Appendix I GRADE profiles and results for 'central neuropathic pain'

Outcome	Profile ID	Follow-up (days)	Number of RCTs	Interventions
Critical				
Patient-reported global improvement[1] (at least moderate improvement)	1a (pg2)	28 +/- 7	1	cannabis sativa extract
	1b (pg3)	56 +/- 7	1	duloxetine
Sleep interference – normalised 10-point scale[2]	2a (pg4)	28 +/- 7	1	cannabis sativa extract
	2b (pg5)	84 +/- 14	1	pregabalin
Withdrawal due to adverse effects	3 (pg6)	All time points	8	cannabis sativa extract, lamotrigine, levetiracetam, pregabalin
Specific adverse effects[3]	3a-t	All time points	See Appendix J	
Important				
30% pain relief	4a (pg10)	84 +/- 14	2	lamotrigine, pregabalin
50% pain relief	5a (pg12)	84 +/- 14	1	pregabalin
Pain relief – normalised 10-point scale	6a (pg13)	28 +/- 7	4	cannabis sativa extract, duloxetine, levetiracetam, pregabalin
	6b (pg16)	56 +/- 7	2	duloxetine, levetiracetam
	6c (pg19)	84 +/- 14	2	levetiracetam, pregabalin

[1] measured using the 7-point PGIC (patient-reported global impression of change) tool

[2] this is the only synthesis possible for the outcome 'patient reported improvement in daily physical and emotional functioning including sleep'

[3] completed for 'all neuropathic pain' only.

(it was not possible to synthesise any results for the outcome 'use of rescue medication')

CRITICAL OUTCOMES (profiles 1 to 3)

Summary GRADE profile 1a: Patient-reported global improvement (at least moderate improvement) (28 +/-7 days) – cannabis sativa extract vs placebo

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Effect/outcome	Quality	Importance
Patient-reported global improvement – at least moderate improvement (28 +/-7 days)	1 RCT[a] n=66	very serious[1]	not applicable[2]	not serious[3]	very serious[4]	OR: 2.52 (95% CI 0.69 to 9.20)	Very low	Critical

[1] treatment groups were not comparable at baseline (more in the intervention group were using concomitant tricyclic anti-depressants and less were using NSAIDs than the placebo group); inadequate length of follow-up (no more than 5 weeks for included studies)

[2] only 1 trial so no possibility of inconsistency

[3] all aspects of PICO conform to review protocol

[4] wide confidence intervals for effect estimate compared to placebo; small study size below optimal information size

[a] cannabis sativa extract vs placebo (n=66): Rog et al. (2005); concomitant drugs permitted

Abbreviations: CI, confidence interval; OR, odds ratio; PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

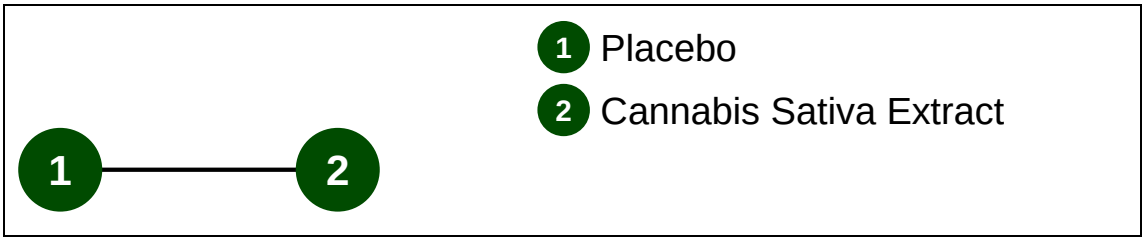

Figure 1 Patient-reported global improvement (at least moderate improvement) - 28 +/-7 days - evidence diagram

Table 1 Patient-reported global improvement (at least moderate improvement) - 28 +/-7 days - notes

- none

Summary GRADE profile 1b: Patient-reported global improvement (at least moderate improvement) (56 +/-7 days) – duloxetine vs placebo

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Effect/outcome	Quality	Importance
Patient-reported global improvement – at least moderate improvement (56 +/-7 days)	1 RCT[a] n=48	not serious[1]	not applicable[2]	not serious[3]	very serious[4]	OR: 2.55 (95% CI 0.51 to 12.82)	Low	Critical

[1] no major concerns with risk of bias

[2] only 1 trial so no possibility of inconsistency

[3] all aspects of PICO conform to review protocol

[4] wide confidence intervals for effect estimate compared to placebo; small number of events; study size below optimal information size

[a] Duloxetine vs placebo (n=48): Vranken et al. (2011); concomitant drugs permitted if stable except anti-depressants

Abbreviations: CI, confidence interval; OR, odds ratio; PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

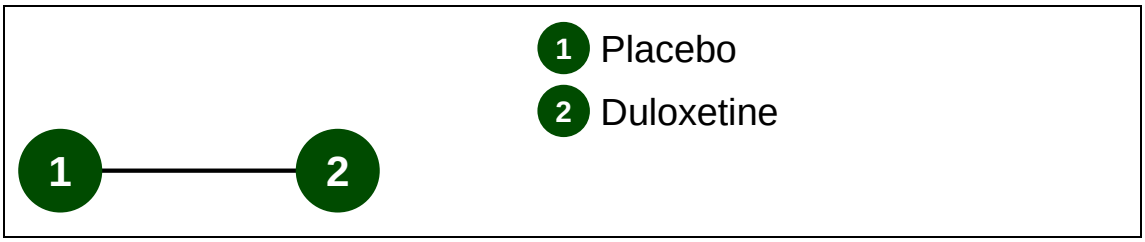

Figure 2 Patient-reported global improvement (at least moderate improvement) - 56 +/-7 days - evidence diagram

Table 2 Patient-reported global improvement (at least moderate improvement) - 56 +/-7 days - notes

- none

Summary GRADE profile 2a: Sleep interference on normalised 10-point scale (28 +/- 7d) – cannabis sativa extract vs placebo

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Effect/outcome	Quality	Importance
Sleep interference on normalised 10-point scale (follow up 28 days)	1 RCT[a] n=65	very serious[1]	not applicable[2]	not serious[3]	serious[4]	MD: -1.74 (95% CI -2.99 to -0.49)	Low	Critical

[1] treatment groups were not comparable at baseline (more in the intervention group were using concomitant tricyclic anti-depressants and less were using NSAIDs than the placebo group); inadequate length of follow-up (no more than 5 weeks for included studies)

[2] only 1 trial so no possibility of inconsistency

[3] all aspects of PICO conform to review protocol

[4] confidence intervals for effect estimate compared to placebo do not cross 'no effect'; small number of events; study size below optimal information size

[a] Cannabis sativa extract vs placebo (n=65): Rog et al. (2005); concomitant amitriptyline permitted

Abbreviations: CI, confidence interval; MD, mean difference; PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

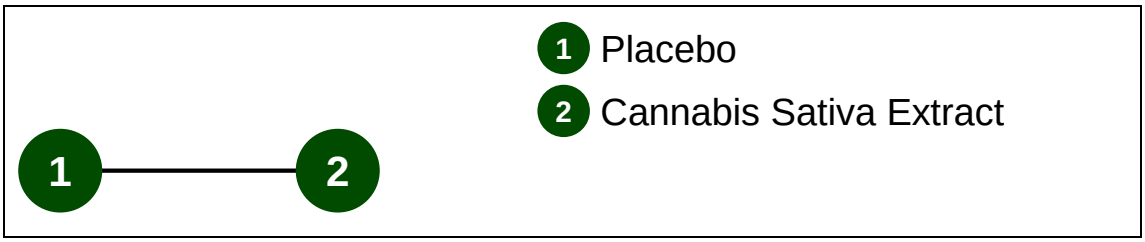

Figure 3 sleep interference - 28 +/-7 days - evidence diagram

Table 3 sleep interference - 28 +/-7 days - notes

- none

Summary GRADE profile 2c: Sleep interference on normalised 10-point scale (84 +/- 14d) – pregabalin vs placebo

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Effect/outcome	Quality	Importance
Sleep interference on normalised 10-point scale (follow up 84 days)	1 RCT[a] n=135	serious[1]	not applicable[2]	not serious[3]	serious[4]	MD: -1.16 (95% CI -2.05 to -0.27)	Low	Critical

[1] allocation concealment unclear; groups appear different at baseline in concomitant medication usage; more patients completed the trial in the placebo group

[2] only 1 trial so no possibility of inconsistency

[3] all aspects of PICO conform to review protocol

[4] confidence intervals for direct effect estimates against placebo appear small enough (do not include appreciable benefit or harm); small number of events; study size below optimal information size

[a] Pregabalin vs placebo (n=135): Siddall et al. (2006); concomitant medications permitted

Abbreviations: CI, confidence interval; MD, mean difference; PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

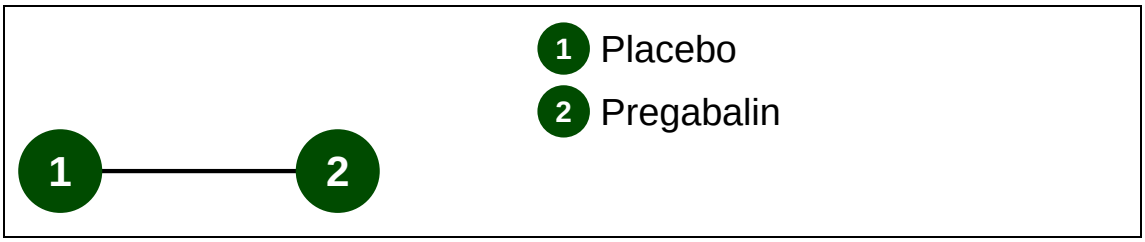

Figure 4 sleep interference - 84 +/- 14 days - evidence diagram

Table 4 sleep interference - 84 +/- 14 days - notes

- none

Summary GRADE profile 3: Network meta-analysis for withdrawal due to adverse effects at any time point

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Quality	Importance
Withdrawal due to adverse effects at any time	8 RCTs[a] n=638	very serious[2]	not serious[3]	not serious[4]	serious[5]	very low	Critical

[1] in 1 study, groups were not comparable at baseline and in 5 studies it was unclear if they were comparable at baseline; concomitant drugs permitted varies across the studies in the network; one study was single-blind

[2] it was not possible to assess heterogeneity for pairwise comparisons; there appeared to be consistency between direct and indirect estimates

[3] all aspects of PICO conform to review protocol

[4] no head-to-head trials; wide confidence intervals for hazard ratios

[a] cannabis sativa extract (n=66): Rog et al. (2005); concomitant medication permitted

lamotrigine (n=96): Breuer et al. (2007), Vestergaard et al. (2001); concomitant medication permitted in one (except anti-convulsants) but not the other

levetiracetam (n=80): Falah et al. (2012), Rossi et al. (2009); concomitant medication not permitted

pregabalin (n=396): Kim et al. (2011), Siddall et al. (2006), Vranken et al. (2008); concomitant medication permitted in all but excluding gabapentin in one

[All compared to placebo]

Abbreviations: PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

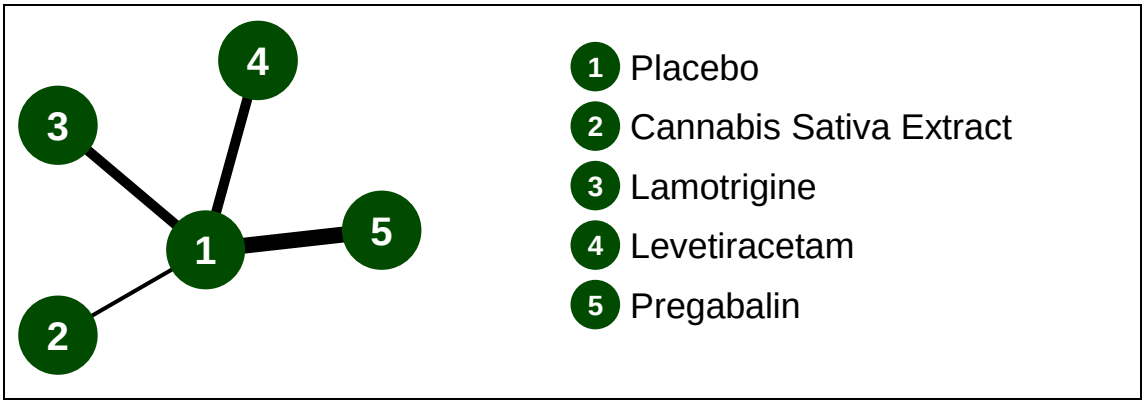

Figure 5 withdrawal due to adverse effects - evidence network

Table 5 withdrawal due to adverse effects - trials included in analysis

	Placebo	Cannabis Sativa Extract	Lamotrigine	Levetiracetam
Cannabis Sativa Extract	1 RCT[4] total n=66			
Lamotrigine	2 RCTs[1,7] total n=96	-		
Levetiracetam	2 RCTs[2,5] total n=80	-	-	
Pregabalin	3 RCTs[3,6,8] total n=396	-	-	-

(1) Breuer et al. (2007); (2) Falah et al. (2012); (3) Kim et al. (2011); (4) Rog et al. (2005); (5) Rossi et al. (2009); (6) Siddall et al. (2006); (7) Vestergaard et al. (2001); (8) Vranken et al. (2008)

Table 6 withdrawal due to adverse effects - relative effectiveness of all pairwise combinations

	Placebo	Cannabis Sativa Extract	Lamotrigine	Levetiracetam	Pregabalin
Placebo		N/A	N/A	N/A	N/A
Cannabis Sativa Extract	5.40 (0.10, 5838.00)		N/A	N/A	N/A
Lamotrigine	9.26 (0.91, 464.30)	1.74 (0.00, 488.70)		N/A	N/A
Levetiracetam	4.99 (0.62, 89.47)	0.92 (0.00, 134.70)	0.54 (0.01, 21.73)		N/A
Pregabalin	1.70 (0.46, 5.91)	0.31 (0.00, 19.26)	0.18 (0.00, 2.53)	0.34 (0.01, 3.70)	

Values given are hazard ratios.

The segment below and to the left of the shaded cells is derived from the network meta-analysis, reflecting direct and indirect evidence of treatment effects (row versus column). The point estimate reflects the mean of the posterior distribution, and numbers in parentheses are 95% credible intervals. Because it is not easily possible to derive analogous estimates of hazard ratios from a frequentist analysis of direct data only, the segment above and to the right of the shaded cells is left blank.

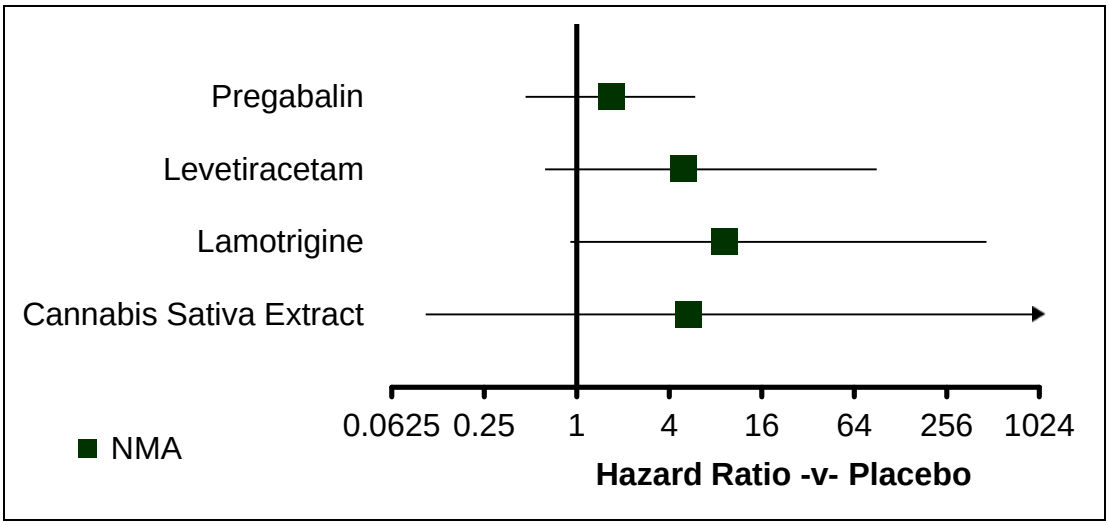

Figure 6 withdrawal due to adverse effects - relative effect of all options compared with placebo

(values less than 1 favour the treatment; values greater than 1 favour placebo; solid error bars are 95% credible intervals)

Table 7 withdrawal due to adverse effects - rankings for each comparator

	Probability best	Median rank (95%CI)
Placebo	0.632	1 (1, 3)
Cannabis Sativa Extract	0.193	4 (1, 5)
Lamotrigine	0.021	4 (2, 5)
Levetiracetam	0.047	4 (1, 5)
Pregabalin	0.107	2 (1, 4)

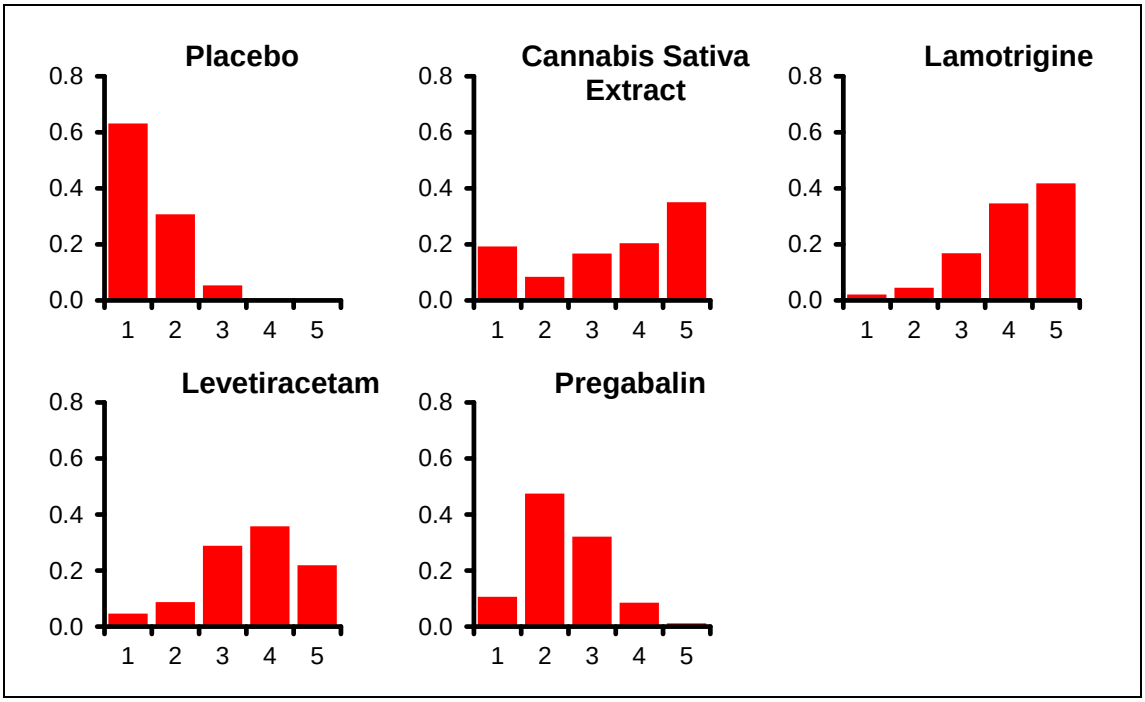

Figure 7 withdrawal due to adverse effects - rank probability histograms

Table 8 withdrawal due to adverse effects - model fit statistics

Residual deviance	Dbar	Dhat	pD	DIC	tau-squared
14.52 (compared to 16 data-points)	57.003	44.788	12.215	69.219	0.000 (95%CrI: 0.001, 6.798)

Table 9 withdrawal due to adverse effects - notes

- Random-effects model was used, with 0.5 added to cells of trials with 1 or more zero cell-count.
- 10000 burn-ins and 50000 iterations.
- Model convergence: there was poor autocorrelation for cannabis sativa and lamotrigine because of small numbers of events in the studies for these interventions.
- Leijon and Bovie (1989) was not included in this network as it had zero events in all study arms.

IMPORTANT OUTCOMES (profiles 4 to 6)

Summary GRADE profile 4a: Network meta-analysis for at least 30% pain relief (84 days +/-14 days)

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Quality	Importance
≥ 30% pain relief on any scale (follow up 84 days)	2 RCTs[a] n=173	very serious[1]	not serious[2]	not serious[3]	very serious[4]	Very low	Important

[1] 1 of 2 studies was a crossover study; groups were not comparable at baseline in one study and it was unclear if they were comparable in another study (including for concomitant medications); unclear about allocation concealment in both studies; concomitant drugs permitted varies across the studies in the network; attrition bias in both studies

[2] only one trial per 'link' so no possibility of inconsistency for each pairwise comparison; no loops in networks so no possibility of inconsistency between direct and indirect estimates

[3] all aspects of PICO conform to review protocol

[4] there are no head-to-head trials; only 1 trial for each 'link' in the network; wide confidence intervals for effect estimate compared to placebo and for the overall ranking within the network

[a] lamotrigine (n=36): Breuer et al. (2007); concomitant opioids, lidocaine patch, gabapentin permitted but use of another anti-convulsants not permitted

pregabalin (n=137): Siddall et al. (2006); concomitant drugs permitted with the exception of gabapentin

[all compared to placebo]

Abbreviations: PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

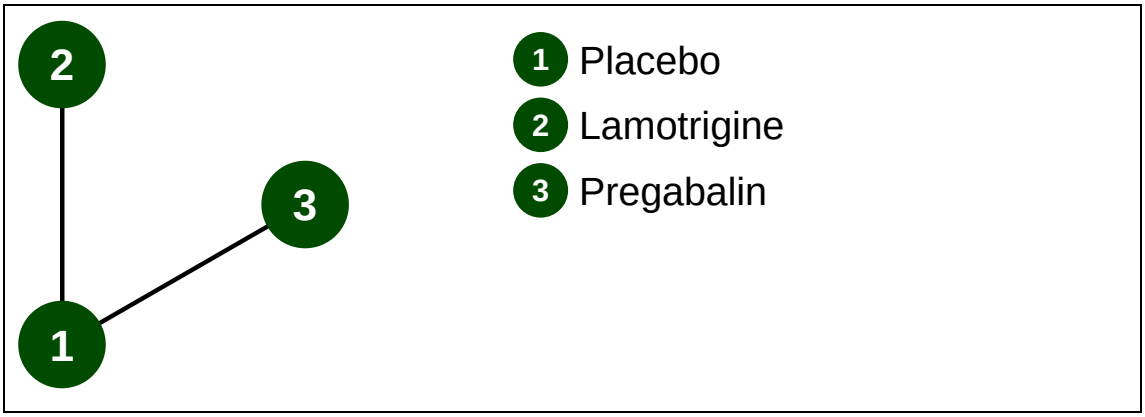

Figure 8 30% pain relief - 84 +/- 14 days - evidence network

Table 10 30% pain relief - 84 +/- 14 days - trials included in analysis

	Placebo	Lamotrigine
Lamotrigine	1 RCT[1] total n=36	
Pregabalin	1 RCT[2] total n=137	-

(1) Breuer et al. (2007); (2) Siddall et al. (2006)

Table 11 30% pain relief - 84 +/- 14 days - relative effectiveness of all pairwise combinations

	Placebo	Lamotrigine	Pregabalin
Placebo		3.08 (0.51, 18.53)	3.60 (1.61, 8.03)
Lamotrigine	3.47 (0.59, 30.16)		-
Pregabalin	3.69 (1.68, 8.54)	1.06 (0.11, 7.57)	

Values given are odds ratios.

The segment below and to the left of the shaded cells is derived from the network meta-analysis, reflecting direct and indirect evidence of treatment effects (row versus column). The point estimate reflects the mean of the posterior distribution, and numbers in parentheses are 95% credible intervals. The segment above and to the right of the shaded cells gives pooled direct evidence (random-effects pairwise meta-analysis), where available (column versus row). Numbers in parentheses are 95% confidence intervals.

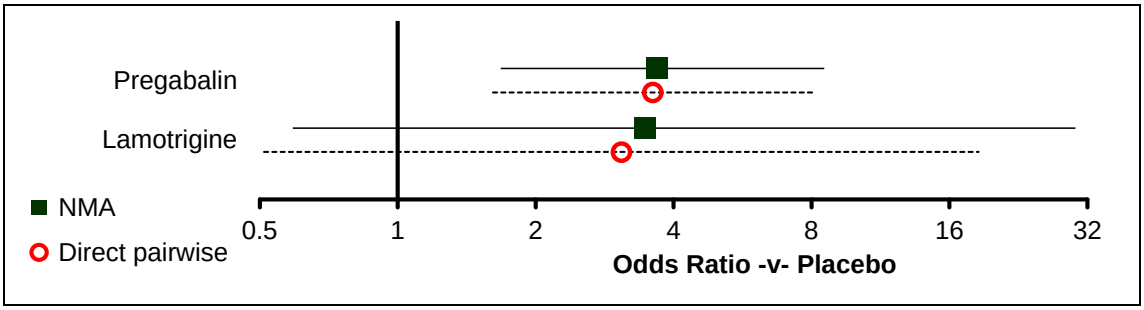

Figure 9 30% pain relief - 84 +/- 14 days - relative effect of all options compared with placebo

(values less than 1 favour placebo; values greater than 1 favour the treatment; solid error bars are 95% credible intervals while dashed error bars are 95% confidence intervals)

Table 12 30% pain relief - 84 +/- 14 days - rankings for each comparator

	Probability best	Median rank (95%CI)
Placebo	0.000	3 (2, 3)
Lamotrigine	0.477	2 (1, 3)
Pregabalin	0.523	1 (1, 2)

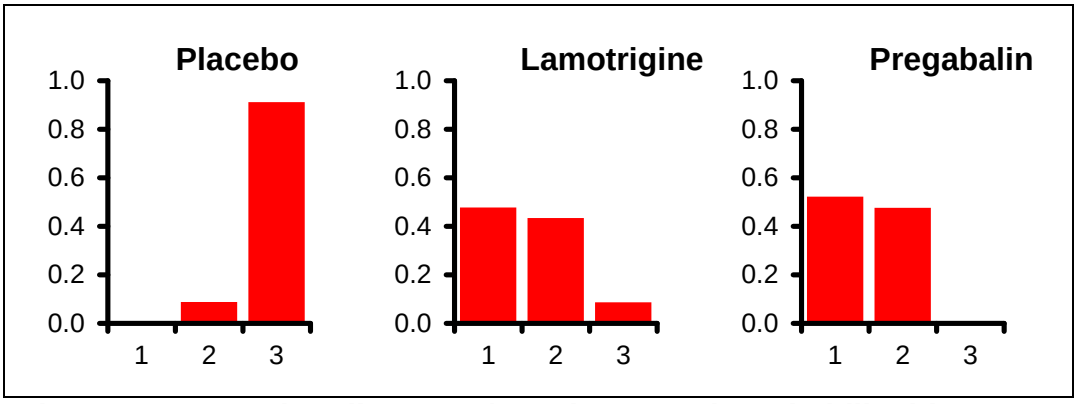

Figure 10 30% pain relief - 84 +/- 14 days - rank probability histograms

Table 13 30% pain relief - 84 +/- 14 days - model fit statistics

Residual deviance	Dbar	Dhat	pD	DIC
4.118 (compared to 4 data-points)	18.523	14.525	3.998	22.522

Table 14 30% pain relief - 84 +/- 14 days - notes

- Fixed-effects model was used.
- 10000 burn-ins and 50000 iterations.

Summary GRADE profile 5a: At least 50% pain relief (84 days +/-14 days) – pregabalin vs placebo

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Effect/outcome	Quality	Importance
≥ 50% pain relief on any scale (follow up 84 days)	1 RCT[a] n=168	serious[1]	not applicable[2]	not serious[3]	very serious[4]	OR: 3.38 (95% CI 1.15 to 9.91)	Very low	Important

[1] allocation concealment unclear; groups appear different at baseline with respect to concomitant medication usage; more patients completed the trial in the placebo group

[2] only 1 trial so no possibility of inconsistency

[3] all aspects of PICO conform to review protocol

[4] wide confidence intervals for effect estimate compared to placebo; small number of events; study size below optimal information size

[a] pregabalin vs placebo (n=168): Siddall et al. (2006); concomitant drugs permitted with the exception of gabapentin

Abbreviations: CI, confidence interval; OR, odds ratio; PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

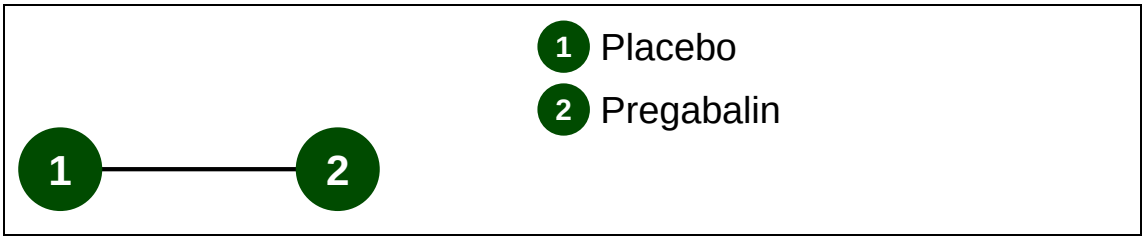

Figure 11 50% pain relief - 84 +/- 14 days - evidence diagram

Table 15 50% pain relief - 84 +/- 14 days - notes

- none

Summary GRADE profile 6a: Network meta-analysis for pain relief on normalised 10-point scale (28 +/- 7 days)

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Quality	Importance
Pain relief on normalised 10-point scale (follow up 28 days)	4 RCTs[a] n=172	serious[1]	not serious[2]	not serious[3]	very serious[4]	Very low	Important

[1] unclear about allocation concealment in 3 studies; concomitant drugs permitted varies across the studies in the network; one study was single-blind

[2] only one trial per 'link' so no possibility of inconsistency for each pairwise comparison; no loops in networks so no possibility of inconsistency between direct and indirect estimates

[3] all aspects of PICO conform to review protocol

[4] no head-to-head trials; only one trial for each 'link'; confidence intervals for the overall ranking in the network is large

[a] cannabis sativa extract (n=65): Rog et al. (2005); concomitant drugs permitted

duloxetine (n=48): Vranken et al. (2011); concomitant drugs permitted if stable except anti-depressants

levetiracetam (n=19): Rossi et al. (2009); concomitant drugs not permitted

pregabalin (n=40): Vranken et al. (2008); concomitant drugs permitted

[all compared to placebo]

Abbreviations: PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

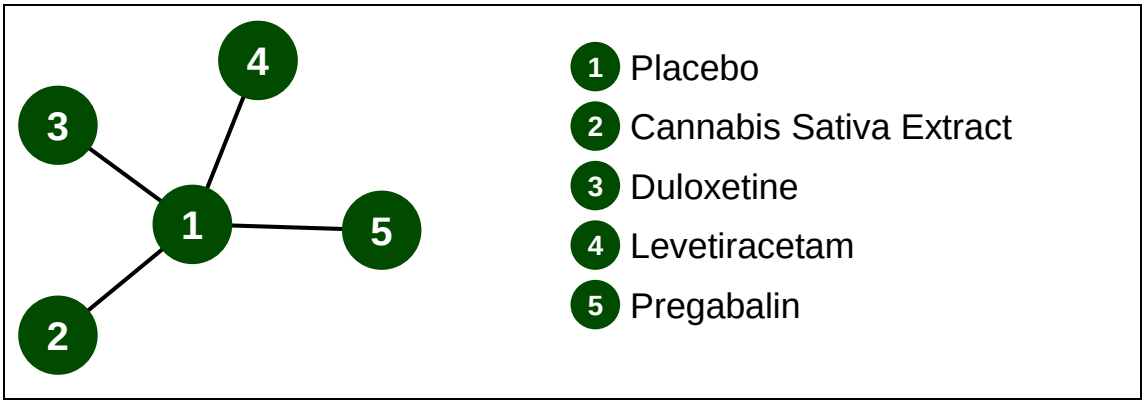

Figure 12 pain (continuous) - 28 +/-7 days - evidence network

Table 16 pain (continuous) - 28 +/-7 days - trials included in analysis

	Placebo	Cannabis Sativa Extract	Duloxetine	Levetiracetam
Cannabis Sativa Extract	1 RCT[1] total n=65			
Duloxetine	1 RCT[4] total n=48	-		
Levetiracetam	1 RCT[2] total n=19	-	-	
Pregabalin	1 RCT[3] total n=40	-	-	-

(1) Rog et al. (2005); (2) Rossi et al. (2009); (3) Vranken et al. (2008); (4) Vranken et al. (2011)

Table 17 pain (continuous) - 28 +/-7 days - relative effectiveness of all pairwise combinations

	Placebo	Cannabis Sativa Extract	Duloxetine	Levetiracetam	Pregabalin
Placebo		-1.32 (-2.28, -0.36)	-0.50 (-1.51, 0.51)	-1.51 (-3.30, 0.28)	-2.40 (-3.77, -1.03)
Cannabis Sativa Extract	-1.32 (-2.28, -0.36)		-	-	-
Duloxetine	-0.50 (-1.51, 0.51)	0.82 (-0.58, 2.22)		-	-
Levetiracetam	-1.52 (-3.31, 0.28)	-0.20 (-2.24, 1.85)	-1.02 (-3.07, 1.04)		-
Pregabalin	-2.40 (-3.78, -1.04)	-1.08 (-2.76, 0.59)	-1.90 (-3.61, -0.20)	-0.88 (-3.15, 1.36)	

Values given are mean differences.

The segment below and to the left of the shaded cells is derived from the network meta-analysis, reflecting direct and indirect evidence of treatment effects (row versus column). The point estimate reflects the mean of the posterior distribution, and numbers in parentheses are 95% credible intervals. The segment above and to the right of the shaded cells gives pooled direct evidence (random-effects pairwise meta-analysis), where available (column versus row). Numbers in parentheses are 95% confidence intervals.

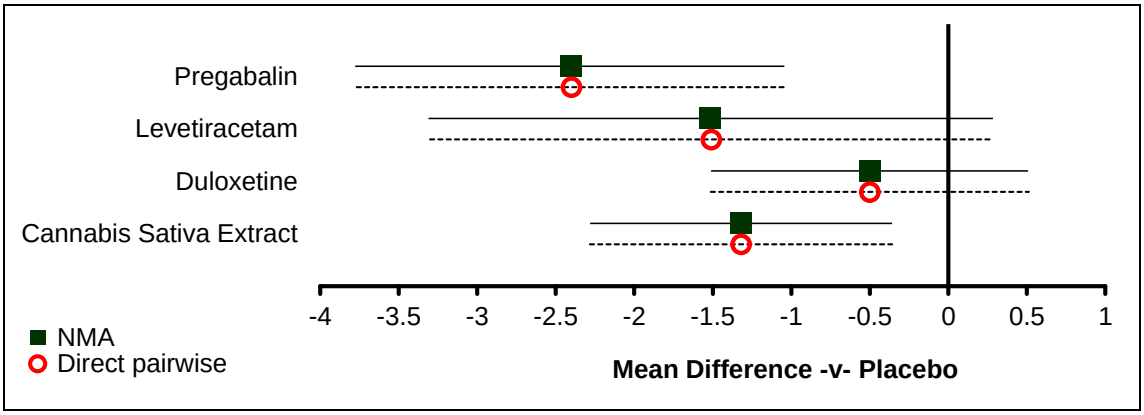

Figure 13 pain (continuous) - 28 +/-7 days - relative effect of all options compared with placebo

(values less than 0 favour the treatment; values greater than 0 favour placebo; solid error bars are 95% credible intervals while dashed error bars are 95% confidence intervals)

Table 18 pain (continuous) - 28 +/-7 days - rankings for each comparator

	Probability best	Median rank (95%CI)
Placebo	0.000	5 (4, 5)
Cannabis Sativa Extract	0.063	3 (1, 4)
Duloxetine	0.003	4 (2, 5)
Levetiracetam	0.205	2 (1, 5)
Pregabalin	0.729	1 (1, 3)

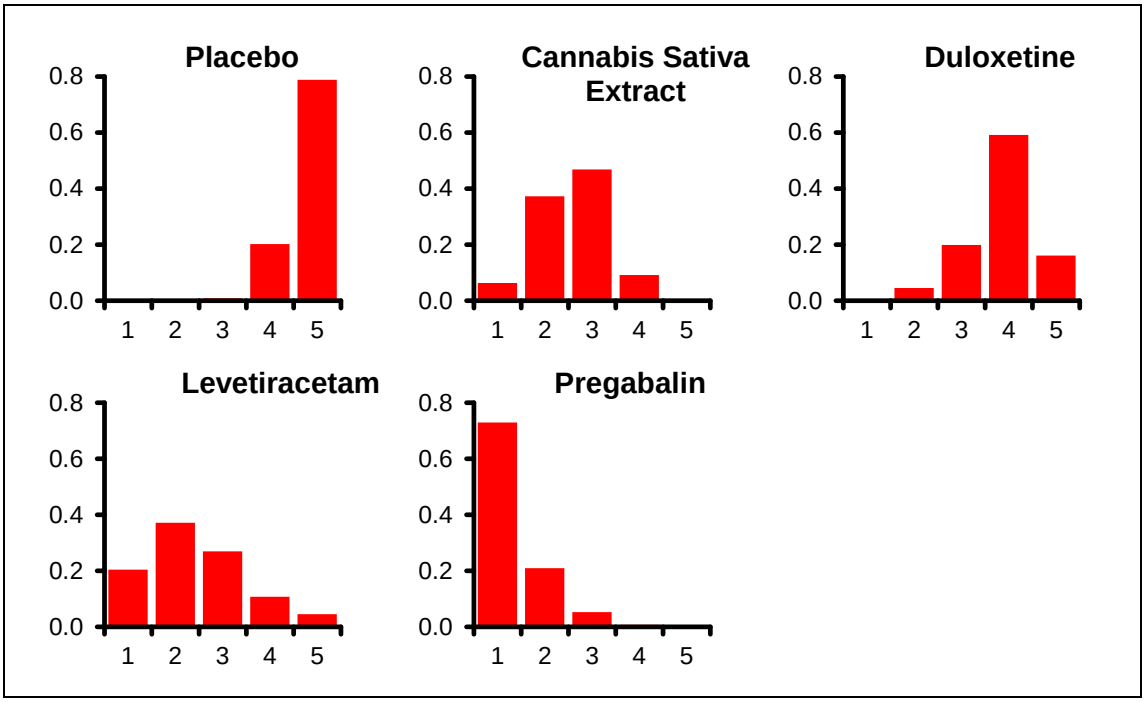

Figure 14 pain (continuous) - 28 +/-7 days - rank probability histograms

Table 19 pain (continuous) - 28 +/-7 days - model fit statistics

Residual deviance	Dbar	Dhat	pD	DIC
8 (compared to 8 data-points)	9.705	1.705	8	17.705

Table 20 pain (continuous) - 28 +/-7 days - notes

- Fixed-effects model was used.
- 10000 burn-ins and 50000 iterations.

Summary GRADE profile 6b: Network meta-analysis for pain relief on normalised 10-point scale (56 +/- 7d)

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Quality	Importance
Pain relief on normalised 10-point scale (follow up 56 days)	2 RCTs[a] n=67	very serious[1]	not serious[2]	not serious[3]	very serious[4]	Very low	Important

[1] unclear about allocation concealment in one study; concomitant drugs permitted varies across the studies in the network; one study was single-blind

[2] only 1 trial for each arm so no possibility of inconsistency between studies for a pairwise comparison; no loops in networks so no possibility of inconsistency between direct and indirect estimates

[3] all aspects of PICO conform to review protocol

[4] no head-to-head trials; only one trial for each 'link'; wide confidence intervals for overall ranking in the network

[a] duloxetine (n=48): Vranken et al. (2011); concomitant drugs permitted if stable except anti-depressants

levetiracetam (n=19): Rossi et al. (2009); concomitant drugs not permitted

[all compared to placebo]

Abbreviations: PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

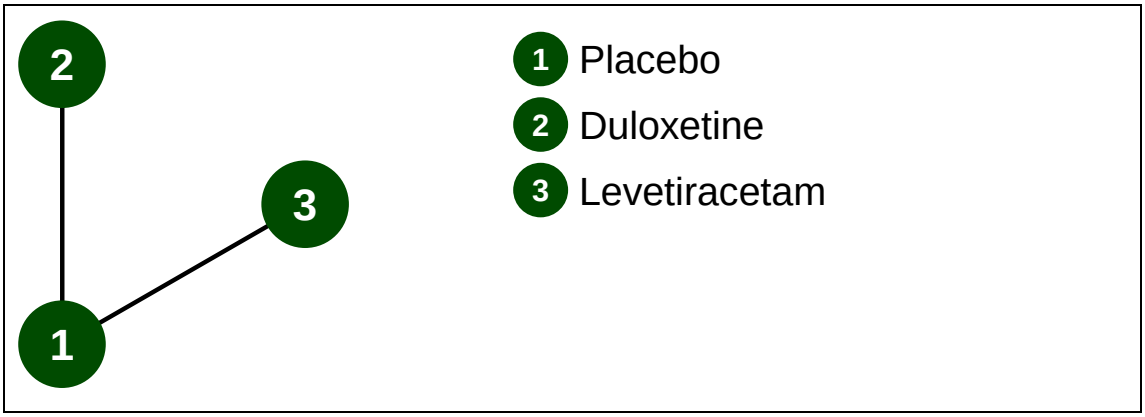

Figure 15 pain (continuous) - 56 +/-7 days - evidence network

Table 21 pain (continuous) - 56 +/-7 days - trials included in analysis

	Placebo	Duloxetine
Duloxetine	1 RCT[2] total n=48	
Levetiracetam	1 RCT[1] total n=19	-

(1) Rossi et al. (2009); (2) Vranken et al. (2011)

Table 22 pain (continuous) - 56 +/-7 days - relative effectiveness of all pairwise combinations

	Placebo	Duloxetine	Levetiracetam
Placebo		-1.00 (-1.91, -0.09)	-2.71 (-4.45, -0.97)
Duloxetine	-1.00 (-1.91, -0.09)		-
Levetiracetam	-2.71 (-4.45, -0.98)	-1.71 (-3.67, 0.25)	

Values given are mean differences.

The segment below and to the left of the shaded cells is derived from the network meta-analysis, reflecting direct and indirect evidence of treatment effects (row versus column). The point estimate reflects the mean of the posterior distribution, and numbers in parentheses are 95% credible intervals. The segment above and to the right of the shaded cells gives pooled direct evidence (random-effects pairwise meta-analysis), where available (column versus row). Numbers in parentheses are 95% confidence intervals.

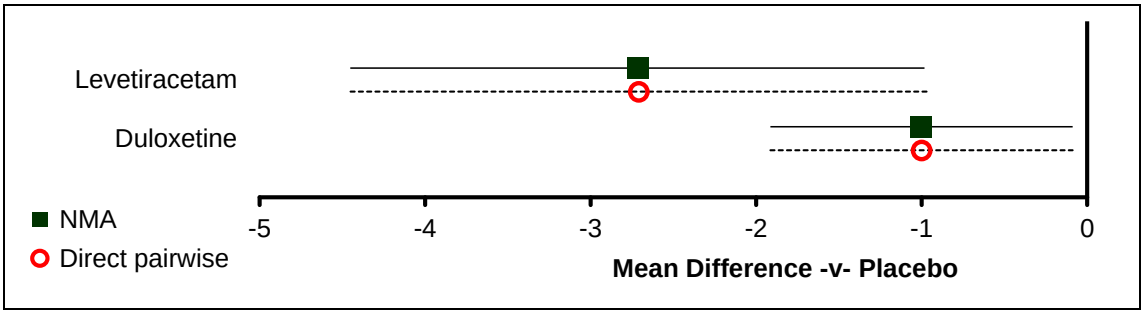

Figure 16 pain (continuous) - 56 +/-7 days - relative effect of all options compared with placebo

(values less than 0 favour the treatment; values greater than 0 favour placebo; solid error bars are 95% credible intervals while dashed error bars are 95% confidence intervals)

Table 23 pain (continuous) - 56 +/-7 days - rankings for each comparator

	Probability best	Median rank (95%CI)
Placebo	0.000	3 (3, 3)
Duloxetine	0.044	2 (1, 2)
Levetiracetam	0.956	1 (1, 2)

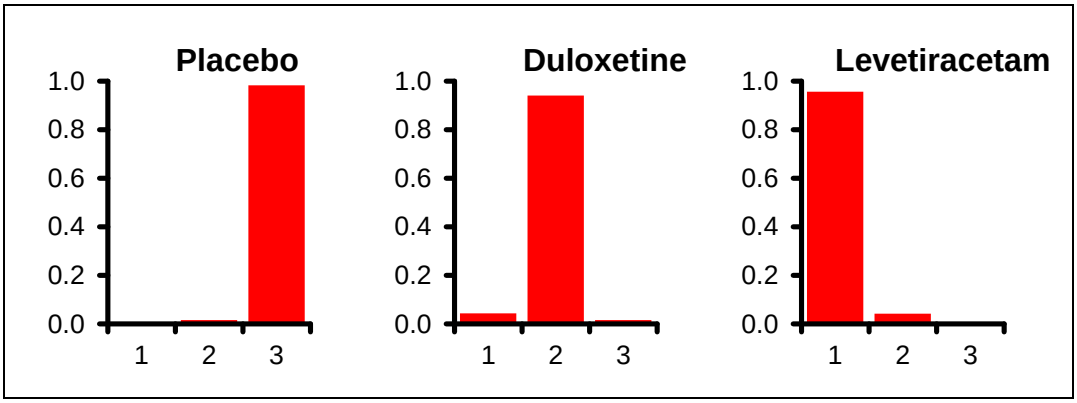

Figure 17 pain (continuous) - 56 +/-7 days - rank probability histograms

Table 24 pain (continuous) - 56 +/-7 days - model fit statistics

Residual deviance	Dbar	Dhat	pD	DIC
3.989 (compared to 4 data-points)	4.91	0.921	3.989	8.899

Table 25 pain (continuous) - 56 +/-7 days - notes

- Fixed-effects model was used.
- 10000 burn-ins and 50000 iterations.

Summary GRADE profile 6c: Network meta-analysis for pain relief on normalised 10-point scale (84 +/- 14days)

Outcome	Number of Studies	Limitations	Inconsistency	Indirectness	Imprecision	Quality	Importance
Pain relief on normalised 10-point scale (follow up 84 days)	2 RCTs[a] n=155	very serious[1]	not applicable[2]	not serious[3]	very serious[4]	Very low	Important

[1] unclear about allocation concealment in both studies; groups appear different at baseline for one study with respect to concomitant medication usage; more patients completed the trial in the placebo group in one study; concomitant drugs permitted varies across the studies in the network; one study was single-blind

[2] only 1 trial for each arm so no possibility of inconsistency between studies for a pairwise comparison; no loops in networks so no possibility of inconsistency between direct and indirect estimates

[3] all aspects of PICO conform to review protocol

[4] no head-to-head trials; only one trial for each 'link'; wide confidence intervals for overall ranking in the network

[a] levetiracetam (n=19): Rossi et al. (2009); concomitant drugs not permitted

pregabalin (n=136): Siddall et al. (2006); concomitant drugs permitted but gabapentin excluded

[all compared to placebo]

Abbreviations: PICO, patient intervention comparator outcome; RCT, randomised controlled trial.

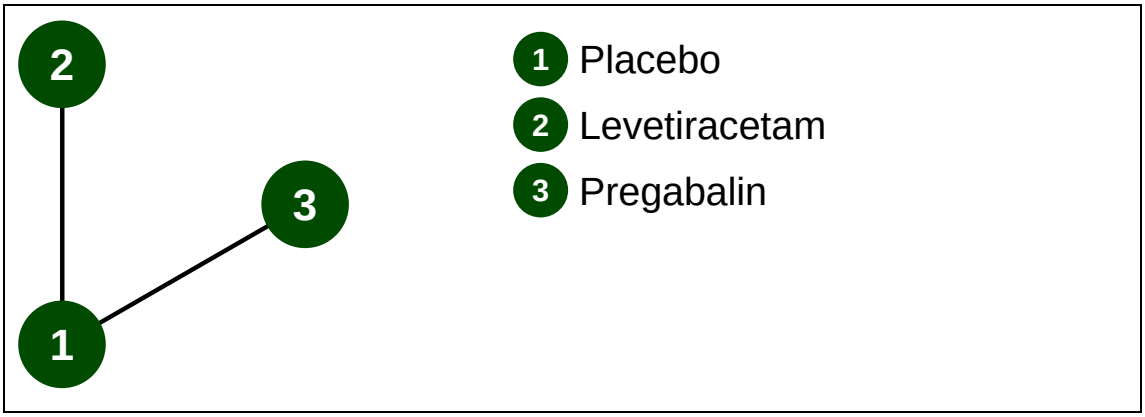

Figure 18 pain (continuous) - 84 +/- 14 days - evidence network

Table 26 pain (continuous) - 84 +/- 14 days - trials included in analysis

	Placebo	Levetiracetam
Levetiracetam	1 RCT[1] total n=18	
Pregabalin	1 RCT[2] total n=136	-

(1) Rossi et al. (2009); (2) Siddall et al. (2006)

Table 27 pain (continuous) - 84 +/- 14 days - relative effectiveness of all pairwise combinations

	Placebo	Levetiracetam	Pregabalin
Placebo		-2.81 (-4.54, -1.08)	-1.46 (-2.08, -0.84)
Levetiracetam	-2.81 (-4.54, -1.08)		-
Pregabalin	-1.46 (-2.08, -0.85)	1.35 (-0.50, 3.19)	

Values given are mean differences.

The segment below and to the left of the shaded cells is derived from the network meta-analysis, reflecting direct and indirect evidence of treatment effects (row versus column). The point estimate reflects the mean of the posterior distribution, and numbers in parentheses are 95% credible intervals. The segment above and to the right of the shaded cells gives pooled direct evidence (random-effects pairwise meta-analysis), where available (column versus row). Numbers in parentheses are 95% confidence intervals.

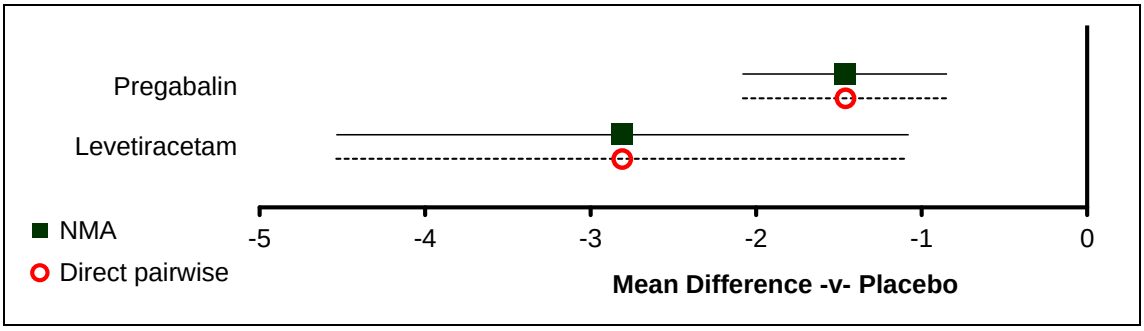

Figure 19 pain (continuous) - 84 +/- 14 days - relative effect of all options compared with placebo

(values less than 0 favour the treatment; values greater than 0 favour placebo; solid error bars are 95% credible intervals while dashed error bars are 95% confidence intervals)

Table 28 pain (continuous) - 84 +/- 14 days - rankings for each comparator

	Probability best	Median rank (95%CI)
Placebo	0.000	3 (3, 3)
Levetiracetam	0.924	1 (1, 2)
Pregabalin	0.076	2 (1, 2)

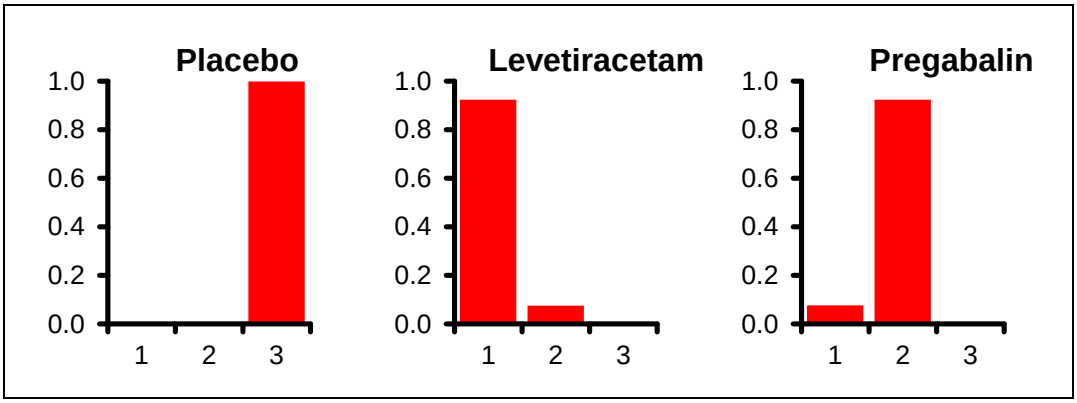

Figure 20 pain (continuous) - 84 +/- 14 days - rank probability histograms

Table 29 pain (continuous) - 84 +/- 14 days - model fit statistics

Residual deviance	Dbar	Dhat	pD	DIC
3.995 (compared to 4 data-points)	3.418	-0.577	3.995	7.412

Table 30 pain (continuous) - 84 +/- 14 days - notes

- Fixed-effects model was used.
- 10000 burn-ins and 50000 iterations.