/kg/day; max. 6 mg/day)	-	-	migraine with and without aura	ICHD second edition	Amitriptylin: 10.1 (2.13) Melatonin: 10.6 (2.44)	Amitriptylin: 47.5 Melatonin: 55.0	Iran	Low
Gelfand 2017[c]	Acceptability	Melatonin (3 mg/day)	-	-	Placebo	migraine	ICHD third edition (beta version)	-	-	USA	Low

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Lakshmi 2007	Efficacy Acceptability	Topiramate (25-100 mg/day in 2 doses [baseline] 100 mg in 2 doses [maintenance phase])	-	-	Placebo Pill	migraine with and without aura	ICHD second edition	Topiramate: 10.95 (1.53) Placebo: 10.14 (1.35)	Topiramate: 14.29 Placebo: 47.62	India	Low
Lewis 2009	Efficacy Acceptability Safety	Topiramate 50 mg/day	Topiramate 100 mg/day	-	Placebo Capsule	migraine	ICHD second edition	Topiramate 50mg: 14.2 (1.6) Topiramate 100mg: 14.2 (1.5) Placebo: 14.4 (1.70)	Topiramate 50mg: 71.43 Topiramate 100mg: 48.57 Placebo: 63.64	US and non-US	Moderate
Ludvigsson 1974	Efficacy	Propranolol (<35kg: max. 60 mg/day in 3 doses; >35kg max 120 mg/day in 3 doses)	-	-	Placebo Pill	migraine	Ad hoc Committee on classification of headache	n.r.	Propranolol:43.75 Placebo: 43.75	Sweden	Moderate
MacLennan 2008	Efficacy Acceptability Safety	Riboflavin (200 mg/day)	-	-	Placebo Pill	migraine with and without aura	ICHD second edition	Riboflavin: 11.1 (2.1) Placebo: 11.5 (2.5)	Riboflavin: 44.44 Placebo: 57.14	Australia	Low

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Oelkers 2008	Efficacy Acceptability Safety	Butterbur root extract (8-9 years: 50mg/day in 2 doses [if no improvement: 75mg/day]; 10-12 years: 100mg/d in 2 doses [if no improvement: 150mg/day])		-	Placebo	migraine with and without aura	ICHD first edition (24h-rule replaced with 18h-rule)	Butterbur root extract: 10.6 (1.2) Placebo: 10.6 (1.5)	Butterbur root extract: 47.4 Placebo: 31.6	Germany	Moderate
Santucci 1986	Efficacy	L-5-Hydroxytryptophan (5mg/kg/day in 3 doses)	-	-	Placebo Identical gelatine capsules	common migraine	In accordance with the ad hoc Committee on classification of headache	Age range? 6-11	< 50% female	Italy	Moderate
Slater 2011	Efficacy Acceptability	CoEnzyme Q10 as chewable tablets (100mg/day)	-	-	Placebo Chewable tablets	migraine with and without aura	ICHD second edition	CoEnzyme Q10: 13.3 (3) Placebo: 14 (2.6)	CoEnzyme Q10: 66.7 Placebo: 63.3	USA	Moderate
Sorge 1985	Efficacy Acceptability Safety	Flunarizine (5 mg/day)	-	-	Placebo	common and classical migraine	Valquist's criteria, clinical observation	Flunarizine: 10.6 (3.25) Placebo: 10.7 (3.29)	Flunarizine: 58.3 Placebo: 54.6	Italy	Moderate

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Talebian 2018	Efficacy Acceptability	Riboflavin 100mg	Riboflavin 200mg	-	Placebo Capsule	migraine with and without aura	ICHD second edition	Riboflavin 100mg: 8.47 (n.r.) Riboflavin 200mg: 8.97 (n.r.) Placebo: 7.9 (n.r.)	Riboflavin 100mg: 43.3 Riboflavin 200mg: 43.3 Placebo 50	Iran	Low
Togha 2012	Efficacy Acceptability Safety	Cinnarizine (6-12years: 37.5mg/day; 12-17 years: 50mg/day in 2 doses)	Propranolol (1 mg/kg/day)	-	-	migraine with and without aura	ICHD second edition	Cinnarizine: 9.8 (2.3) Propranolol: 8.9 (2.7)	Cinnarizine: 33.3 Propranolol: 32.1	Iran	Moderate
Tonekaboni 2013	Efficacy Acceptability Safety	Topiramate (50-100 mg/day)	Propranolol (20-80 mg/day)	-	-	migraine	ICHD second edition	Topiramate: 8.5 (2.9) Propranolol: 8.3 (2.8)	Topiramate: 50 Propranolol: 52.5	Iran	Moderate
Winner 2005[d]	Efficacy Acceptability Safety	Topiramate (15 mg/day [week 1], 30 mg/day [week 2], 50 mg/day [week 3], in 2 doses)	-	-	Placebo	migraine with and without aura	ICHD 1997 proposed revision	Topiramate: 11.3 (2.5) Placebo: 10.7 (2.6)	Topiramate: 53.1 Placebo: 53.1	USA	Moderate

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias[a]
Powers 2017[d]	Efficacy Acceptability Safety	Amitriptylin (1 mg/kg/day in 2 doses)	Topiramate (2 mg/kg/day in 2 doses)	-	Placebo	migraine with and without aura	ICHD second edition	Amitriptylin: 14.2 (2.4) Topiramate: 14.2 (2.5) Placebo: 14.2 (2.5)	Amitriptylin: 67 Topiramate: 69.7 Placebo: 68.06	USA	Low

Note. *ICHD* = International Classification of Headache Disorders

[a] Based on adequacy of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, usage of observer-rated outcomes, completeness of outcome data, specification of main outcomes a priori, reporting on all outcomes, and conduction of ITT-analyses. Individual items were summarized to produce a total score of 1 (low risk of bias), 2 (moderate/unclear risk of bias), or 3 (high risk of bias).

[b] This study did not report efficacy data in a usable way (i.e., no baseline data reported).

[c] This study did report efficacy data; however, the study was unconnected to the efficacy network.

[d] These studies reported long-term outcomes and were not included in the main analysis but only in the long-term analysis

eTable 1b. Study design and outcomes

						Dichotomous outcome		Continuous outcome	
Study ID	**Number of study sites**	**Study design**	**Treatment duration**	**Co-intervention**	**Randomized per group**	**Responder criterion**	**Reported time point(s)**	**Types of outcome**	**Reported time point(s)**
Apostol 2008	38	Parallel	10 weeks plus 2 weeks titration	No	250 mg: 83 500 mg: 74 1000 mg: 75 Placebo: 73	≥50% reduction in migraine frequency within 4 weeks	2-4 months	Migraine frequency within 3 months prior to screening	2-4 months
Ashrafi 2005	n.r.	Parallel	≥ 12 weeks	No	Sodium Valporate: 60 Propranolol: 60	≥ 50% reduction of baseline headache frequency per month	up to 2 months	Headache frequency	2-4 months
Ashrafi 2014	1	Parallel	12 weeks	No	Cinnarizine: 34 Placebo: 34	≥50% reduction of baseline headache frequency per month	2-4 months	Headache frequency per month	2-4 months
Bakhshandeh Bali 2015	1	Parallel	at least 8 weeks	Yes	Pregabalin: 46 Propranolol: 45	>=50% reduction of severity and frequency of headache per month	up to 2 months	Headache frequency per month	up to 2 months
Battistella 1990	n.r.	Crossover	12 weeks, 4 weeks washout crossover, 12 weeks	No	Nimodipine: 18 Placebo: 19	n.r.	n.r.	Headache frequency (attacks per month)	2-4 months
Bidabadi 2010	1	Parallel	4 to 6 months	No	Propranolol: 32 Sodium Valpoate: 31	Headache frequency: Reduction of baseline headache frequency by >50%	2-4 months	Headache frequency per month	2-4 months
Bruijn 2010	2	Crossover	16 weeks, 4 weeks washout, 16 weeks	Yes	Riboflavin: 20 Placebo: 22	n.r.	n.r.	Mean frequency of migraine attacks in the last 4 weeks at the end of the riboflavin and placebo phase	2-4 months

eTable 1b. Study design and outcomes. Continued.

						Dichotomous outcome		Continuous outcome	
Study ID	**Number of study sites**	**Study design**	**Treatment duration**	**Co-intervention**	**Randomized per group**	**Responder criterion**	**Reported time point(s)**	**Types of outcome**	**Reported time point(s)**
Fallah 2013	1	Parallel	3 months	No	Topiramate: 50 Propranolol: 50	≥50% reduction in monthly headache frequency	2-4 months	Headache frequency monthly	2-4 months
Fallah 2018	1	Parallel	12 weeks	No	Melatonin: 45 Amitriptylin: 46	More than 50% decrease in monthly headache frequency during the follow-up period	n.r.	Monthly headache frequency	n.r.
Gelfand 2017	1	Parallel	12 weeks	Yes	Melatonin: 13 Placebo: 13	n.r.	n.r.	Mean migraine days	2-4 months
Lakshmi 2007	1	Parallel	12 weeks	No	Topiramate: 22 Placebo: 22	≥50% reduction in monthly migraine days	2-4 months	Migraine frequency	2-4 months
Lewis 2009	31	Parallel	4 weeks titration and 12 weeks maintenance	No	Topiramate 50mg: 35 Topiramate 100mg: 35 Placebo: 33	≥50% reduction in the monthly migraine attack rate (48-hour-rule: a single migraine episode defined as all recurrences of migraine symptoms within 48 hours after onset)	2-4 months	Migraine attacks per month	2-4 months
Ludvigsson 1974	n.r.	Crossover	2 x13 weeks including titration phase of 1 week each	No	Propranolol: 16 Placebo: 16	Headache frequency reduction responder (66,6% reduction)	2-4 months	Frequency of headache attacks during a 3-month period	2-4 months
MacLennan 2008	1	Parallel	12 weeks	No	Riboflavin: 27 Placebo: 21	≥50% reduction in the number of migraine attacks per 4 weeks at the end of the study period, compared with the baseline month	up to 2 months	Migraine frequency per month	n.r.

eTable 1b. Study design and outcomes. Continued**.**

						Dichotomous outcome		Continuous outcome	
Study ID	**Number of study sites**	**Study design**	**Treatment duration**	**Co-intervention**	**Randomized per group**	**Responder criterion**	**Reported time point(s)**	**Types of outcome**	**Reported time point(s)**
Oelkers 2008	1	Parallel	12 weeks	Yes	Butterbur root extract: 20 Placebo: 19	≥50% reduction of headache frequency compared with baseline	n.r.	Attack frequency per 28 days	Up to 2 months and 5-6 months
Santucci 1986	n.r.	Crossover	4 weeks	No	n.r.	n.r.	n.r.	Frequency of migraine attacks per 4 weeks	2-4 months
Slater 2011	1	Crossover	2 x16 weeks	No	CoEnzyme Q10: 60 Placebo: 60	CoEnzyme Q10: Migraine episodes -50% or more Placebo: n.r.	n.r.	Headache frequency	Up to 2 months and 2-4 months
Sorge 1985	1	Parallel	12 weeks	No	Flunarizine: 24 Placebo: 24	>50% reduction in migraine frequency	n.r.	Headache frequency	2-4 months
Talebian 2018	1	Parallel	12 weeks	No	Riboflavin 100mg: 30 Riboflavin 200mg: 30 Placebo: 30	≥50% reduction in headache days	2-4 months	Frequency of migraine attacks	2-4 months
Togha 2012	3	Parallel	12 weeks	No	Cinnarizine: 60 Propranolol: 60	≥ 50% reduction of baseline headache frequency per month	Up to 2 months and 2-4 months	Migraine frequency attacks per month	2-4 months
Tonekaboni 2013	1	Parallel	4weeks/16weeks	No	Topiramate: 44 Propranolol: 42	n.r.	n.r.	Frequency, average number of headaches	up to 2 months and 2-4 months

eTable 1b. Study design and outcomes. Continued.

						Dichotomous outcome		Continuous outcome	
Study ID	**Number of study sites**	**Study design**	**Treatment duration**	**Co-intervention**	**Randomized per group**	**Responder criterion**	**Reported time point(s)**	**Types of outcome**	**Reported time point(s)**
Powers 2017*	31	Crossover	12 weeks	unclear	Amitriptylin: 144 Topiramate: 145 Placebo: 72	≥50%reduction in number of headache days compared with baseline	4-6 months	Headache days per 28 days	4-6 months
Winner 2005*	17	Parallel	8 weeks titration (increasing dose), 12 weeks maintenance	No	Topiramate: 112 Placebo: 50	>50% baseline vs. last 28 days	4-6 months	Number of migraine days per months	4-6 months

* These studies reported long-term outcomes and were not included in the main analysis but only in the long-term analysis

eTable 2a. Head-to-head comparisons of efficacy of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]
Butterbur root extract [1]							0.00 [-1.15; 1.15]					
Cinnarizine [2]	-0.52 [-1.88; 0.85]						0.23 [-0.74; 1.20]		0.17 [-0.74; 1.08]			
CoEnzyme Q10 [3]	-0.30 [-1.76; 1.17]	0.22 [-0.94; 1.38]					0.30 [-0.61; 1.21]					
Flunarizine [4]	-0.93 [-2.49; 0.63]	-0.41 [-1.69; 0.87]	-0.63 [-2.02; 0.75]				0.93 [-0.12; 1.98]					
L-5-Hydroxytryptophan (L-5HTP) [5]	0.21 [-1.45; 1.87]	0.73 [-0.68; 2.13]	0.51 [-1.00; 2.01]	1.14 [-0.45; 2.73]			-0.21 [-1.40; 0.99]					
Nimodipine [6]	-0.00 [-1.56; 1.56]	0.52 [-0.76; 1.80]	0.30 [-1.09; 1.69]	0.93 [-0.55; 2.42]	-0.21 [-1.80; 1.39]		0.00 [-1.05; 1.05]					
Placebo [7]	-0.00 [-1.15; 1.15]	0.52 [-0.21; 1.25]	0.30 [-0.61; 1.21]	0.93 [-0.12; 1.98]	-0.21 [-1.40; 0.99]	-0.00 [-1.05; 1.05]			-1.51 [-2.81; -0.20]	-0.19 [-0.78; 0.39]	-0.10 [-0.98; 0.77]	-0.55 [-1.25; 0.14]
Pregabalin [8]	-0.81 [-2.40; 0.77]	-0.30 [-1.47; 0.88]	-0.52 [-1.93; 0.90]	0.12 [-1.40; 1.63]	-1.02 [-2.64; 0.60]	-0.81 [-2.33; 0.70]	-0.81 [-1.90; 0.28]		0.21 [-0.72; 1.14]			
Propranolol [9]	-0.60 [-1.89; 0.68]	-0.08 [-0.80; 0.63]	-0.30 [-1.37; 0.77]	0.33 [-0.86; 1.52]	-0.81 [-2.13; 0.52]	-0.60 [-1.80; 0.60]	-0.60 [-1.17; -0.03]	0.21 [-0.72; 1.14]			0.32 [-0.35; 0.98]	-0.02 [-0.68; 0.63]

eTable 2a. Head-to-head comparisons of efficacy of the included prophylactic treatments. Continued.

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]
Riboflavin [10]	-0.19 [-1.49; 1.10]	0.32 [-0.61; 1.26]	0.10 [-0.97; 1.18]	0.74 [-0.46; 1.94]	-0.40 [-1.73; 0.93]	-0.19 [-1.40; 1.01]	-0.19 [-0.78; 0.39]	0.62 [-0.62; 1.86]	0.41 [-0.41; 1.22]			
Sodium Valproate [11]	-0.22 [-1.54; 1.10]	0.30 [-0.55; 1.15]	0.08 [-1.03; 1.19]	0.71 [-0.52; 1.94]	-0.42 [-1.78; 0.93]	-0.22 [-1.45; 1.01]	-0.22 [-0.86; 0.42]	0.60 [-0.49; 1.69]	0.38 [-0.19; 0.95]	-0.02 [-0.89; 0.84]		
Topiramate [12]	-0.59 [-1.87; 0.69]	-0.07 [-0.89; 0.75]	-0.29 [-1.36; 0.78]	0.34 [-0.85; 1.53]	-0.80 [-2.12; 0.52]	-0.59 [-1.78; 0.60]	-0.59 [-1.15; -0.03]	0.22 [-0.85; 1.30]	0.01 [-0.54; 0.56]	-0.40 [-1.21; 0.42]	-0.37 [-1.09; 0.34]	

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets.
Cells contain the network estimates (SMDs) from network meta-analysis in the lower triangle and the direct treatment estimates (SMDs) from pairwise comparisons in the upper triangle.

eTable 2b. Head-to-head comparisons of acceptability of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]						1.17 [0.39; 3.57]							
Butterbur root extract [2]	0.62 [0.02; 25.02]							0.95 [0.06; 14.13]					
Cinnarizine [3]	0.52 [0.03; 8.60]	0.84 [0.04; 16.20]						2.00 [0.39; 10.20]		0.75 [0.18; 3.21]			
CoEnzyme Q10 [4]	0.70 [0.05; 8.98]	1.13 [0.07; 17.17]	1.35 [0.37; 4.84]					0.84 [0.58; 1.22]					
Flunarizine [5]	0.59 [0.03; 11.12]	0.95 [0.04; 20.82]	1.14 [0.16; 7.87]	0.84 [0.18; 3.94]				1.00 [0.22; 4.47]					
Melatonin [6]	1.17 [0.39; 3.57]	1.90 [0.06; 64.83]	2.27 [0.17; 30.11]	1.69 [0.17; 16.89]	2.00 [0.13; 30.44]			0.50 [0.05; 4.86]					
Nimodipine [7]	0.74 [0.04; 13.07]	1.20 [0.06; 24.56]	1.44 [0.23; 8.90]	1.07 [0.26; 4.32]	1.26 [0.17; 9.49]	0.63 [0.04; 8.90]		0.79 [0.21; 3.06]					
Placebo [8]	0.59 [0.05; 7.38]	0.95 [0.06; 14.13]	1.14 [0.33; 3.87]	0.84 [0.58; 1.22]	1.00 [0.22; 4.47]	0.50 [0.05; 4.86]	0.79 [0.21; 3.06]				2.03 [0.51; 8.12]	0.58 [0.25; 1.32]	1.31 [0.58; 2.96]
Pregabalin [9]	0.62 [0.04; 10.97]	1.00 [0.05; 20.61]	1.20 [0.28; 5.25]	0.89 [0.22; 3.64]	1.06 [0.14; 7.97]	0.53 [0.04; 7.46]	0.84 [0.12; 5.68]	1.06 [0.27; 4.10]		0.98 [0.40; 2.38]			

eTable 2b. Head-to-head comparisons of acceptability of the included prophylactic treatments. Continued.

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	0.61 [0.04; 9.32]	0.98 [0.05; 17.63]	1.18 [0.36; 3.81]	0.87 [0.29; 2.59]	1.03 [0.17; 6.34]	0.52 [0.04; 6.26]	0.82 [0.15; 4.46]	1.03 [0.37; 2.88]	0.98 [0.40; 2.38]			0.98 [0.24; 3.98]	0.40 [0.10; 1.69]
Riboflavin [11]	1.19 [0.07; 21.37]	1.93 [0.09; 40.12]	2.31 [0.36; 14.68]	1.71 [0.41; 7.18]	2.03 [0.26; 15.62]	1.02 [0.07; 14.56]	1.61 [0.23; 11.13]	2.03 [0.51; 8.12]	1.92 [0.28; 13.36]	1.96 [0.35; 11.00]			
Sodium Valproate [12]	0.39 [0.03; 5.51]	0.63 [0.04; 10.48]	0.76 [0.20; 2.88]	0.56 [0.24; 1.31]	0.67 [0.12; 3.58]	0.33 [0.03; 3.67]	0.53 [0.11; 2.49]	0.67 [0.31; 1.43]	0.63 [0.16; 2.49]	0.65 [0.23; 1.83]	0.33 [0.07; 1.60]		
Topiramate [13]	0.58 [0.04; 8.18]	0.94 [0.06; 15.55]	1.13 [0.30; 4.29]	0.84 [0.36; 1.93]	0.99 [0.19; 5.30]	0.50 [0.05; 5.45]	0.79 [0.17; 3.69]	0.99 [0.47; 2.10]	0.94 [0.24; 3.72]	0.96 [0.34; 2.75]	0.49 [0.10; 2.36]	1.49 [0.54; 4.07]	

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets.
Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle.
Shaded Area = Direct Comparisons

eTable 2c. Head-to-head comparisons of safety of the included prophylactic treatments

	Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
Butterbur root extract					0.95 [0.02; 45.63]				
Cinnarizine	0.54 [0.00; 201.21]					1.00 [0.02; 49.59]			
Flunarizine	0.14 [0.00; 17.23]	0.25 [0.00; 52.10]			7.00 [0.38; 128.47]				
Nimodipine	0.90 [0.00; 214.72]	1.66 [0.00; 616.22]	6.64 [0.05; 840.10]		1.05 [0.02; 50.43]				
Placebo	0.95 [0.02; 45.63]	1.75 [0.02; 153.87]	7.00 [0.38; 128.47]	1.05 [0.02; 50.43]			1.28 [0.03; 61.88]	0.35 [0.05; 2.74]	0.35 [0.04; 2.82]
Propranolol	0.54 [0.01; 46.23]	1.00 [0.02; 49.59]	3.99 [0.10; 151.99]	0.60 [0.01; 51.11]	0.57 [0.06; 5.08]			0.98 [0.06; 15.48]	0.45 [0.07; 3.12]
Riboflavin	1.22 [0.01; 291.78]	2.24 [0.01; 836.87]	8.95 [0.07; 1142.76]	1.35 [0.01; 322.72]	1.28 [0.03; 61.88]	2.24 [0.03; 192.64]			
Sodium Valproate	0.40 [0.01; 28.53]	0.73 [0.01; 63.41]	2.92 [0.09; 90.18]	0.44 [0.01; 31.54]	0.42 [0.07; 2.57]	0.73 [0.08; 6.36]	0.33 [0.00; 23.63]		
Topiramate	0.28 [0.00; 20.59]	0.52 [0.01; 37.59]	2.09 [0.07; 65.21]	0.31 [0.00; 22.77]	0.30 [0.05; 1.87]	0.52 [0.09; 2.98]	0.23 [0.00; 17.06]	0.72 [0.08; 6.49]	

Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle.
Shaded Area = Direct Comparisons

eTable 3a. Head-to-head comparisons of long-term efficacy of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]								0.14 [-0.72; 1.00]					0.00 [-0.84; 0.84]
Butterbur root extract [2]	0.22 [-1.15; 1.59]							0.00 [-1.13; 1.13]					
Cinnarizine [3]	-0.21 [-1.23; 0.80]	-0.43 [-1.77; 0.90]						0.23 [-0.72; 1.18]		0.17 [-0.72; 1.06]			
CoEnzyme Q10 [4]	-0.08 [-1.25; 1.09]	-0.30 [-1.73; 1.14]	0.13 [-1.00; 1.26]					0.30 [-0.58; 1.18]					
Flunarizine [5]	-0.71 [-1.99; 0.57]	-0.93 [-2.46; 0.60]	-0.50 [-1.75; 0.75]	-0.63 [-1.99; 0.72]				0.93 [-0.10; 1.96]					
L-5-Hydroxytryptophan (L-5HTP) [6]	0.43 [-0.98; 1.83]	0.21 [-1.43; 1.84]	0.64 [-0.73; 2.01]	0.51 [-0.97; 1.98]	1.14 [-0.43; 2.70]			-0.21 [-1.38; 0.97]					
Nimodipine [7]	-0.24 [-1.53; 1.05]	-0.46 [-1.99; 1.08]	-0.03 [-1.28; 1.23]	-0.16 [-1.52; 1.20]	0.47 [-0.99; 1.94]	-0.66 [-2.24; 0.91]		0.46 [-0.58; 1.50]					
Placebo [8]	0.22 [-0.54; 0.98]	0.00 [-1.13; 1.13]	0.43 [-0.27; 1.14]	0.30 [-0.58; 1.18]	0.93 [-0.10; 1.96]	-0.21 [-1.38; 0.97]	0.46 [-0.58; 1.50]			-1.51 [-2.79; -0.22]	-0.20 [-0.77; 0.37]	-0.10 [-0.95; 0.75]	-0.21 [-0.66; 0.24]
Pregabalin [9]	-0.43 [-1.69; 0.83]	-0.65 [-2.19; 0.89]	-0.22 [-1.36; 0.92]	-0.35 [-1.72; 1.02]	0.28 [-1.18; 1.75]	-0.86 [-2.43; 0.72]	-0.19 [-1.66; 1.28]	-0.65 [-1.69; 0.39]		0.21 [-0.69; 1.12]			

eTable 3a. Head-to-head comparisons of long-term efficacy of the included prophylactic treatments. Continued.

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	-0.22 [-1.09; 0.65]	-0.44 [-1.68; 0.81]	-0.01 [-0.70; 0.69]	-0.14 [-1.16; 0.89]	0.49 [-0.66; 1.65]	-0.64 [-1.93; 0.64]	0.02 [-1.14; 1.18]	-0.44 [-0.96; 0.08]	0.21 [-0.69; 1.12]			0.32 [-0.34; 0.97]	-0.02 [-0.66; 0.62]
Riboflavin [11]	0.02 [-0.93; 0.98]	-0.20 [-1.47; 1.07]	0.23 [-0.67; 1.14]	0.10 [-0.95; 1.15]	0.73 [-0.44; 1.91]	-0.40 [-1.71; 0.90]	0.26 [-0.92; 1.45]	-0.20 [-0.77; 0.37]	0.45 [-0.74; 1.64]	0.24 [-0.53; 1.01]			
Sodium Valproate [12]	0.11 [-0.84; 1.05]	-0.11 [-1.40; 1.17]	0.32 [-0.51; 1.15]	0.18 [-0.89; 1.26]	0.82 [-0.38; 2.01]	-0.32 [-1.65; 1.01]	0.34 [-0.86; 1.55]	-0.11 [-0.73; 0.50]	0.54 [-0.52; 1.60]	0.32 [-0.23; 0.87]	0.08 [-0.75; 0.92]		
Topiramate [13]	-0.07 [-0.83; 0.69]	-0.29 [-1.50; 0.91]	0.14 [-0.62; 0.89]	0.00 [-0.97; 0.98]	0.64 [-0.47; 1.75]	-0.50 [-1.75; 0.75]	0.16 [-0.95; 1.28]	-0.29 [-0.70; 0.12]	0.36 [-0.68; 1.39]	0.14 [-0.36; 0.65]	-0.10 [-0.80; 0.61]	-0.18 [-0.83; 0.47]	

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets.
Cells contain the network estimates (SMDs) from network meta-analysis in the lower triangle and the direct treatment estimates (SMDs) from pairwise comparisons in the upper triangle.
Shaded Area = Direct Comparisons

eTable 3b. Head-to-head comparisons of long-term acceptability of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]						1.17 [0.39; 3.57]		1.46 [0.83; 2.57]					0.89 [0.61; 1.29]
Butterbur root extract [2]	1.29 [0.08; 19.92]							0.95 [0.06; 14.13]					
Cinnarizine [3]	1.00 [0.28; 3.59]	0.78 [0.04; 15.01]						2.00 [0.39; 10.20]		0.75 [0.18; 3.21]			
CoEnzyme Q10 [4]	1.45 [0.81; 2.60]	1.13 [0.07; 17.17]	1.45 [0.41; 5.15]					0.84 [0.58; 1.22]					
Flunarizine [5]	1.22 [0.26; 5.85]	0.95 [0.04; 20.82]	1.22 [0.18; 8.40]	0.84 [0.18; 3.94]				1.00 [0.22; 4.47]					
Melatonin [6]	1.35 [0.50; 3.69]	1.05 [0.06; 19.13]	1.35 [0.27; 6.70]	0.93 [0.30; 2.88]	1.11 [0.18; 6.94]			0.50 [0.05; 4.86]					
Nimodipine [7]	1.55 [0.37; 6.44]	1.20 [0.06; 24.56]	1.54 [0.25; 9.49]	1.07 [0.26; 4.32]	1.26 [0.17; 9.49]	1.14 [0.20; 6.39]		0.79 [0.21; 3.06]					
Placebo [8]	1.22 [0.78; 1.93]	0.95 [0.06; 14.13]	1.22 [0.36; 4.12]	0.84 [0.58; 1.22]	1.00 [0.22; 4.47]	0.90 [0.31; 2.63]	0.79 [0.21; 3.06]				2.03 [0.51; 8.12]	0.58 [0.25; 1.32]	0.78 [0.53; 1.14]
Pregabalin [9]	1.14 [0.29; 4.45]	0.88 [0.04; 17.86]	1.13 [0.26; 4.93]	0.78 [0.20; 3.10]	0.93 [0.13; 6.86]	0.84 [0.16; 4.49]	0.74 [0.11; 4.88]	0.93 [0.25; 3.49]		0.98 [0.40; 2.38]			

eTable 3b. Head-to-head comparisons of long-term acceptability of the included prophylactic treatments. Continued.

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	1.11 [0.40; 3.13]	0.86 [0.05; 15.27]	1.11 [0.35; 3.57]	0.77 [0.27; 2.19]	0.91 [0.15; 5.44]	0.82 [0.20; 3.40]	0.72 [0.14; 3.82]	0.91 [0.34; 2.42]	0.98 [0.40; 2.38]			0.98 [0.24; 3.98]	0.40 [0.10; 1.69]
Riboflavin [11]	2.49 [0.58; 10.69]	1.93 [0.09; 40.12]	2.48 [0.39; 15.66]	1.71 [0.41; 7.18]	2.03 [0.26; 15.62]	1.84 [0.32; 10.55]	1.61 [0.23; 11.13]	2.03 [0.51; 8.12]	2.19 [0.32; 14.86]	2.23 [0.41; 12.21]			
Sodium Valproate [12]	0.79 [0.33; 1.89]	0.61 [0.04; 10.13]	0.79 [0.21; 2.99]	0.54 [0.23; 1.26]	0.65 [0.12; 3.46]	0.58 [0.16; 2.14]	0.51 [0.11; 2.41]	0.65 [0.30; 1.38]	0.69 [0.18; 2.69]	0.71 [0.26; 1.97]	0.32 [0.07; 1.54]		
Topiramate [13]	0.92 [0.64; 1.31]	0.71 [0.05; 10.85]	0.91 [0.26; 3.17]	0.63 [0.37; 1.07]	0.75 [0.16; 3.50]	0.68 [0.24; 1.93]	0.59 [0.15; 2.41]	0.75 [0.51; 1.09]	0.80 [0.21; 3.04]	0.82 [0.31; 2.21]	0.37 [0.09; 1.55]	1.16 [0.51; 2.65]	

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets.
Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle.
Shaded Area = Direct Comparisons

eTable 3c. Head-to-head comparisons of long-term safety of the included prophylactic treatments

	Amitriptylin	Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
Amitriptylin						3.50 [0.44; 27.91]				0.88 [0.33; 2.37]
Butterbur root extract	2.43 [0.04; 145.18]					0.95 [0.02; 45.63]				
Cinnarizine	1.65 [0.02; 129.09]	0.68 [0.00; 224.72]					1.00 [0.02; 49.59]			
Flunarizine	0.33 [0.01; 8.07]	0.14 [0.00; 17.23]	0.20 [0.00; 36.62]			7.00 [0.38; 128.47]				
Nimodipine	2.19 [0.04; 130.69]	0.90 [0.00; 214.72]	1.33 [0.00; 438.70]	6.64 [0.05; 840.10]		1.05 [0.02; 50.43]				
Placebo	2.31 [0.61; 8.70]	0.95 [0.02; 45.63]	1.40 [0.02; 105.46]	7.00 [0.38; 128.47]	1.05 [0.02; 50.43]			1.28 [0.03; 61.88]	0.35 [0.05; 2.74]	0.43 [0.15; 1.24]
Propranolol	1.65 [0.24; 11.52]	0.68 [0.01; 49.65]	1.00 [0.02; 49.59]	5.00 [0.16; 157.52]	0.75 [0.01; 54.89]	0.71 [0.11; 4.56]			0.98 [0.06; 15.48]	0.45 [0.07; 3.12]
Riboflavin	2.95 [0.05; 178.06]	1.22 [0.01; 291.78]	1.79 [0.01; 595.87]	8.95 [0.07; 1142.76]	1.35 [0.01; 322.72]	1.28 [0.03; 61.88]	1.79 [0.02; 131.92]			
Sodium Valproate	1.04 [0.13; 8.47]	0.43 [0.01; 30.30]	0.63 [0.01; 51.51]	3.16 [0.10; 95.30]	0.48 [0.01; 33.50]	0.45 [0.08; 2.65]	0.63 [0.08; 4.82]	0.35 [0.00; 25.10]		

eTable 3c. Head-to-head comparisons of long-term safety of the included prophylactic treatments. Continued.

	Amitriptylin	Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
Topiramate	0.93 [0.35; 2.44]	0.38 [0.01; 20.92]	0.56 [0.01; 39.73]	2.81 [0.13; 61.39]	0.42 [0.01; 23.12]	0.40 [0.14; 1.12]	0.56 [0.10; 3.08]	0.31 [0.01; 17.33]	0.89 [0.13; 5.96]	

Note: The league table contains the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

eReferences.

1. IntHout J, Ioannidis JP, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open. 2016;6(7):e010247.
2. Chaimani A, Salanti G. Using network meta-analysis to evaluate the existence of small-study effects in a network of interventions. Res Synth Methods. 2012;3(2):161-176.
3. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. PLoS One. 2014;9(7):e99682.
4. CINeMA: Confidence in Network Meta-Analysis [computer program]. Version 1.4.1. http://cinema.ispm.ch/ 2017.
5. https://handbook-5-1.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm
6. Cuijpers P, Noma H, Karyotaki E, Cipriani A, Furukawa TA. Effectiveness and acceptability of cognitive behavior therapy delivery formats in adults with depression: a network meta-analysis. JAMA Psychiatry. Published online April 17, 2019. doi:10.1001/jamapsychiatry.2019.0268