Supplementary Table 15

Comparison: Dihydroergotamine nasal spray vs Placebo											
Outcome: Duration, intensity, frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DHE	Placebo	Effect	Certainty	Importance of outcome
Andersson & Jespersen 1986	Cross-over trial	Serious	Serious	Not serious	Serious	None	137 attacks	133 attacks	No effect on duration and frequency of attacks, but intensity significantly lower	Low	Critical

Supplementary Table 16

Comparison: Lidocaine vs Placebo								
Outcome: Duration, intensity, frequency of attacks								
Certainty assessment							Summary of findings	
Manuscript	Study design	Risk of bias	Incon-sistency	Indirect-ness	Imprecision	Other considerations	Certainty	Importance of outcome
No controlled studies	Case reports	Very Serious	Very Serious	NA	NA	None	Very Low	Critical

Supplementary Table 17

Comparison: Verapamil vs Placebo											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Verapamil	Placebo Or Lithium	Effect	Certainty	Importance of outcome
Bussone et al. 1990; Leone et al. 2000	Cross-over trial & RCT	Not serious	Not serious	Not serious	Not serious	None	24 (Bussone et al. 1990) 15 (Leone et al. 2000)	24 Lithium 15 Placebo	Significant effect of Verapamil over placebo; similar effect but less side-effects than lithium	Moderate	Critical

Supplementary Table 18

Comparison: Lithium vs Placebo (or Verapamil)											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lithium	Placebo Or other drugs	Effect	Certainty	Importance of outcome
Bussone et al. 1990; Medina et al. 1980; Steiner et al. 1997	RCT	Serious	Serious[a]	Not serious	Not serious	None	24 (Bussone et al. 1990) 13 (Steiner et al. 1997) 12 (Medina et al. 1980)	24 Verapamil 14 Placebo 6 “other drugs”	No significant effect of lithium over placebo; similar effect to Verapamil; but more side-effects	Low	Critical

Supplementary Table 19

Comparison: Topiramate vs Placebo								
Outcome: Frequency of attacks								
Certainty assessment							Summary of findings	
Manuscript	Study design	Risk of bias	Incon-sistency	Indirect-ness	Imprecision	Other considerations	Certainty	Importance of outcome
No controlled studies	Case reports	Very Serious	Very Serious	NA	NA	None	Very Low	Critical

Supplementary Table 20

Comparison: Frovatriptan vs placebo											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Frovatriptan	Placebo	Effect	Certainty	Importance of outcome
Pageler et al. 2011	RCT	Serious[a]	Serious[a]	Not serious	Not serious	None	11		Not evaluated	Very low	Critical

Supplementary Table 21

Comparison: Melatonin vs Placebo											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Placebo	Effect	Certainty	Importance of outcome
Leone et al. 1996	RCT	Not serious	Not serious	Not serious	Serious	None	10 Melatonin	10 Placebo	5 responders, 5 non-responders	Low	Critical

Supplementary Table 22

Comparison: VNS vs placebo											
Outcome: Pain relief during attacks or frequency of attacks											
Certainty assessment						Summary of findings					
Manuscript	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	VNS	Sham	Effect	Certainty	Importance of outcome
Silber-stein et al. 2016; Goadsby et al. 2018	RCT	Not serious	Not serious	Not serious	Not serious	None	50 patients (Goadsby et al. 2018) 73 (Silber-stein et al. 2016)	52 77	VNS significantly better effect than sham in episodic cluster headache; no significant difference for chronic cluster headache	Moderate	Critical
Gaul et al. 2016	RCT	Not serious	Not serious	Not serious	Not serious	None	45	48	Significant reduction of attacks.	Moderate	Critical

Supplementary Table 23

Comparison: DBS vs placebo											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	In-consistency	In-directness	Im-precision	Other con-siderations	DBS	Placebo	Effect	Certainty	Importance of outcome
Fontaine et al. 2010	RCT ()	Not serious	Not serious	Not serious	Serious	None	12 patients, random placebo stimulation		Not significantly reduced	Low	Critical

Supplementary Table 24

Comparison: GON block vs placebo											
Outcome: Frequency of attacks											
Certainty assessment							Summary of findings				
Manuscript	Study design	Risk of bias	In-consistency	In-directness	Imprecision	Other con-siderations	GON block	Sham	Effect	Certainty	Importance of outcome
Ambrosini et al. 2005; Leroux et al. 2011	RCT	Not serious	Not serious	Not serious	Not serious	None	13 (Ambrosini et al. 2005) 19 (Leroux et al. 2011)	10 18	GON block significantly better than placebo	High	