

The comparative effectiveness of drugs for migraine prevention: a systematic review and network meta-analysis

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Supplement 1 – Search strategy

Search Strategies

PRISMA Initial Results: total number of results before duplicates removed

Database [Platform] Searches run August 13, 2022. <i>No date, language limits used.</i>	Results
OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present [Ovid]	5,913
Embase 1974 to 2022 August 12 [Ovid]	5,983
EBM Reviews - Cochrane Central Register of Controlled Trials July 2022 [Ovid]	3,267
TOTAL	15,163

ClinicalTrials.gov Results Searched August 13, 2022.

Studies With Results Interventional Studies Migraine Disorders various treatment terms [see strategies below in document]	94
TOTAL	94

ClinicalTrials.gov Search Strategies

1 Study found for: CGRP monoclonal antibodies | Studies With Results | Interventional Studies | Migraine Disorders
8 Studies found for: adrenergic beta-antagonists | Studies With Results | Interventional Studies | Migraine Disorders
1 Study found for: Calcium Channel Blocker | Studies With Results | Interventional Studies | Migraine Disorders
22 Studies found for: Anticonvulsants | Studies With Results | Interventional Studies | Migraine Disorders
39 Studies found for: Anti-Inflammatory Agents, Non-Steroidal | Studies With Results | Interventional Studies | Migraine Disorders
1 Study found for: angiotensin receptor antagonists | Studies With Results | Interventional Studies | Migraine Disorders
5 Studies found for: antidepressive agents | Studies With Results | Interventional Studies | Migraine Disorders
11 Studies found for: Botulinum Toxins, Type A | Studies With Results | Interventional Studies | Migraine Disorders
No Studies found for: coenzyme Q10 | Studies With Results | Interventional Studies | Migraine Disorders
3 Studies found for: Magnesium | Studies With Results | Interventional Studies | Migraine Disorders
3 Studies found for: Melatonin | Studies With Results | Interventional Studies | Migraine Disorders

MEDLINE(R) 1996 to August 12, 2022

Search Strategy:

#	Searches	Results
1	exp Migraine Disorders/	22110
2	(migraine or migraines or sick headache or sick headaches or hemicrania or migrainous headache or status hemicranicus).tw,kf.	28623
3	or/1-2	30802
4	("cgrp monoclonal antibodies" or "calcitonin gene-related peptide antibodies (cgrp) monoclonal antibodies (mabs)" or "cgrp mabs").tw,kf.	127
5	calcitonin gene related peptide.tw,kf.	8169

6	Calcitonin Gene-Related Peptide Receptor Antagonists/	848
7	exp Antibodies, Monoclonal/	191819
8	6 and 7	274
9	adrenergic beta-antagonists/	24650
10	("adrenergic beta antagonist*" or "adrenergic beta blocker*" or "adrenergic beta receptor blockader*" or "beta adrenergic antagonist*" or "beta adrenergic blocker*" or "beta adrenergic blocking agent*" or "beta adrenergic blocking drug" or "beta adrenergic receptor antagonist*" or "beta adrenergic receptor blockader*" or "beta adrenergic receptor blocker*" or "beta adrenoceptor antagonist*" or "beta adrenoceptor blocker*" or "beta adrenoceptor blocking agent*" or "beta adrenoceptor blocking drug*" or "beta adrenolytic" or "beta antagonist*" or "beta antiadrenergic agent*" or "beta blocker" or "beta blocking adrenergic agent*" or "beta blocking agent*" or "beta blocking drug*" or "beta receptor adrenergic blocking agent*" or "beta receptor blocker*" or "beta receptor blocking agent*" or "beta sympathicolytic agent*" or "beta sympathicolitics" or "beta sympatholytic agent*" or "betasympatholytic agent*").tw,kf.	14206
11	alprenolol/ or brimonidine tartrate, timolol maleate drug combination/ or bunolol/ or bupranolol/ or carteolol/ or carvedilol/ or dihydroalprenolol/ or iodocyanopindolol/ or labetalol/ or levobunolol/ or metipranolol/ or nadolol/ or oxprenolol/ or penbutolol/ or pindolol/ or propranolol/ or sotalol/ or timolol/	14502
12	(alprenolol or bucindolol or bunolol or bupranolol or carazolol or carpindolol or carteolol or carvedilol or cloranolol or dexpropranolol or dichlorisoprenaline or dihydroalprenolol or dilevalol or iodocyanopindolol or isamoltane or labetalol or levobunolol or metipranolol or nadolol or nifenalol or oxprenolol or penbutolol or pindolol or propranolol or sotalol or spirendolol or tertatolol or tilisolol or timolol).tw,kf.	19291
13	adrenergic beta-1 receptor antagonists/	1281
14	acebutolol/ or atenolol/ or betaxolol/ or bisoprolol/ or celiprolol/ or metoprolol/ or practolol/	6735
15	(acebutolol or atenolol or bendacalol or betaxolol or bevantolol or bisoprolol or celiprolol or cetamolol or cyanoiodopindolol or cyanopindolol or dramedilol or epanolol or esmolol or flusoxolol or landiolol or metoprolol or nebivolol or practolol or propranolol or ritodrine or salcardolol or sandoz 204545 or sotalol or talinolol or vortioxetine).tw,kf.	22643
16	Calcium Channel Blockers/	25268
17	("calcium blocker" or "calcium blocking agent*" or "calcium channel antagonist*" or "calcium channel blocker*" or "calcium channel blocking drug*" or "calcium entry blocker" or "calcium entry blocking agent*" or "calcium inhibitor" or "exogenous calcium antagonist*" or "exogenous calcium blockader*").tw,kf.	12479
18	Anticonvulsants/	40862
19	("anti convulsant agent*" or "anti convulsive agent*" or "anti convulsive drug*" or "anti epileptic*" or "anticonvulsant*" or "anticonvulsive agent*" or "anticonvulsive drug*" or "anticonvulsivum" or "antiepileptic" or "antiepileptics" or "antiepileptiform drug*").tw,kf.	34720
20	acetazolamide/ or bromides/ or cannabidiol/ or carbamazepine/ or chlormethiazole/ or clobazam/ or clonazepam/ or clorazepate dipotassium/ or diazepam/ or dimethadione/ or estazolam/ or ethosuximide/ or felbamate/ or flunarizine/ or gabapentin/ or lacosamide/ or lamotrigine/ or levetiracetam/ or lorazepam/ or magnesium sulfate/ or medazepam/ or mephenytoin/ or	57455

	mephobarbital/ or meprobamate/ or nitrazepam/ or oxcarbazepine/ or paraldehyde/ or phenobarbital/ or phenytoin/ or pregabalin/ or primidone/ or riluzole/ or thiopental/ or tiagabine/ or tiletamine/ or topiramate/ or trimethadione/ or valproic acid/ or vigabatrin/ or zonisamide/	
21	(acetazolamide or albutoin or alprazolam or ascorbate magnesium or belnacasan or brexanolone or brivaracetam or bromides or cannabidiol or cannabidivarin or carabersat or carbamazepine or carisbamate or cenobamate or chlormethiazole or clobazam or clomethiazole or clonazepam or clorazepate dipotassium or darigabat or dextromethorphan or dezinamide or diazepam or diclofenamide or dimethadione or elpetrigine or estazolam or eterobarb or ethosuximide or ethotoin or etiracetam or felbamate or fenfluramine or flunarizine or gabapentin or ganaxolone or guaifenesin or "ica 105665" or imepitoin or imidazenil or lacosamide or lamotrigine or lanicemine or levetiracetam or licarbazepine or lorazepam or loreclezole or losigamone or magnesium sulfate or medazepam or mephenytoin or mephobarbital or meprobamate or mesuximide or metharbital or midazolam or nitrazepam or oxcarbazepine or padsevonil or paraldehyde or paramethadione or pentoxyverine or perampanel or phenobarbital or phenytoin or pregabalin or primidone or progabide or remacemide or retigabine or riluzole or ropizine or rufinamide or safinamide or seletracetam or sodium bromide or stiripentol or sultiame or talampanel or thiopental or tiagabine or tiletamine or topiramate or trimethadione or valproic acid or valpromide or valroceamide or vigabatrin or vixotrigine or zaleplon or zonisamide).tw,kf.	82787
22	exp Anti-Inflammatory Agents, Non-Steroidal/	138244
23	("anti inflammatory analgesic*" or "aspirin like agent*" or "non steroid antiinflammatory agent*" or "non steroid antiinflammatory drug*" or "non steroidal anti inflammatory agent*" or "non steroidal anti inflammatory drug*" or "nonsteroid antiinflammatory agent*" or "nonsteroid antiinflammatory drug" or "nonsteroid antirheumatic agent" or "nonsteroidal anti inflammatory agent*" or "nonsteroidal anti inflammatory drug*" or "nonsteroidal antiinflammatory agent*" or "nonsteroidal antiinflammatory drug*" or "nsaid" or "nsaids").tw,kf.	36916
24	Acetaminophen/ or Antipyrine/ or Aspirin/ or Celecoxib/ or Clonixin/ or Curcumin/ or Diclofenac/ or dipyrrone/ or Ibuprofen/ or Indomethacin/ or Ketoprofen/ or Ketorolac/ or Ketorolac Tromethamine/ or Mesalamine/ or Naproxen/ or salicylates/ or Sulfasalazine/ or Tolmetin/	96692
25	(acalabrutinib or aceclofenac or acemetacin or acetaminophen or acetaminosalol or acetylsalicylic acid or actarit or adalimumab or alemtuzumab or antipyrine or apremilast or ascriptin or aspirin or azathioprine or azelaic acid or balsalazide or belimumab or brimonidine or celecoxib or clonixin lysine or clonixin or curcumin or dexibuprofen or dexketoprofen or diclofenac or dipyrrone or etodolac or etoricoxib or fenoprofen or flurbiprofen or ibuprofen or icosapentaenoic acid or indometacin or indomethacin or ketoprofen or ketorolac or leflunomide or lornoxicam or loxoprofen or lumiracoxib or meclofenamic acid or mefenamic acid or meloxicam or mesalamine or mesalazine or methotrexate or nabumetone or naproxen or natalizumab or nimesulide or parecoxib or phenylbutazone or piroxicam or pirprofen or rasagiline or rituximab or rofecoxib or ruxolitinib or salazosulfapyridine or salicylates or salicylic acid or satralizumab or sulfasalazine or sulindac or tenoxicam or teriflunomide or tofacitinib or tolmetin or valdecoxib).tw,kf.	203782
26	exp Angiotensin Receptor Antagonists/	24152

27	("angiotensin ii receptor antagonist*" or "angiotensin ii receptor blocker*" or "angiotensin ii receptor blocking agent*" or "angiotensin receptor antagonist" or "angiotensin receptor blocker*" or "angiotensin receptor blocking agent*").tw,kf.	12160
28	irbesartan/ or olmesartan medoxomil/ or telmisartan/ or valsartan/	6612
29	("angiotensin 1 receptor antagonist" or "angiotensin 2 receptor antagonist" or azilsartan or candesartan or eprosartan or fimasartan or irbesartan or losartan or olmesartan or sartan derivative or tasosartan or telmisartan or trv027 or valsartan).tw,kf.	17916
30	exp Antidepressive Agents/	94901
31	("anti depressant agent*" or "antidepressant*" or "antidepression drug*" or "antidepressive agent*" or "antidepressive drug*" or "neurothymoleptic agent*" or "psychoenergizer" or "thymoanaleptic" or "thymoanaleptics" or thymoleptic or thymoleptics or "thymolytic agent").tw,kf.	52365
32	Aripiprazole/ or Duloxetine Hydrochloride/ or Lithium Carbonate/ or Lithium Compounds/ or Mirtazapine/ or Moclobemide/ or Phenelzine/ or Pizotiline/ or Quetiapine Fumarate/ or Sertraline/ or Tranylcypromine/	16745
33	Bupropion/ or Citalopram/ or Fluoxetine/ or Mianserin/ or Paroxetine/ or Sulpiride/ or Trazodone/ or Tryptophan/ or Venlafaxine Hydrochloride/	38437
34	Amitriptyline/ or Clomipramine/ or Desipramine/ or Dothiepin/ or Doxepin/ or Imipramine/ or Nortriptyline/ or Opipramol/	7959
35	(agomelatine or amitriptyline or aprepitant or aripiprazole or asenapine or "botulinum toxin a" or bupropion or citalopram or clomipramine or desipramine or dothiepin or doxepin or duloxetine hydrochloride or esketamine or fluoxetine or gepirone or imipramine or indalpine or ipsapirone or lithium acetate or lithium carbonate or lithium chloride or lithium compounds or lithium salt or mianserin or mifepristone or minaprine or mirtazapine or moclobemide or monoamine oxidase inhibitor* or noradrenalin uptake inhibitor* or nortriptyline or opipramol or paroxetine or phenelzine or pizotiline or quetiapine fumarate or serotonin uptake inhibitor* or sertraline or sulpiride or tetracyclic antidepressant* or tranylcypromine or trazodone or tricyclic antidepressant* or tryptophan or venlafaxine hydrochloride).tw,kf.	84436
36	Botulinum Toxins, Type A/	10631
37	("abobotulinum toxin a" or "abobotulinumtoxin a" or "abobotulinumtoxina" or "agn 151607" or "agn151607" or "alluzience" or "ant 1207" or "ant 1401" or "ant 1403" or "ant1207" or "ant1401" or "ant1403" or "azzalure" or "bocouture" or "boe-tox" or "bont a" or "bont serotype a" or "botox" or "botulin a" or "botulin toxin a" or "botulinium a toxin" or "botulinum a exotoxin" or "botulinum a toxin" or "botulinum neurotoxin a" or "botulinum toxin a" or "btxa" or "clostridium botulinum a toxin" or "clostridium botulinum endotoxin" or "clostridium botulinum neurotoxin a" or "clostridium botulinum toxin type a" or "clostridium botulinum type a neurotoxin" or "cnt 52120" or "cnt52120" or "daxibotulinum toxin a" or "daxibotulinumtoxin a" or "daxibotulinumtoxina" or "dwp 450" or "dwp450" or "dyslor" or "dysport" or "evabotulinum toxin a" or "evabotulinumtoxin a" or "evabotulinumtoxina" or "evosyal" or "gemibotulinum toxin a" or "gemibotulinumtoxin a" or "gemibotulinumtoxina" or "gsk 1358820" or "gsk1358820" or "incobotulinum toxin a" or "incobotulinumtoxin a" or "incobotulinumtoxina" or "ipn 59011" or "ipn59011" or "jeuveau" or "letibotulinum toxin a" or "letibotulinumtoxin a" or "letibotulinumtoxina" or "meditoxin" or "mt 10109" or "mt10109" or "nabota" or "neuronox" or "nivobotulinum toxin a" or "nivobotulinumtoxin a" or "nivobotulinumtoxina" or "nt 201" or "nt201" or "nuceiva" or "oculium" or "onabotulinum toxin a" or "onabotulinumtoxin a" or	7610

	"onabotulinumtoxina" or "onaclostox" or "pm 12759" or "pm12759" or "prabotulinum toxin a" or "prabotulinumtoxin a" or "prabotulinumtoxina" or "prosigne" or "purtox" or "qm 1114" or "qm1114" or "relabotulinum toxin a" or "relabotulinumtoxin a" or "relabotulinumtoxina" or "reloxin" or "rtt 150" or "rtt150" or "vistabel" or "vistabex" or "xeomeen" or "xeomin").tw,kf.	
38	(caomet or "coenzyme 910" or "coenzyme q 10" or "coenzyme Q10" or decorenone or mitocor or neuquinone or "quinone q 10" or ubidecarenone or ubimaioir or "ubiquinone (10)" or "ubiquinone 10" or "ubiquinone 50" or ubiten).tw,kf.	4064
39	Magnesium/	24624
40	(magnesium or romag).tw,kf.	32593
41	Melatonin/	17282
42	("apl 510" or "apl510" or ceyesto or circadin or "jan 13004" or "jan13004" or "ki 1001" or "ki1001" or melatonin or melatonina or melovine or orlogin or slenyto or "sp 13004" or "sp13004" or waferest).tw,kf.	20405
43	or/4-5,8-42	696356
44	3 and 43 [migraines AND prophylaxis]	6793
45	randomized controlled trial.pt.	480050
46	controlled clinical trial.pt.	49673
47	randomized.ab.	460234
48	placebo.ab.	169835
49	drug therapy.fs.	1880993
50	randomly.ab.	294766
51	trial.ab.	482925
52	groups.ab.	1714791
53	45 or 46 or 47 or 48 or 49 or 50 or 51 or 52	3949647
54	animals/ not humans.sh.	2817192
55	53 not 54	3422601
56	44 and 55 [migraines AND prophylaxis AND RCTs]	4566
57	remove duplicates from 56	4540

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

#	Searches	Results
1	exp Migraine Disorders/	30669
2	(migraine or migraines or sick headache or sick headaches or hemicrania or migrainous headache or status hemicranicus).tw,kf.	40663
3	or/1-2	44880
4	("cgrp monoclonal antibodies" or "calcitonin gene-related peptide antibodies (cgrp) monoclonal antibodies (mabs)" or "cgrp mabs").tw,kf.	167
5	calcitonin gene related peptide.tw,kf.	12349

6	Calcitonin Gene-Related Peptide Receptor Antagonists/	869
7	exp Antibodies, Monoclonal/	267646
8	6 and 7	274
9	adrenergic beta-antagonists/	41510
10	("adrenergic beta antagonist*" or "adrenergic beta blocker*" or "adrenergic beta receptor blockader*" or "beta adrenergic antagonist*" or "beta adrenergic blocker*" or "beta adrenergic blocking agent*" or "beta adrenergic blocking drug" or "beta adrenergic receptor antagonist*" or "beta adrenergic receptor blockader*" or "beta adrenergic receptor blocker*" or "beta adrenoceptor antagonist*" or "beta adrenoceptor blocker*" or "beta adrenoceptor blocking agent*" or "beta adrenoceptor blocking drug*" or "beta adrenolytic" or "beta antagonist*" or "beta antiadrenergic agent*" or "beta blocker" or "beta blocking adrenergic agent*" or "beta blocking agent*" or "beta blocking drug*" or "beta receptor adrenergic blocking agent*" or "beta receptor blocker*" or "beta receptor blocking agent*" or "beta sympatholytic agent*" or "beta sympatholytics" or "beta sympatholytic agent*" or "betasympatholytic agent*").tw,kf.	28363
11	alprenolol/ or brimonidine tartrate, timolol maleate drug combination/ or bunolol/ or bupranolol/ or carteolol/ or carvedilol/ or dihydroalprenolol/ or iodocyanopindolol/ or labetalol/ or levobunolol/ or metipranolol/ or nadolol/ or oxprenolol/ or penbutolol/ or pindolol/ or propranolol/ or sotalol/ or timolol/	48975
12	(alprenolol or bucindolol or bunolol or bupranolol or carazolol or carpindolol or carteolol or carvedilol or cloranolol or dexpropranolol or dichlorisoprenaline or dihydroalprenolol or dilevalol or iodocyanopindolol or isamoltane or labetalol or levobunolol or metipranolol or nadolol or nifenalol or oxprenolol or penbutolol or pindolol or propranolol or sotalol or spirendolol or tertatolol or tilisolol or timolol).tw,kf.	51527
13	adrenergic beta-1 receptor antagonists/	1328
14	acebutolol/ or atenolol/ or betaxolol/ or bisoprolol/ or celiprolol/ or metoprolol/ or practolol/	14374
15	(acebutolol or atenolol or bendacalol or betaxolol or bevantolol or bisoprolol or celiprolol or cetamolol or cyanoiodopindolol or cyanopindolol or dramedilol or epanolol or esmolol or flusoxolol or landiolol or metoprolol or nebivolol or practolol or propranolol or ritodrine or salcardolol or sandoz 204545 or sotalol or talinolol or vortioxetine).tw,kf.	54958
16	Calcium Channel Blockers/	37478
17	("calcium blocker" or "calcium blocking agent*" or "calcium channel antagonist*" or "calcium channel blocker*" or "calcium channel blocking drug*" or "calcium entry blocker" or "calcium entry blocking agent*" or "calcium inhibitor" or "exogenous calcium antagonist*" or "exogenous calcium blockader*").tw,kf.	20506
18	Anticonvulsants/	54979
19	("anti convulsant agent*" or "anti convulsive agent*" or "anti convulsive drug*" or "anti epileptic*" or "anticonvulsant*" or "anticonvulsive agent*" or "anticonvulsive drug*" or "anticonvulsivum" or "antiepileptic" or "antiepileptics" or "antiepileptiform drug*").tw,kf.	52702
20	acetazolamide/ or bromides/ or cannabidiol/ or carbamazepine/ or chlormethiazole/ or clobazam/ or clonazepam/ or clorazepate dipotassium/ or diazepam/ or dimethadione/ or estazolam/ or ethosuximide/ or felbamate/ or flunarizine/ or gabapentin/ or lacosamide/ or lamotrigine/ or levetiracetam/ or lorazepam/ or magnesium sulfate/ or medazepam/ or mephenytoin/ or	121063

	mephobarbital/ or meprobamate/ or nitrazepam/ or oxcarbazepine/ or paraldehyde/ or phenobarbital/ or phenytoin/ or pregabalin/ or primidone/ or riluzole/ or thiopental/ or tiagabine/ or tiletamine/ or topiramate/ or trimethadione/ or valproic acid/ or vigabatrin/ or zonisamide/	
21	(acetazolamide or albutoin or alprazolam or ascorbate magnesium or belnacasan or brexanolone or brivaracetam or bromides or cannabidiol or cannabidivarin or carabersat or carbamazepine or carisbamate or cenobamate or chlormethiazole or clobazam or clomethiazole or clonazepam or clorazepate dipotassium or darigabat or dextromethorphan or dezinamide or diazepam or diclofenamide or dimethadione or elpetrigine or estazolam or eterobarb or ethosuximide or ethotoin or etiracetam or felbamate or fenfluramine or flunarizine or gabapentin or ganaxolone or guaifenesin or "ica 105665" or imepitoin or imidazenil or lacosamide or lamotrigine or lanicemine or levetiracetam or licarbazepine or lorazepam or loreclezole or losigamone or magnesium sulfate or medazepam or mephenytoin or mephobarbital or meprobamate or mesuximide or metharbital or midazolam or nitrazepam or oxcarbazepine or padsevonil or paraldehyde or paramethadione or pentoxyverine or perampanel or phenobarbital or phenytoin or pregabalin or primidone or progabide or remacemide or retigabine or riluzole or ropizine or rufinamide or safinamide or seletracetam or sodium bromide or stiripentol or sultiame or talampanel or thiopental or tiagabine or tiletamine or topiramate or trimethadione or valproic acid or valpromide or valroceamide or vigabatrin or vixotrigine or zaleplon or zonisamide).tw,kf.	148034
22	exp Anti-Inflammatory Agents, Non-Steroidal/	211076
23	("anti inflammatory analgesic*" or "aspirin like agent*" or "non steroid antiinflammatory agent*" or "non steroid antiinflammatory drug*" or "non steroidal anti inflammatory agent*" or "non steroidal anti inflammatory drug*" or "nonsteroid antiinflammatory agent*" or "nonsteroid antiinflammatory drug" or "nonsteroid antirheumatic agent" or "nonsteroidal anti inflammatory agent*" or "nonsteroidal anti inflammatory drug*" or "nonsteroidal antiinflammatory agent*" or "nonsteroidal antiinflammatory drug*" or "nsaid" or "nsaids").tw,kf.	51073
24	Acetaminophen/ or Antipyrine/ or Aspirin/ or Celecoxib/ or Clonixin/ or Curcumin/ or Diclofenac/ or dipyrrone/ or Ibuprofen/ or Indomethacin/ or Ketoprofen/ or Ketorolac/ or Ketorolac Tromethamine/ or Mesalamine/ or Naproxen/ or salicylates/ or Sulfasalazine/ or Tolmetin/	156025
25	(acalabrutinib or aceclofenac or acemetacin or acetaminophen or acetaminosalol or acetylsalicylic acid or actarit or adalimumab or alemtuzumab or antipyrine or apremilast or ascriptin or aspirin or azathioprine or azelaic acid or balsalazide or belimumab or brimonidine or celecoxib or clonixin lysine or clonixin or curcumin or dexibuprofen or dexketoprofen or diclofenac or dipyrrone or etodolac or etoricoxib or fenoprofen or flurbiprofen or ibuprofen or icosapentaenoic acid or indometacin or indomethacin or ketoprofen or ketorolac or leflunomide or lornoxicam or loxoprofen or lumiracoxib or meclofenamic acid or mefenamic acid or meloxicam or mesalamine or mesalazine or methotrexate or nabumetone or naproxen or natalizumab or nimesulide or parecoxib or phenylbutazone or piroxicam or pirprofen or rasagiline or rituximab or rofecoxib or ruxolitinib or salazosulfapyridine or salicylates or salicylic acid or satralizumab or sulfasalazine or sulindac or tenoxicam or teriflunomide or tofacitinib or tolmetin or valdecoxib).tw,kf.	307676
26	exp Angiotensin Receptor Antagonists/	26926

27	("angiotensin ii receptor antagonist*" or "angiotensin ii receptor blocker*" or "angiotensin ii receptor blocking agent*" or "angiotensin receptor antagonist" or "angiotensin receptor blocker*" or "angiotensin receptor blocking agent*").tw,kf.	14264
28	irbesartan/ or olmesartan medoxomil/ or telmisartan/ or valsartan/	6658
29	("angiotensin 1 receptor antagonist" or "angiotensin 2 receptor antagonist" or azilsartan or candesartan or eprosartan or fimasartan or irbesartan or losartan or olmesartan or sartan derivative or tasosartan or telmisartan or trv027 or valsartan).tw,kf.	20660
30	exp Antidepressive Agents/	157396
31	("anti depressant agent*" or "antidepressant*" or "antidepression drug*" or "antidepressive agent*" or "antidepressive drug*" or "neurothymoleptic agent*" or "psychoenergizer" or "thymoanaleptic" or "thymoanaleptics" or thymoleptic or thymoleptics or "thymolytic agent").tw,kf.	73764
32	Aripiprazole/ or Duloxetine Hydrochloride/ or Lithium Carbonate/ or Lithium Compounds/ or Mirtazapine/ or Moclobemide/ or Phenelzine/ or Pizotiline/ or Quetiapine Fumarate/ or Sertraline/ or Tranylcypromine/	21662
33	Bupropion/ or Citalopram/ or Fluoxetine/ or Mianserin/ or Paroxetine/ or Sulpiride/ or Trazodone/ or Tryptophan/ or Venlafaxine Hydrochloride/	61997
34	Amitriptyline/ or Clomipramine/ or Desipramine/ or Dothiepin/ or Doxepin/ or Imipramine/ or Nortriptyline/ or Opipramol/	24431
35	(agomelatine or amitriptyline or aprepitant or aripiprazole or asenapine or "botulinum toxin a" or bupropion or citalopram or clomipramine or desipramine or dothiepin or doxepin or duloxetine hydrochloride or esketamine or fluoxetine or gepirone or imipramine or indalpine or ipsapirone or lithium acetate or lithium carbonate or lithium chloride or lithium compounds or lithium salt or mianserin or mifepristone or minaprine or mirtazapine or moclobemide or monoamine oxidase inhibitor* or noradrenalin uptake inhibitor* or nortriptyline or opipramol or paroxetine or phenelzine or pizotiline or quetiapine fumarate or serotonin uptake inhibitor* or sertraline or sulpiride or tetracyclic antidepressant* or tranylcypromine or trazodone or tricyclic antidepressant* or tryptophan or venlafaxine hydrochloride).tw,kf.	143344
36	Botulinum Toxins, Type A/	10662
37	("abobotulinum toxin a" or "abobotulinumtoxin a" or "abobotulinumtoxina" or "agn 151607" or "agn151607" or "alluzience" or "ant 1207" or "ant 1401" or "ant 1403" or "ant1207" or "ant1401" or "ant1403" or "azzalure" or "bocouture" or "boe-tox" or "bont a" or "bont serotype a" or "botox" or "botulin a" or "botulin toxin a" or "botulinium a toxin" or "botulinum a exotoxin" or "botulinum a toxin" or "botulinum neurotoxin a" or "botulinum toxin a" or "btxa" or "clostridium botulinum a toxin" or "clostridium botulinum endotoxin" or "clostridium botulinum neurotoxin a" or "clostridium botulinum toxin type a" or "clostridium botulinum type a neurotoxin" or "cnt 52120" or "cnt52120" or "daxibotulinum toxin a" or "daxibotulinumtoxin a" or "daxibotulinumtoxina" or "dwp 450" or "dwp450" or "dyslor" or "dysport" or "evabotulinum toxin a" or "evabotulinumtoxin a" or "evabotulinumtoxina" or "evosyal" or "gemibotulinum toxin a" or "gemibotulinumtoxin a" or "gemibotulinumtoxina" or "gsk 1358820" or "gsk1358820" or "incobotulinum toxin a" or "incobotulinumtoxin a" or "incobotulinumtoxina" or "ipn 59011" or "ipn59011" or "jeuveau" or "letibotulinum toxin a" or "letibotulinumtoxin a" or "letibotulinumtoxina" or "meditoxin" or "mt 10109" or "mt10109" or "nabota" or "neuronox" or "nivobotulinum toxin a" or "nivobotulinumtoxin a" or "nivobotulinumtoxina" or "nt 201" or "nt201" or "nuceiva" or "oculium" or "onabotulinum toxin a" or "onabotulinumtoxin a" or	9189

	"onabotulinumtoxina" or "onaclostox" or "pm 12759" or "pm12759" or "prabotulinum toxin a" or "prabotulinumtoxin a" or "prabotulinumtoxina" or "prosigne" or "purtox" or "qm 1114" or "qm1114" or "relabotulinum toxin a" or "relabotulinumtoxin a" or "relabotulinumtoxina" or "reloxin" or "rtt 150" or "rtt150" or "vistabel" or "vistabex" or "xeomeen" or "xeomin").tw,kf.	
38	(caomet or "coenzyme 910" or "coenzyme q 10" or "coenzyme Q10" or decorenone or mitocor or neuquinone or "quinone q 10" or ubidecarenone or ubimaio or "ubiquinone (10)" or "ubiquinone 10" or "ubiquinone 50" or ubiten).tw,kf.	5376
39	Magnesium/	69283
40	(magnesium or romag).tw,kf.	66468
41	Melatonin/	22186
42	("apl 510" or "apl510" or ceyesto or circadin or "jan 13004" or "jan13004" or "ki 1001" or "ki1001" or melatonin or melatonina or melovine or orlogin or slenyto or "sp 13004" or "sp13004" or waferest).tw,kf.	28086
43	or/4-5,8-42	1183314
44	3 and 43 [migraines AND prophylaxis]	9301
45	randomized controlled trial.pt.	574929
46	controlled clinical trial.pt.	94985
47	randomized.ab.	571967
48	placebo.ab.	230792
49	drug therapy.fs.	2519979
50	randomly.ab.	389035
51	trial.ab.	612187
52	groups.ab.	2393254
53	45 or 46 or 47 or 48 or 49 or 50 or 51 or 52	5433260
54	animals/ not humans.sh.	5002581
55	53 not 54	4733125
56	44 and 55 [migraines AND prophylaxis AND RCTs]	5941
57	remove duplicates from 56	5913

EBM Reviews - Cochrane Central Register of Controlled Trials July 2022

Search Strategy:

#	Searches	Results
1	exp Migraine Disorders/	3020
2	(migraine or migraines or sick headache or sick headaches or hemicrania or migrainous headache or status hemicanicus).tw,kw.	9024
3	1 or 2	9137
4	("cgrp monoclonal antibodies" or "calcitonin gene-related peptide antibodies (cgrp) monoclonal antibodies (mabs)" or "cgrp mabs").tw,kw.	13
5	calcitonin gene related peptide.tw,kw.	1062
6	Calcitonin Gene-Related Peptide Receptor Antagonists/	81

7	exp Antibodies, Monoclonal/	15809
8	6 and 7	42
9	adrenergic beta-antagonists/	4417
10	("adrenergic beta antagonist*" or "adrenergic beta blocker*" or "adrenergic beta receptor blockader*" or "beta adrenergic antagonist*" or "beta adrenergic blocker*" or "beta adrenergic blocking agent*" or "beta adrenergic blocking drug" or "beta adrenergic receptor antagonist*" or "beta adrenergic receptor blockader*" or "beta adrenergic receptor blocker*" or "beta adrenoceptor antagonist*" or "beta adrenoceptor blocker*" or "beta adrenoceptor blocking agent*" or "beta adrenoceptor blocking drug*" or "beta adrenolytic" or "beta antagonist*" or "beta antiadrenergic agent*" or "beta blocker" or "beta blocking adrenergic agent*" or "beta blocking agent*" or "beta blocking drug*" or "beta receptor adrenergic blocking agent*" or "beta receptor blocker*" or "beta receptor blocking agent*" or "beta sympathicolytic agent*" or "beta sympathicolytics" or "beta sympatholytic agent*" or "betasympatholytic agent*").tw,kw.	6202
11	alprenolol/ or "brimonidine tartrate, timolol maleate drug combination"/ or bunolol/ or bupranolol/ or carteolol/ or carvedilol/ or dihydroalprenolol/ or iodocyanopindolol/ or labetalol/ or levobunolol/ or metipranolol/ or nadolol/ or oxprenolol/ or penbutolol/ or pindolol/ or propranolol/ or sotalol/ or timolol/	6240
12	(alprenolol or bucindolol or bunolol or bupranolol or carazolol or carpindolol or carteolol or carvedilol or cloranolol or dexpropranolol or dichlorisoprenaline or dihydroalprenolol or dilevalol or iodocyanopindolol or isamoltane or labetalol or levobunolol or metipranolol or nadolol or nifenalol or oxprenolol or penbutolol or pindolol or propranolol or sotalol or spirendolol or tertatolol or tilisolol or timolol).tw,kw.	10888
13	adrenergic beta-1 receptor antagonists/	215
14	acebutolol/ or atenolol/ or betaxolol/ or bisoprolol/ or celiprolol/ or metoprolol/ or practolol/	4201
15	(acebutolol or atenolol or betaxolol or bevantolol or bisoprolol or celiprolol or cetamolol or cyanoiodopindolol or cyanopindolol or esmolol or landiolol or metoprolol or nebivolol or practolol or propranolol or ritodrine or sotalol or talinolol or vortioxetine).tw,kw.	13586
16	Calcium Channel Blockers/	2876
17	("calcium blocker" or "calcium blocking agent*" or "calcium channel antagonist*" or "calcium channel blocker*" or "calcium channel blocking drug*" or "calcium entry blocker" or "calcium entry blocking agent*" or "calcium inhibitor" or "exogenous calcium antagonist*" or "exogenous calcium blockader*").tw,kw.	3325
18	Anticonvulsants/	2440
19	("anti convulsant agent*" or "anti convulsive agent*" or "anti convulsive drug*" or "anti epileptic*" or "anticonvulsant*" or "anticonvulsive agent*" or "anticonvulsive drug*" or "anticonvulsivum" or "antiepileptic" or "antiepileptics" or "antiepileptiform drug*").tw,kw.	4495
20	acetazolamide/ or bromides/ or cannabidiol/ or carbamazepine/ or chlormethiazole/ or clobazam/ or clonazepam/ or clorazepate dipotassium/ or diazepam/ or dimethadione/ or estazolam/ or ethosuximide/ or felbamate/ or flunarizine/ or gabapentin/ or lacosamide/ or lamotrigine/ or levetiracetam/ or lorazepam/ or magnesium sulfate/ or medazepam/ or mephentyoin/ or mephobarbital/ or meprobamate/ or nitrazepam/ or oxcarbazepine/ or paraldehyde/ or phenobarbital/	11619

	or phenytoin/ or pregabalin/ or primidone/ or riluzole/ or thiopental/ or tiagabine/ or tiletamine/ or topiramate/ or trimethadione/ or valproic acid/ or vigabatrin/ or zonisamide/	
21	(acetazolamide or albutoin or alprazolam or ascorbate magnesium or belnacasan or brexanolone or brivaracetam or bromides or cannabidiol or cannabidivarin or carabersat or carbamazepine or carisbamate or cenobamate or chlormethiazole or clobazam or clomethiazole or clonazepam or clorazepate dipotassium or darigabat or dextromethorphan or dezinamide or diazepam or diclofenamide or dimethadione or elpetrigine or estazolam or eterobarb or ethosuximide or ethotoin or etiracetam or felbamate or fenfluramine or flunarizine or gabapentin or ganaxolone or guaifenesin or "ica 105665" or imepitoin or imidazenil or lacosamide or lamotrigine or lanicemine or levetiracetam or licarbazepine or lorazepam or loreclezole or losigamone or magnesium sulfate or medazepam or mephentyoin or mephobarbital or meprobamate or mesuximide or metharbital or midazolam or nitrazepam or oxcarbazepine or padsevonil or paraldehyde or paramethadione or pentoxyverine or perampanel or phenobarbital or phenytoin or pregabalin or primidone or progabide or remacemide or retigabine or riluzole or ropizine or rufinamide or safinamide or seletracetam or sodium bromide or stiripentol or sultiame or talampanel or thiopental or tiagabine or tiletamine or topiramate or trimethadione or valproic acid or valpromide or valroceamide or vigabatrin or vixotrigine or zaleplon or zonisamide).tw,kw.	34246
22	exp Anti-Inflammatory Agents, Non-Steroidal/	21883
23	("anti inflammatory analgesic*" or "aspirin like agent*" or "non steroid antiinflammatory agent*" or "non steroid antiinflammatory drug*" or "non steroidal anti inflammatory agent*" or "non steroidal anti inflammatory drug*" or "non steroidal antiinflammatory agent*" or "non steroidal antiinflammatory drug*" or "nonsteroid antiinflammatory agent*" or "nonsteroid antiinflammatory drug" or "nonsteroid antirheumatic agent" or "nonsteroidal anti inflammatory agent*" or "nonsteroidal anti inflammatory drug*" or "nonsteroidal antiinflammatory agent*" or "nonsteroidal antiinflammatory drug*" or "nsaid" or "nsaids").tw,kw.	11038
24	Acetaminophen/ or Antipyrine/ or Aspirin/ or Celecoxib/ or Clonixin/ or Curcumin/ or Diclofenac/ or dipyrrone/ or Ibuprofen/ or Indomethacin/ or Ketoprofen/ or Ketorolac/ or Ketorolac Tromethamine/ or Mesalamine/ or Naproxen/ or salicylates/ or Sulfasalazine/ or Tolmetin/	19158
25	(acalabrutinib or aceclofenac or acemetacin or acetaminophen or acetaminosalol or acetylsalicylic acid or actarit or adalimumab or alemtuzumab or antipyrine or apremilast or ascriptin or aspirin or azathioprine or azelaic acid or balsalazide or belimumab or brimonidine or celecoxib or clonixin lysine or clonixin or curcumin or dexibuprofen or dexketoprofen or diclofenac or dipyrrone or etodolac or etoricoxib or fenoprofen or flurbiprofen or ibuprofen or icosapentaenoic acid or indometacin or indomethacin or ketoprofen or ketorolac or leflunomide or lornoxicam or loxoprofen or lumiracoxib or meclofenamic acid or mefenamic acid or meloxicam or mesalamine or mesalazine or methotrexate or nabumetone or naproxen or natalizumab or nimesulide or parecoxib or phenylbutazone or piroxicam or piroprofen or rasagiline or rituximab or rofecoxib or ruxolitinib or salazosulfapyridine or salicylates or salicylic acid or satralizumab or sulfasalazine or sulindac or tenoxicam or teriflunomide or tofacitinib or tolmetin or valdecoxib).tw,kw.	70589
26	exp angiotensin receptor antagonists/	4178
27	("angiotensin ii receptor antagonist*" or "angiotensin ii receptor blocker*" or "angiotensin ii receptor blocking agent*" or "angiotensin receptor antagonist" or "angiotensin receptor blocker*" or "angiotensin receptor blocking agent*").tw,kw.	3582
28	irbesartan/ or olmesartan medoxomil/ or telmisartan/ or valsartan/	2080

29	("angiotensin 1 receptor antagonist" or "angiotensin 2 receptor antagonist" or azilsartan or candesartan or eprosartan or fimasartan or irbesartan or losartan or olmesartan or sartan derivative or tasosartan or telmisartan or trv027 or valsartan).tw,kw.	8620
30	exp antidepressive agents/	15881
31	("anti depressant agent*" or "antidepressant*" or "antidepression drug*" or "antidepressive agent*" or "antidepressive drug*" or "neurothymoleptic agent*" or "psychoenergizer" or "thymoanaleptic" or "thymoanaleptics" or thymoleptic or thymoleptics or "thymolytic agent").tw,kw.	13906
32	Aripiprazole/ or Duloxetine Hydrochloride/ or Lithium Carbonate/ or Lithium Compounds/ or Mirtazapine/ or Moclobemide/ or Phenelzine/ or Pizotiline/ or Quetiapine Fumarate/ or Sertraline/ or Tranylcypromine/	4101
33	Bupropion/ or Citalopram/ or Fluoxetine/ or Mianserin/ or Paroxetine/ or Sulpiride/ or Trazodone/ or Tryptophan/ or Venlafaxine Hydrochloride/	6608
34	Amitriptyline/ or Clomipramine/ or Desipramine/ or Dothiepin/ or Doxepin/ or Imipramine/ or Nortriptyline/ or Opipramol/	3410
35	(agomelatine or amitriptyline or aprepitant or aripiprazole or asenapine or "botulinum toxin a" or bupropion or citalopram or clomipramine or desipramine or dothiepin or doxepin or duloxetine hydrochloride or esketamine or fluoxetine or gepirone or imipramine or indalpine or ipsapirone or lithium acetate or lithium carbonate or lithium chloride or lithium compounds or lithium salt or mianserin or mifepristone or minaprine or mirtazapine or moclobemide or monoamine oxidase inhibitor* or noradrenalin uptake inhibitor* or nortriptyline or opipramol or paroxetine or phenelzine or pizotiline or quetiapine fumarate or serotonin uptake inhibitor* or sertraline or sulpiride or tetracyclic antidepressant* or tranylcypromine or trazodone or tricyclic antidepressant* or tryptophan or venlafaxine hydrochloride).tw,kw.	25811
36	Botulinum Toxins, Type A/	1835
37	("abobotulinum toxin a" or "abobotulinumtoxin a" or "abobotulinumtoxina" or "agn 151607" or "agn151607" or "alluzience" or "ant 1207" or "ant 1401" or "ant 1403" or "ant1207" or "ant1401" or "ant1403" or "azzalure" or "bocouture" or "boe-tox" or "bont a" or "bont serotype a" or "botox" or "botulin a" or "botulin toxin a" or "botulinium a toxin" or "botulinum a exotoxin" or "botulinum a toxin" or "botulinum neurotoxin a" or "botulinum toxin a" or "btxa" or "clostridium botulinum a toxin" or "clostridium botulinum endotoxin" or "clostridium botulinum neurotoxin a" or "clostridium botulinum toxin type a" or "clostridium botulinum type a neurotoxin" or "cnt 52120" or "cnt52120" or "daxibotulinum toxin a" or "daxibotulinumtoxin a" or "daxibotulinumtoxina" or "dwp 450" or "dwp450" or "dyslor" or "dysport" or "evabotulinum toxin a" or "evabotulinumtoxin a" or "evabotulinumtoxina" or "evosyal" or "gemibotulinum toxin a" or "gemibotulinumtoxin a" or "gemibotulinumtoxina" or "gsk 1358820" or "gsk1358820" or "incobotulinum toxin a" or "incobotulinumtoxin a" or "incobotulinumtoxina" or "ipn 59011" or "ipn59011" or "jeuveau" or "letibotulinum toxin a" or "letibotulinumtoxin a" or "letibotulinumtoxina" or "meditoxin" or "mt 10109" or "mt10109" or "nabota" or "neuronox" or "nivobotulinum toxin a" or "nivobotulinumtoxin a" or "nivobotulinumtoxina" or "nt 201" or "nt201" or "nuceiva" or "oculinum" or "onabotulinum toxin a" or "onabotulinumtoxin a" or "onabotulinumtoxina" or "onaclostox" or "pm 12759" or "pm12759" or "prabotulinum toxin a" or "prabotulinumtoxin a" or "prabotulinumtoxina" or "prosigne" or "purtox" or "qm 1114" or "qm1114" or "relabotulinum toxin a" or "relabotulinumtoxin a" or "relabotulinumtoxina" or "reloxin" or "rtt 150" or "rtt150" or "vistabel" or "vistabex" or "xeomeen" or "xeomin").tw,kw.	3672

38	(caomet or "coenzyme 910" or "coenzyme q 10" or "coenzyme Q10" or decorenone or mitocor or neuquinone or "quinone q 10" or ubidecarenone or ubimaio or "ubiquinone (10)" or "ubiquinone 10" or "ubiquinone 50" or ubiten).tw,kw.	1080
39	Magnesium/	1229
40	(magnesium or romag).tw,kw.	7739
41	Melatonin/	1328
42	("apl 510" or "apl510" or ceyesto or circadin or "jan 13004" or "jan13004" or "ki 1001" or "ki1001" or melatonin or melatonina or melovine or orlogin or slenyo or "sp 13004" or "sp13004" or waferest).tw,kw.	3246
43	or/4-5,8-42	197886
44	3 and 43	3267

Supplement 2 – Risk of bias criteria

Bias from the randomization process	
Issues to consider: Random sequence generation Allocation concealment	
Definitely low risk of bias	Trials that assign participants to alternative interventions using a randomly generated sequence and maintain allocation concealment. Examples of methods for developing a randomly generated allocation sequence include a random number generator, random number table, coin tossing, shuffling cards or envelopes, and throwing dice. If a trial is described as 'randomized' without any additional details related to how the allocation sequence was developed, we will assume that the allocation sequence was appropriately developed. Examples of methods for maintaining allocation concealment include using central allocation via a computer or phone system, pharmacy-controlled allocation, opaque sealed envelopes, and sequentially numbered drug containers. <i>Note that an explicit description of random sequence generation is not necessary for a rating of low risk of bias.</i>
Probably low risk of bias	Trials in which healthcare providers were blind to the intervention but which provide no information on allocation concealment. <i>Note that an explicit description of random sequence generation is not necessary for a rating of probably low risk of bias.</i>
Probably high risk of bias	Trials in which healthcare providers were not blind to the intervention and which provide no information on allocation concealment. Trials in which there are substantial baseline differences between trial arms that suggest a problem with the randomization process but there are no other limitations related to randomization.
Definitely high risk of bias	Trials in which allocation is by judgment of the clinician, by preference of the participant, by availability of the intervention, based on the results of a laboratory test, or other non-random rules (e.g., birthdate, etc.). Trials in which investigators enrolling participants could possibly foresee the arm to which each subsequent patient would be randomized, such as allocation using an open allocation schedule (e.g. a list of random numbers), assignment envelopes used without appropriate safeguards (e.g. use of unsealed, non-opaque or not sequentially numbered envelopes), alternation between arms, case record number, or any other explicitly unconcealed procedure, rate as high risk.
Bias due to deviations from the intended intervention	
Issues to consider: Blinding of healthcare providers/clinicians and participants Imbalances in cointerventions or behaviors	

Definitely low risk of bias	Trials in which healthcare providers are blind to the intervention administered and in which there are no significant differences in administered co-interventions. Trials that are described as double or triple blind.
Probably low risk of bias	
Probably high risk of bias	Trials in which healthcare providers are not blind to the intervention administered. Trials in which healthcare providers are blind to the intervention administered but there are significant differences in administered co-interventions that suggests that blinding may have been compromised. Trials in which healthcare providers are described as being blind to the intervention but allocation concealment was inadequate.
Definitely high risk of bias	Trials in which healthcare providers are not blind to the intervention and in which there are significant differences in administered co-interventions.
Bias due to missing data	
Issues to consider: Missing outcome measures Loss to follow-up	
Definitely low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) < 10%.
Probably low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is unlikely to be related to the true outcome and there is no imbalance in numbers of or reasons for missing data across intervention groups.
Probably high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is likely to be related to the true outcome or there are imbalances in numbers of or reasons for missing data across intervention groups.
Definitely high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) > 15%.
Bias due to measurement of the outcome	
Issues to consider: Blinding of outcome adjudicators Objectivity of outcome <i>Note that the judgments may differ across outcomes.</i>	
Definitely low risk of bias	Trials in which patients are blind to the intervention and in which outcomes are patient-reported. Trials in which outcomes are measured by a third-party (investigator or clinician) and in which the third-party is blind to the intervention. Trials in which the outcomes are objective (e.g., mortality, hospitalization). Trials that are described as double or triple blind.
Probably low risk of bias	

Probably high risk of bias	
Definitely high risk of bias	Trials in which patients are not blind and in which outcomes are patient-reported (e.g., ACQ). Trials in which outcome adjudicators are not blind and the outcomes are not objective (e.g., adverse events leading to discontinuation).
Bias in selection of the reported results	
Issues to consider: Selective reporting of timepoints Selective reporting of outcome measures <i>Note that we are only interested in selective reporting for the outcomes for which we are extracting data.</i> <i>Note that the judgments may differ across outcomes.</i>	
Definitely low risk of bias	Results for outcomes that were analyzed and reported according to a pre-specified statistical analysis plan or protocol (including the timepoint for the measurement of the outcome).
Probably low risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is consistent with the timepoint for other outcomes in the trial report or there is little reason to believe the outcome was selectively reported. Please note that outcomes that were not prespecified in a protocol or statistical analysis plan and that are reported in the trial preprint or publication should be rated at probably low risk of bias unless there are other important reasons to suspect that results for those outcomes were selectively reported (e.g., results are presented at timepoints that don't match the timepoints reported for other outcomes).
Probably high risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is not consistent with the timepoint for other outcomes in the trial report or there are other reasons to believe that the outcome is selectively reported.
Definitely high risk of bias	Results for outcomes that were analyzed and reported for which there are inconsistencies with the statistical analysis plan or protocol. These inconsistencies may include outcome measures of interest or the timepoints for the measurement of outcomes.

Supplement 3 – Sensitivity analysis restricted to recommended therapeutic doses of drugs

We performed a sensitivity analysis in which we restricted trial arms to only those that tested recommended therapeutic doses of drugs.

Drugs	Minimum dose
Amitriptyline	10 mg/day
Beta-blocker	Bisoprolol: 5 mg/day Propranolol: 40 mg/day
Calcium channel blocker	Flunarizine: 5 mg/day Cinnarizine: 15 mg/day
Carisbamate	100 mg/day
Eptinezumab	100 mg/month
Erenumab	70 mg/month
Fremanezumab	225 mg/month or 675 mg/3 months
Gabapentin	100 mg/day
Galcanezumab	120 mg/month
Gepant	Atogepant: 10 mg/day Rimegepant: 75 mg/day Telcagepant: 280 mg/day
Oxcarbazepine	300 mg/day
Topiramate	50 mg/day
Valproate	500 mg/day

Ducros A, de Gaalon S, Roos C, Donnet A, Giraud P, Guégan-Massardier E, Lantéri-Minet M, Lucas C, Mawet J, Moisset X, Valade D, Demarquay G. Revised guidelines of the French headache society for the diagnosis and management of migraine in adults. Part 2: Pharmacological treatment. Rev Neurol (Paris). 2021 Sep;177(7):734-752. doi: 10.1016/j.neurol.2021.07.006. Epub 2021 Jul 30. PMID: 34340810.

Supplement 4 – Table of trial characteristics

Study	Trial Name	Registration	Funding	Country	Age	% Male	Duration of Migraine (years)	% Aura	% With Previous Prophylaxis	Migraine/ Headache Days Per Month	Interventions
Ailani, 2021 (1)	ADVANCE	NCT03777059	Allergan	United States	41.6	11.2	NR	NR	70.3	7.4	Atogepant (10mg): 10 mg/day for 12 weeks, oral Atogepant (30mg): 30 mg/day for 12 weeks, oral Atogepant (60mg): 60 mg/day for 12 weeks, oral Placebo
Ashina, 2020 (2)	PROMISE-1	NCT02559895	H. Lundbeck A/S	United States	39.8	15.7	17.4	NR	NR	8.6	Eptinezumab (30mg): 30 mg, q12w, IV Eptinezumab (100mg): 100 mg, q12w, IV Eptinezumab (300mg): 300 mg, q12w, IV Placebo
Ashina, 2022 (3)	DELIVER	NCT04418765	H. Lundbeck A/S	Belgium, Bulgaria, Czechia, Denmark, Finland, France, Georgia, Germany, Hungary, Italy, Poland, Russia, Slovakia, Spain, Sweden, United Kingdom, United States	43.8	10.1	14.6	29.6	100.0	13.8	Eptinezumab (100mg): 100 mg, day 0 and week 12, IV Eptinezumab (300mg): 300 mg, day 0 and week 12, IV Placebo
Bigal, 2015 (4)	NR	NCT02025556	Teva Pharmaceuticals	United States	41.2	12.1	19.0	NR	29.0	11.4	Fremanezumab (225mg): 225 mg/day q28d for 12 weeks, SC Fremanezumab (675mg): 675mg q28d for 12 weeks, SC Placebo
Bigal, 2016 (5)	NR	NCT02021773	Teva Pharmaceuticals	United States	40.7	14.1	18.3	NR	40.3	16.8	Fremanezumab (675/225mg): 675 mg loading dose, 225 mg/day q28d for 12 weeks, SC Fremanezumab (900mg): 900 mg, q28d for 12 weeks, SC Placebo
Bostani, 2013 (6)	NR	IRCT201102055729N2	Kermanshah University of Medical Sciences	Iran	32.1	31.7	6.4	17.3	NR	6.8	Valproate: 200 mg/day for 12 weeks, oral Cinnarizine: 25 mg/day for 12 weeks, oral

Brandes, 2004 (7)	MIGR-002	NCT00231595	Johnson and Johnson Pharmaceutical Research and Development	Canada, United States	38.9	13.2	NR	NR	NR	6.5	Topiramate (50mg): 50 mg titrated over 8 weeks, maintained for 18 weeks, oral Topiramate (100mg): 100 mg titrated over 8 weeks, maintained for 18 weeks, oral Topiramate (200mg): 200 mg titrated over 8 weeks, maintained for 18 weeks, oral Placebo
Cady, 2009 (8)	NR	NCT00109083	Johnson and Johnson Pharmaceutical Research and Development	Germany, Spain, United States	41.3	14.6	19.2	46.8	NR	8.1	Carisbamate (100mg): 100 mg/day titrated over 2 weeks, maintained for 12 weeks, oral Carisbamate (300mg): 300 mg/day titrated over 2 weeks, maintained for 12 weeks, oral Carisbamate (600mg): 600 mg/day titrated over 2 weeks, maintained for 12 weeks, oral Placebo
Camporeale, 2018 (9)	NR	NCT02614287	Eli Lilly and Company	Belgium, Canada, France, Hungary, United States	42.0	17.4	20.8	NR	62.6	10.6	Galcanzumab (120mg): 120 mg/month for 52 weeks, SC Galcanzumab (240 mg): 240 mg/month for 52 weeks, SC
Chowdhury, 2021 (10)	TOP-PRO	CTRI/2019/05/018997	None	India	33.0	4.6	6.0	4.6	NR	17.4	Topiramate: 100 mg/day titrated over 4 weeks, maintained for 20 weeks, oral Propranolol: 80 mg/day titrated over 4 weeks, maintained for 20 weeks, oral
Couch, 1979 (11)	NR	NR	Merck Laboratories	United States	NR	16.0	NR	NR	NR	NR	Amitriptyline: 100 mg/day or MTD, titrated over 4 weeks, maintained for 4 weeks, oral Placebo
Couch, 2011 (12)	NR	NR	Merck, Sharp, and Dohme Research Laboratories	United States	34.9	19.0	NR	NR	NR	NR	Amitriptyline: 100 mg/day or MTD, titrated over 4 weeks, maintained for 12 weeks, oral Placebo
Croop, 2021 (13)	NR	NCT03732638	Biohaven Pharmaceuticals	United States	41.2	17.0	NR	40.0	NR	10.1	Rimegepant: 75 mg every other day for 12 weeks, oral Placebo
Detke, 2018 (14)	REGAIN	NCT02614261	Eli Lilly and Company	Argentina, Canada, Czech Republic, Germany, Israel, Italy, Mexico, Netherlands, Spain, Taiwan, United Kingdom, United States	41.0	15.0	21.1	54.3	77.8	19.5	Galcanzumab (120mg): 120 mg, q4w for 12 weeks, SC Galcanzumab (240mg): 240 mg, q4w for 12 weeks, SC Placebo

Diener, 1996 (15)	NR	NR	NR	NR	39.0	22.0	19.0	26.2	NR	4.0	Propranolol: 120 mg/day for 12 weeks, oral Placebo
Diener, 2002 (16)	NR	NR	Janssen	Belgium, Denmark, France, Germany, Italy, Portugal, Spain, Switzerland	37.0 *	18.6	10.0*	28.2	NR	NR	Flunarizine (5mg): 5 mg/day for 16 weeks, oral Flunarizine (10mg): 10 mg/day for 16 weeks (placebo administered on 2/7 days), oral Propranolol: 160 mg/day titrated over 1 weeks and maintained for 8 weeks, oral
Diener, 2004 (17)	MIGR-003	NCT00236561	Johnson & Johnson Pharmaceutical Research and Development	Australia, Denmark, Finland, France, Germany, Italy, Korea, Netherlands, South African, Spain, Sweden, Taiwan, United Kingdom	40.9	20.3	NR	NR	NR	6.1	Topiramate (100mg): 100 mg/day titrated over 8 weeks and maintained for 18 weeks, oral Topiramate (200mg): 200 mg/day titrated over 8 weeks and maintained for 18 weeks, oral Propranolol (160mg): 160 mg/day titrated over 8 weeks and maintained for 18 weeks, oral Placebo
Diener, 2007 (18)	PROMPT	NR	Janssen-Cilag EMEA	Austria, Belgium, Bulgaria, Czech Republic, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Norway, Poland, Portugal, Russia, Saudi Arabia, Slovenia, Spain, Switzerland, Turkey, UK	39.8	13.0	NR	NR	NR	8.9	Topiramate:100mg/day or MTD, titrated over 4 weeks and maintained for 12 weeks, oral Placebo
Dodick, 2007(19)	NR	NR	Ortho-McNeil Janssen	United States	38.2	14.7	9.2	NR	NR	17.1	Topiramate: 100 mg/day or MTD, titrated over 4 weeks maintained for 12 weeks, oral Placebo
Dodick, 2009 (20)	NR	NR	Ortho-McNeil Janssen	United States	38.8	15.1	NR	NR	NR	7.3	Topiramate: 100 mg/day or MTD, titrated over 4 weeks and maintained for 22 weeks, oral Amitriptyline: 100 mg/day or MTD titrated over 4 weeks and maintained for 22 weeks, oral
Dodick, 2014 (21)	NR	NCT01625988	Arteaus Therapeutics	United States	41.4	15.2	NR	41.5	NR	6.9	Galcanezumab: 150 mg, q2w for 12 weeks, SC Placebo
Dodick, 2014 (22)	NR	NCT01772524	Alder Biopharmaceuticals	United States	38.8	18.4	NR	NR	NR	8.6	Eptinezumab: 1000 mg once for 12 weeks, IV Placebo

Dodick, 2018 (23)	NR	NCT02629861	Teva Pharmaceuticals	Canada, Czech Republic, Finland, Israel, Japan, Poland, Russia, Spain, United States	41.8	15.2	20.2	NR	20.8	9.1	Fremanezumab (225mg): 225 mg, q4w for 12 weeks, SC Fremanezumab (675mg): 675 mg once for 12 weeks, SC Placebo
Dodick, 2018 (24)	ARISE	NCT02483585	Amgen	Denmark, France, Greece, Portugal, Russia, Spain, Switzerland, United States	42.0	14.7	21.0	50.3	46.1	8.3	Erenumab: 70 mg, q4w for 12 weeks, SC Placebo
Dodick, 2019 (25)	NR	NCT02275117	Alder Biopharmaceuticals	Australia, Georgia, New Zealand, United States	36.6	13.2	17.9	NR	45.6	16.5	Eptinezumab (10mg): 10 mg, once for 12 weeks, IV Eptinezumab (30mg): 30 mg, once for 12 weeks, IV Eptinezumab (100mg): 100 mg, once for 12 weeks, IV Eptinezumab (300mg): 300 mg, once for 12 weeks, IV Placebo
Ferrari, 2019 (26)	FOCUS	NCT03308968	Teva Pharmaceuticals	Belgium, Czechia, Denmark, Finland, France, Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, United Kingdom, United States	46.2	16.5	24.9	NR	100.0	14.2	Fremanezumab (monthly): 225 mg q4w, SC Fremanezumab (quarterly): 675 mg once, SC Placebo
Freitag, 2002 (27)	NR	NR	Abbott Laboratories	United States	40.5	21.1	20.2	36.3	20.6	4.3	Valproate: 500-1000 mg/day, for 12 weeks, oral Placebo
Ghasami, 2009 (28)	NR	NR	Arak University of Medical Sciences	Iran	NR	31.8	NR	NR	NR	NR	Valproate (15 mg/kg): 1-3 pills/day for 24 weeks, oral Propranolol/antidepressant: 40-80mg/day propranolol with 50mg amitriptyline or 25-50mg/day nortriptyline
Ghobadi, 2013 (29)	NR	NR	NR	NR	47.0	16.7	NR	NR	NR	15.0	Propranolol: 40 mg/day for 24 weeks, oral Nimodipine: 30 mg/day for 24 weeks, oral
Goadsby, 2017 (30)	STRIVE	NR	Novartis, Amgen	United States	40.5	21.1	20.2	36.3	20.6	4.3	Erenumab (70mg): 70 mg, q4w for 24 weeks, SC Erenumab (140mg): 140 mg, q4w for 24 weeks, SC Placebo
Goadsby, 2020 (31)	NR	NCT02638103	Teva Pharmaceuticals	Canada, Czechia, Finland, Israel, Japan, Poland, Russian Confederation, Spain, United States	43.5	13.0	21.6	NR	23.9	13.4	Fremanezumab (q12w): 675mg q12w for 52 weeks, SC Fremanezumab (675/225 q4w chronic): 675 mg loading dose, 225 q4w for 52 weeks, SC Fremanezumab (225mg q4w episodic): 225 mg q4w for 52 weeks, SC
Goadsby, 2020 (32)	NR	NCT02848326	Allergan	United States	40.1	13.5	19.4	22.3	28.1	7.7	Atogepant (10mg): 10 mg/day for 12 weeks, oral Atogepant (30mg): 30 mg/day for 12 weeks, oral Atogepant (60mg): 60 mg/day for 12 weeks, oral Atogepant (30mg B.I.D): 30mg twice/day for 12 weeks, oral Atogepant (60mg B.I.D): 60 mg twice/day for 12

												weeks, oral Placebo
Goncalves, 2016(33)	NR	NCT01357031	Fundação de Amparo a Pesquisa de São Paulo	Brazil	36.9	24.6	22.2	16.1	NR	7.3	Amitriptyline: 25 mg/day for 12 weeks Placebo	
Hesami, 2017(34)	NR	IRCT2012070310178N1	NR	Iran	36.0	10.2	NR	NR	NR	10.3	Pregabalin (100mg): 100mg/day for 12 weeks, oral Valproate (400mg): 400 mg/day for 12 weeks, oral	
Ho, 2014(35)	NR	NCT00797667	Merck & Co.	United States	41.3	16.0	NR	46.6	29.1	8.2	Telcagepant (280 mg): 280mg/day for 12 weeks, oral Telcagepant (560 mg): 560mg/day for 12 weeks, oral Placebo	
Holroyd, 2010 (36)	NR	NCT00910689	National Institutes of Health	United States	38.2	21.0	15.0	22.0	NR	8.5	Propranolol: 180 mg titrated over 12 weeks or MTD, offered nadolol if propranolol was not tolerated, maintained for 12 weeks, oral Placebo	
Hu, 2022 (37)	PERSIST	NCT03963232	Eli Lilly and Company	China, India, Russia	37.0	26.2	12.6	NR	44.6	6.3	Galcanezumab: 240 mg loading dose, 120 mg q4w for 12 weeks, SC Placebo	
Kalita, 2013 (38)	NR	NR	NR	India	31.9	19.7	7.3	6.3	NR	10.8	Valproate: 500-1000mg/day or MTD for 22 weeks, oral Amitriptyline: 25-50mg/day or MTD for 22 weeks, oral	
Klapper, 1997 (39)	NR	NR	Abbott Laboratories	United States	40.8	11.0	21.6	40.3	53.0	NR	Valproate (500mg): 500 mg/day, titrated over 4 weeks, maintained for 8 weeks, oral Valproate (1000mg): 1000 mg/day, titrated over 4 weeks, maintained for 8 weeks, oral Valproate (1500mg): 1500 mg/day, titrated over 4 weeks, maintained for 8 weeks, oral Placebo	
Lipton, 2011 (40)	INTREPID	NCT00212810	Ortho-Mcneil Janssen	NR	40.3	10.9	NR	NR	NR	11.7	Topiramate: 100 mg/day titrated over 6 weeks, maintained for 20 weeks, oral Placebo	

Lipton, 2020 (41)	PROMISE-2	NCT02974153	H. Lundbeck A/S	Belgium, Czechia, Denmark, Georgia, Germany, Hungary, Italy, Russia, Slovakia, Ukraine, United Kingdom, United States	40.5	11.8	18.1	NR	NR	16.1	Eptinezumab (100mg): 100 mg, day 0 and week 12, IV Eptinezumab (300mg): 300 mg, day 0 and week 12, IV Placebo
Lucking, 1988 (42)	Trial 1	NR	NR	NR	42.1	19.5	NR	NR	NR	NR	Flunarizine: 10 mg/day for 16 weeks, oral Propranolol: 120mg/day titrated over 2 weeks, maintained for 14 weeks, oral
Lucking, 1988 (42)	Trial 2	NR	NR	NR	42.1	19.5	NR	NR	NR	NR	Flunarizine: 10 mg/day for 16 weeks, oral Propranolol: 120mg/day titrated over 2 weeks, maintained for 14 weeks, oral
Luo, 2012 (43)	NR	NR	National Natural Science Foundation of China	China	43.0	28.6	4.5	NR	NR	4.5	Flunarizine (5mg): 5 mg/day for 52 weeks, oral Topiramate: 100mg/day or MTD for 52 weeks Flunarizine and Topiramate: 5 mg/day of flunarizine with 25-100 mg/day of topiramate for 52 weeks
Mansoureh, 2008 (44)	NR	NR	NR	NR	34.1	19.2	NR	NR	NR	7.2	Cinnarizine: 75 mg/day for 12 weeks, oral Valproate: 600 mg/day for 12 weeks, oral
Mathew, 1981 (45)	NR	NR	NR	NR	34.0	9.5	NR	NR	NR	NR	Propranolol: 160mg/day or MTD for 28 weeks, oral Amitriptyline: 50-75mg or MTD for 28 weeks, oral
Mathew, 1995 (46)	NR	NR	Abbott Laboratories	United States	45.6	22.4	25.0	27.0	NR	6.1	Valproate: 750 mg/day titrated over 4 weeks, maintained for 8 weeks, oral Placebo
Mathew, 2001 (47)	NR	NR	NR	NR	39.6	17.2	20.8	43.7	NR	4.9	Gabapentin: 2400 mg/day titrated over 4 weeks, maintained for 8, oral Placebo
Mei 2004 (48)	NR	NR	NR	Italy	39.2	45.8	NR	19.4	NR	5.5	Topiramate: 100mg/day titrated over 4 weeks maintained for 12, oral Placebo
Misra, 2013 (49)	NR	NR	NR	NR	32.0 *	22.8	5.0*	4.0	NR	6.1	Valproate: 500-750 mg/day for 24 weeks, oral Amitriptyline: 25-50 mg/day for 24 weeks, oral
Mulleners, 2020 (50)	CONQUER	NR	Eli Lilly and Company	Belgium, Canada, Czechia, France, Germany, Hungary, Japan, Korea Republic, Netherlands, Spain, United Kingdom, United States	45.8	14.1	23.3	44.2	100.0	13.2	Galcanzumab: 240 mg loading dose, 120 mg q4w for 12 weeks, SC Placebo
Reuter, 2018 (51)	LIBERTY	NCT03096834	Novartis	Australia, Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Norway,	44.4	18.7	NR	35.4	100.0	9.3	Erenumab: 70 mg q4w for 12 weeks, SC Placebo

				Netherlands, Spain, Sweden, Switzerland, United Kingdom							
Reuter, 2022 (52)	HER-MES	NCT03828539	Novartis	Germany	40.7	14.2	21.9	34.27	40.7	10.4	Erenumab: 140mg q4w for 24 weeks, SC Topiramate: 50–100 mg/day for 24 weeks, oral
Sakai, 2019 (53)	NR	NCT02630459	Amgen, Novartis	Japan	NR	15.8	NR	26.1	66.3	7.8	Erenumab (28mg): 28 mg, q4w for 24 weeks, SC Erenumab (70mg): 70 mg, q4w for 24 weeks, SC Erenumab (140mg): 140 mg, q4w for 24 weeks, SC Placebo
Sakai, 2020 (54)	NR	NCT02959177	Eli Lilly and Company	Japan	44.1	15.7	21.4	NR	60.6	8.7	Galcanezumab (120mg): 120 mg, q4w for 24 weeks, SC Galcanezumab (240mg): 240 mg, q4w for 24 weeks, SC Placebo
Sakai, 2021 (55)	NR	NCT03303079	Otsuka Pharmaceutical	Japan, Korea	42.8	13.7	18.7	NR	21.0	15.7	Fremanezumab (monthly) 675mg loading dose, 225mg q4w for 12 weeks, SC Fremanezumab (quarterly): 675mg once for 12 weeks, SC Placebo
Sakai, 2021 (56)	NR	NCT03303092	Otsuka Pharmaceutical	Japan, Korea	43.5	15.4	19.9	NR	19.3	8.8	Fremanezumab (monthly): 225 mg q4w, SC Fremanezumab (quarterly): 3 doses of 225 mg at baseline, SC Placebo
Sargent, 1985 (57)	NR	NR	NR	NR	30.0	21.0	20.0	NR	NR	NR	Propranolol: 120mg/day for 12 weeks Valproate: 1100mg/day for 12 weeks Placebo

Silberstein, 2004 (58)	NR	NR	Johnson & Johnson Pharmaceutical Research and Development	NR	40.4	11.3	NR	NR	NR	6.5	Topiramate (50mg): 50 mg/day titrated over 8 weeks, maintained for 18 weeks, oral Topiramate (100mg): 100 mg/day, titrated over 8 weeks, maintained for 18 weeks, oral Topiramate (200mg): 200 mg/day titrated over 8 weeks, maintained for 18 weeks, oral Placebo
Silberstein, 2006 (59)	NR	NR	Ortho-Mcneil Neurologics	United States	40.5	14.2	NR	35.6	NR	4.9	Topiramate: 200 mg/day, titrated over 8 weeks, maintained for 12 weeks, oral Placebo
Silberstein, 2008 (60)	NR	NR	Novartis	United States	40.5	15.3	NR	NR	NR	NR	Oxcarbazepine: 1200 mg/day titrated over 6 weeks, maintained for 8 weeks, oral Placebo
Silberstein, 2009 (61)	NR	NCT00210912	Ortho-McNeil Janssen	United States	38.2	NR	NR	NR	NR	NR	Topiramate: 100 mg/day titrated over 4 weeks, maintained for 12 weeks, oral Placebo
Silberstein, 2012 (62)	NR	NCT00772031	National Institute of Neurological Disorders and Stroke	United States	42.0 *	10.0	NR	NR	NR	18.0	Propranolol: total dose of 240 mg/day for 6 months, oral Placebo
Silberstein, 2013 (63)	NR	NCT00742209	GlaxoSmithKline	Canada, United States	39.2	18.0	NR	NR	NR	9.2	Gabapentin (1200mg): 1200 mg/day for 20 weeks, oral Gabapentin (1800mg): 1800 mg/day for 20 weeks, oral Gabapentin (2400mg): 2400 mg/day for 20 weeks, oral Gabapentin (3000mg): 3000 mg/day for 20 weeks, oral Placebo
Silberstein, 2017 (64)	NR	NCT02621931	Teva Pharmaceuticals	Canada, Czechia, Finland, Israel, Poland, Russia, Spain, United States,	40.7	12.3	19.9	NR	21.2	16.2	Fremanezumab (quarterly): 675 mg q8w for 12 weeks, SC Fremanezumab (monthly): 675 mg loading dose, 225 q4w for 12 weeks, SC Placebo
Skljarevski, 2018 (65)	EVOLVE-2	NCT02614196	Eli Lilly and Company	Argentina, Czechia, Germany, Israel, Korea, Mexico, Netherlands, Spain, Taiwan, United Kingdom, United States	41.9	14.6	20.6	NR	66.2	9.1	Galcanezumab (120mg): 120 mg q4w 24 weeks, SC Galcanezumab (240mg): 240 mg, q4w for 24 weeks, SC Placebo

Skljarevski, 2018 (66)	NR	NCT02163993	Eli Lilly and Company	United States	40.2	17.1	NR	NR	NR	6.7	Galcanezumab (5mg): 5 mg, q4w for 12 weeks, SC Galcanezumab (50mg): 50 mg, q4w for 12 weeks SC Galcanezumab (120mg): 120 mg, q4w for 12 weeks, SC Galcanezumab (300mg): 300 mg, q4w for 12 weeks, SC Placebo
Sorensen, 1991 (67)	NR	NR	Janssen Pharmaceuticals	Denmark	42.0	20.8	17.0*	26.2	54.4	NR	Flunarizine: 10 mg/day for 16 weeks, oral Metoprolol: 200 mg/day for 16 weeks, oral
Sudilovsky, 1987(68)	NR	NR	NR	United States	39.3	24.5	20.7	NR	NR	5.3	Nadalol (80mg): 80 mg/day for 12 weeks, oral Nadolol (160mg): 160 mg/day for 12 weeks, oral Propranolol: 160 mg/day for 12 weeks, oral
Sun, 2016 (69)	NR	NCT01952574	Amgen	Canada, United States, Denmark, Finland, Germany, Norway, Sweden, Portugal	41.1	19.5	20.4	NR	57.6	8.7	Erenumab (7mg): 7 mg, q4w for 12 weeks, SC Erenumab (21mg): 21 mg, q4w for 12 weeks, SC Erenumab (70mg): 70 mg, q4w for 12 weeks, SC Placebo
Takeshima, 2021 (70)	NR	NCT03812224	Amgen	Japan	44.4	13.0	NR	NR	77.4	12.1	Erenumab: 70 mg q4w for 24 weeks, SC Placebo
Tepper, 2017 (71)	NR	NCT02066415	Amgen	Canada, Czech Republic, Denmark, Finland, Germany, Norway, Poland, Sweden, UK, United States	42.1	17.2	21.7	41.4	NR	18	Erenumab (70mg): 70mg q4w for 12 weeks, SC Erenumab (140mg): 140mg q4w for 12 weeks, SC Placebo
van de Ven, 1997 (72)	NR	NR	Merck KGaA	Belgium, France, The Netherlands, Spain	38.7	17.7	NR	22.6	NR	5.5	Bisoprolol (5mg): 5 mg/day for 12 weeks, oral Bisoprolol (10mg): 10 mg/day for 12 weeks, oral Placebo
Wang, 2021 (73)	EMPOWER	NCT03333109	Novartis	NR	37.5	18.1	11.7	69.9	53.2	9.3	Erenumab (70mg): 70 mg, q4w for 12 weeks, SC Erenumab (140mg): 140 mg, q4w for 12 weeks, SC Placebo

Supplement 5 – Risk of bias judgements for mean monthly migraine days

Trial	Randomization	Deviations from the intended intervention	Missing outcome data	Measurement of outcome	Selection of the reported results
Ailani 2021	●	●	●	●	●
Ashina 2020	●	●	●	●	●
Ashina 2022	●	●	●	●	●
Bigal 2015	●	●	●	●	●
Bigal 2015	●	●	●	●	●
Bostani 2013	●	●	●	●	●
Brandes 2004	●	●	●	●	●
Camporeale 2018	●	●	●	●	●
Chowdhury 2021	●	●	●	●	●
Croop 2021	●	●	●	●	●
Detke 2018	●	●	●	●	●
Diener 2002	●	●	●	●	●
Diener 2004	●	●	●	●	●
Diener 2007	●	●	●	●	●
Dodick 2009	●	●	●	●	●
Dodick 2014 (galcanezumab)	●	●	●	●	●
Dodick 2014 (eptinezumab)	●	●	●	●	●
Dodick 2018	●	●	●	●	●
Dodick 2018	●	●	●	●	●
Dodick 2019	●	●	●	●	●
Ferrari 2019	●	●	●	●	●
Freitag 2002	●	●	●	●	●
Ghobadi 2013	●	●	●	●	●
Goadsby 2020 (atogepant)	●	●	●	●	●
Goadsby 2020 (fremanezumab)	●	●	●	●	●
Goasby 2017	●	●	●	●	●
Goncalves 2016	●	●	●	●	●
Hesami 2018	●	●	●	●	●
Ho 2014	●	●	●	●	●
Holroyd 2010	●	●	●	●	●
Hu 2022	●	●	●	●	●
Lipton 2011	●	●	●	●	●
Lipton 2020	●	●	●	●	●
Lucking 1988	●	●	●	●	●
Luo 2012	●	●	●	●	●
Mansoureh 2008	●	●	●	●	●
Mathew 1995	●	●	●	●	●
Mathew 2001	●	●	●	●	●
Mulleners 2020	●	●	●	●	●
Reuter 2018	●	●	●	●	●
Reuter 2022	●	●	●	●	●
Sakai 2019	●	●	●	●	●
Sakai 2020	●	●	●	●	●
Sakai 2021 (episodic)	●	●	●	●	●
Sakai 2021 (chronic)	●	●	●	●	●
Sargent 1985	●	●	●	●	●
Silberstein 2004	●	●	●	●	●
Silberstein 2006	●	●	●	●	●
Silberstein 2008	●	●	●	●	●
Silberstein 2009	●	●	●	●	●
Silberstein 2012	●	●	●	●	●
Silberstein 2013	●	●	●	●	●
Silberstein 2017	●	●	●	●	●
Skjjaevski 2018 (EVOLVE-2)	●	●	●	●	●
Skjjaevski 2018	●	●	●	●	●
Sorensen 1991	●	●	●	●	●
Sun 2016	●	●	●	●	●
Takeshima 2021	●	●	●	●	●
Tepper 2017	●	●	●	●	●
van de Ven 1997	●	●	●	●	●
Wang 2021	●	●	●	●	●

Low risk of bias ●
 Probably low risk of bias ●
 Probably high risk of bias ●
 High risk of bias ●

Supplement 6 – Risk of bias judgements for adverse events leading to discontinuation

Trial	Randomization	Deviations from the intended intervention	Missing outcome data	Measurement of outcome	Selection of the reported results
Ailani 2021	●	●	●	●	●
Ashina 2020	●	●	●	●	●
Ashina 2022	●	●	●	●	●
Bigal 2015	●	●	●	●	●
Bigal 2015	●	●	●	●	●
Bostani 2013	●	●	●	●	●
Brandes 2004	●	●	●	●	●
Cady 2009	●	●	●	●	●
Camporeale 2018	●	●	●	●	●
Chowdhury 2021	●	●	●	●	●
Couch 1979	●	●	●	●	●
Couch 2011	●	●	●	●	●
Croop 2021	●	●	●	●	●
Detke 2018	●	●	●	●	●
Diener 1996	●	●	●	●	●
Diener 2002	●	●	●	●	●
Diener 2004	●	●	●	●	●
Diener 2007	●	●	●	●	●
Dodick 2009	●	●	●	●	●
Dodick 2014 (galcanezumab)	●	●	●	●	●
Dodick 2014 (eptinezumab)	●	●	●	●	●
Dodick 2018 (fremanezumab)	●	●	●	●	●
Dodick 2018 (erenumab)	●	●	●	●	●
Dodick 2019	●	●	●	●	●
Ferrari 2019	●	●	●	●	●
Freitag 2002	●	●	●	●	●
Ghobadi 2013	●	●	●	●	●
Goadsby 2020	●	●	●	●	●
Goadsby 2020	●	●	●	●	●
Goadsby 2017	●	●	●	●	●
Ho 2014	●	●	●	●	●
Holroyd 2010	●	●	●	●	●
Hu 2022	●	●	●	●	●
Kalita 2013	●	●	●	●	●
Klapper 1997	●	●	●	●	●
Lipton 2011	●	●	●	●	●
Lipton 2020	●	●	●	●	●
Lucking 1988	●	●	●	●	●
Luo 2012	●	●	●	●	●
Mansoureh 2008	●	●	●	●	●
Mathew 1981	●	●	●	●	●
Mathew 1995	●	●	●	●	●
Mathew 2001	●	●	●	●	●
Mei 2004	●	●	●	●	●
Misra 2013	●	●	●	●	●
Mulleners 2020	●	●	●	●	●
Reuter 2018	●	●	●	●	●
Reuter 2022	●	●	●	●	●
Sakai 2019	●	●	●	●	●
Sakai 2020	●	●	●	●	●
Sakai 2021 (chronic)	●	●	●	●	●
Sakai 2021 (episodic)	●	●	●	●	●
Sargent 1985	●	●	●	●	●
Silberstein 2004	●	●	●	●	●
Silberstein 2006	●	●	●	●	●
Silberstein 2008	●	●	●	●	●
Silberstein 2009	●	●	●	●	●
Silberstein 2013	●	●	●	●	●
Silberstein 2017	●	●	●	●	●
Skjarevski 2018	●	●	●	●	●
Skjarevski 2018 (EVOLVE-2)	●	●	●	●	●
Sorensen 1991	●	●	●	●	●
Sudilovsky 1987	●	●	●	●	●
Sun 2016	●	●	●	●	●
Takeshima 2021	●	●	●	●	●
Tepper 2017	●	●	●	●	●
van de Ven 1997	●	●	●	●	●
Wang 2021	●	●	●	●	●

Low risk of bias ●
 Probably low risk of bias ●
 Probably high risk of bias ●
 High risk of bias ●

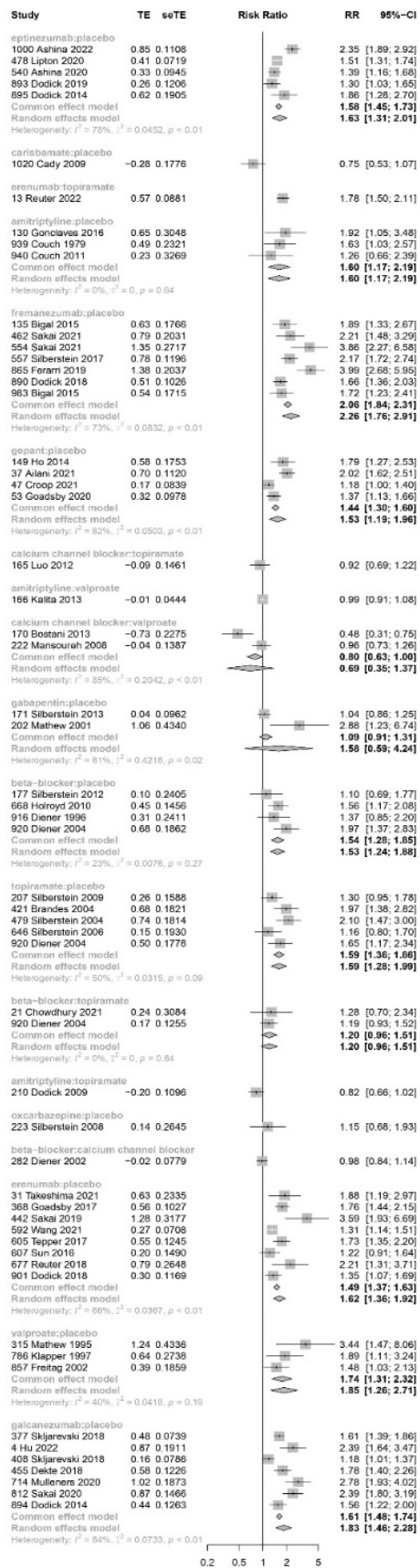
Supplement 7 – Comparisons and GRADE ratings for network meta-analysis of 50% or more reduction in monthly migraine days

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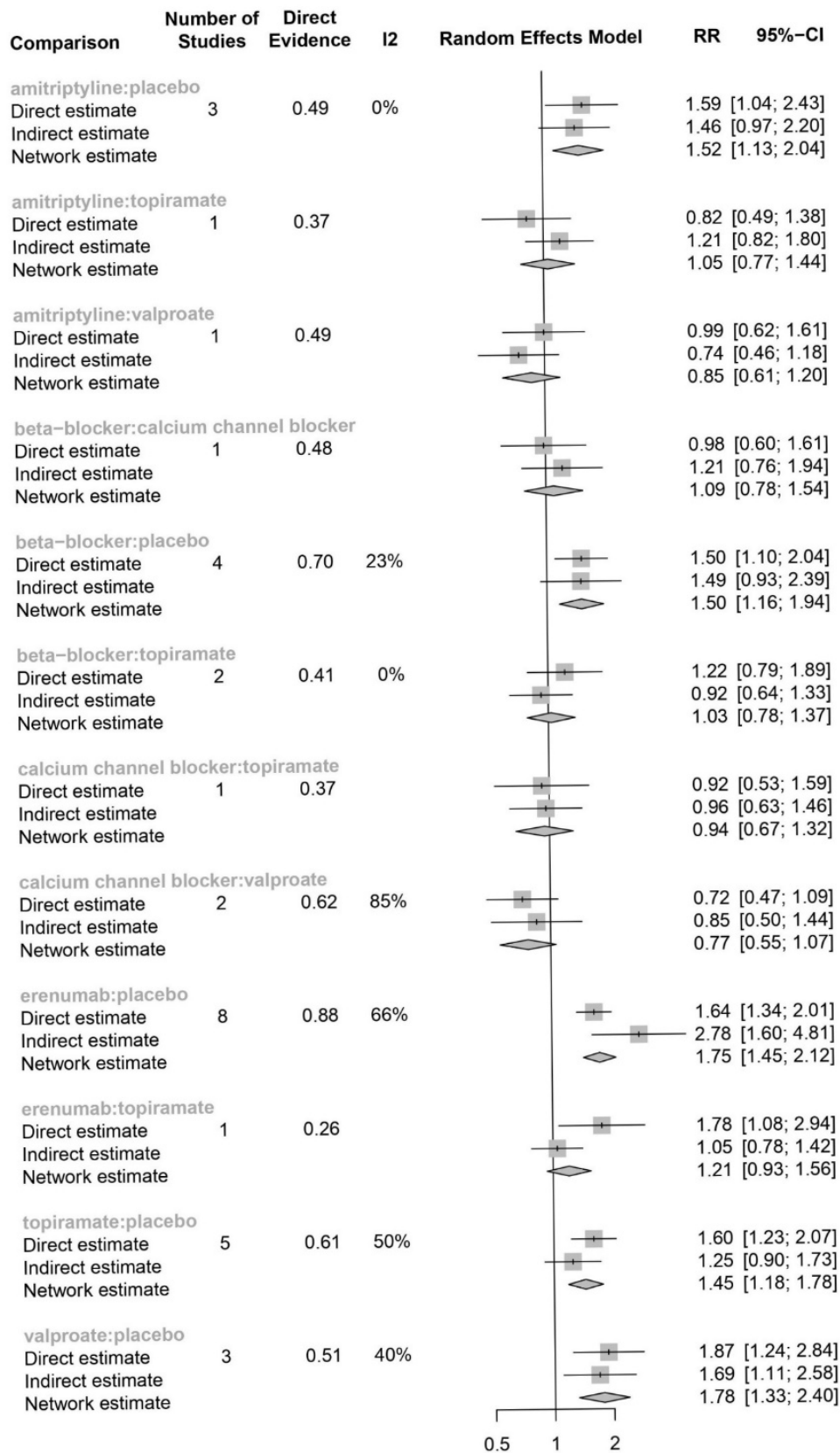
gabapentin	placebo	1.291479165	0.823209499	2.026116601	80.1567703	-48.6173877	282.1820653	Serious	No concerns	No concerns	Not assessed	Moderate	Serious	Low							1.291479165	0.823209499	2.026116601	80.1567703	-48.6173877	282.1820653	Moderate	Serious	Low
gabapentin	topiramate																				0.891300683	0.540409464	1.461912168	43.3134398	181.937727	184.0582386	Moderate	Serious	Low
gabapentin	valproate																				0.724868305	0.422890952	1.243489164	134.808779	282.761104	118.8671828	Moderate	Serious	Low
galcanezumab	oxcarbazepine																				1.579797905	0.760942234	3.273610873	182.6909401	75.7917684	719.0294385	High	Serious	Moderate
galcanezumab	placebo	1.814928509	1.479876729	2.224366311	223.9409401	131.9661004	336.7007356	No concerns	No concerns	No concerns	Not assessed	High	No concerns	High							1.814928509	1.479876729	2.224366311	223.9409401	131.9661004	336.7007356	High	No concerns	High
galcanezumab	topiramate																				1.352139627	0.9137800134	1.671841992	100.47013	-34.7847935	267.7090198	High	Serious	Low
galcanezumab	valproate																				1.018327592	0.710951014	1.458597098	8.9797971	-141.6223598	224.6944883	Moderate	Serious	Low
oxcarbazepine	placebo	1.15	0.570545114	2.31795868	41.25	118.100094	362.4386371	No concerns	No concerns	No concerns	Not assessed	High	Serious	Moderate							1.15	0.570545114	2.31795868	41.25	118.100094	362.4386371	High	Serious	Moderate
oxcarbazepine	topiramate																				0.793860334	0.382356354	1.647407502	-82.2202101	-246.112594	257.9726034	High	Serious	Moderate
oxcarbazepine	valproate																				0.645460139	0.301605059	1.381338889	-171.710543	-342.185985	186.8408993	Moderate	Serious	Low
topiramate	placebo	1.395573127	1.227009551	2.074844183	163.7826101	62.42762654	295.5821449	No concerns	No concerns	No concerns	Not assessed	High	No concerns	High	1.246644931	0.897923731	1.73079887	High			1.448882542	1.180349381	1.778753442	123.4702101	46.59867986	214.1571985	High	No concerns	High
topiramate	valproate																				0.812260999	0.586439010	1.127837796	91.4903329	202.628563	62.63547595	Moderate	Serious	Low
valproate	placebo	1.874103043	1.238030311	2.835601898	240.3783367	65.6233356	504.7904671	Serious	No concerns	No concerns	Not assessed	Moderate	No concerns	Moderate	1.690051854	1.106997569	2.580200129	Moderate			1.781674702	1.325246878	2.395300677	214.960543	89.44289139	383.7076861	Moderate	No concerns	Moderate

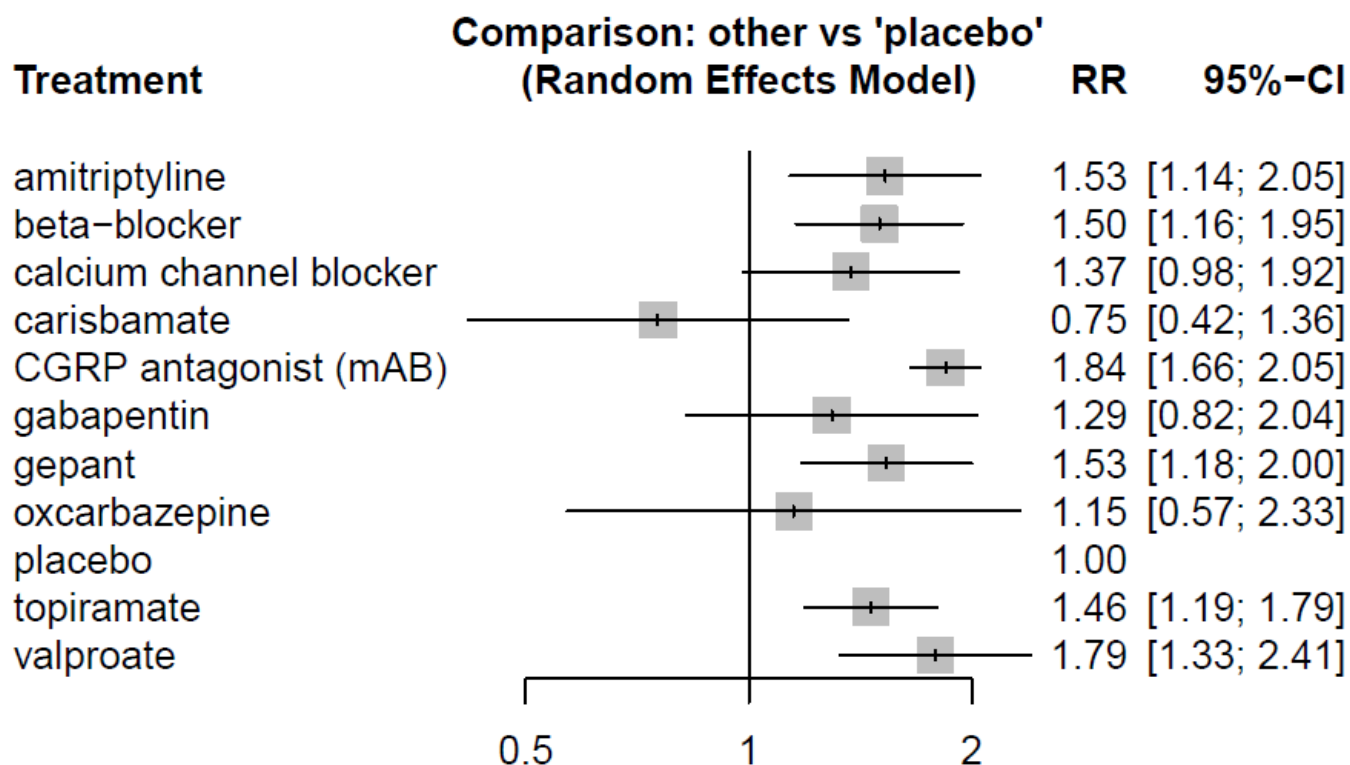
Full table also available at: <https://osf.io/g3u26>

Supplement 8 – Pairwise meta-analyses for 50% or more reduction in monthly migraine days

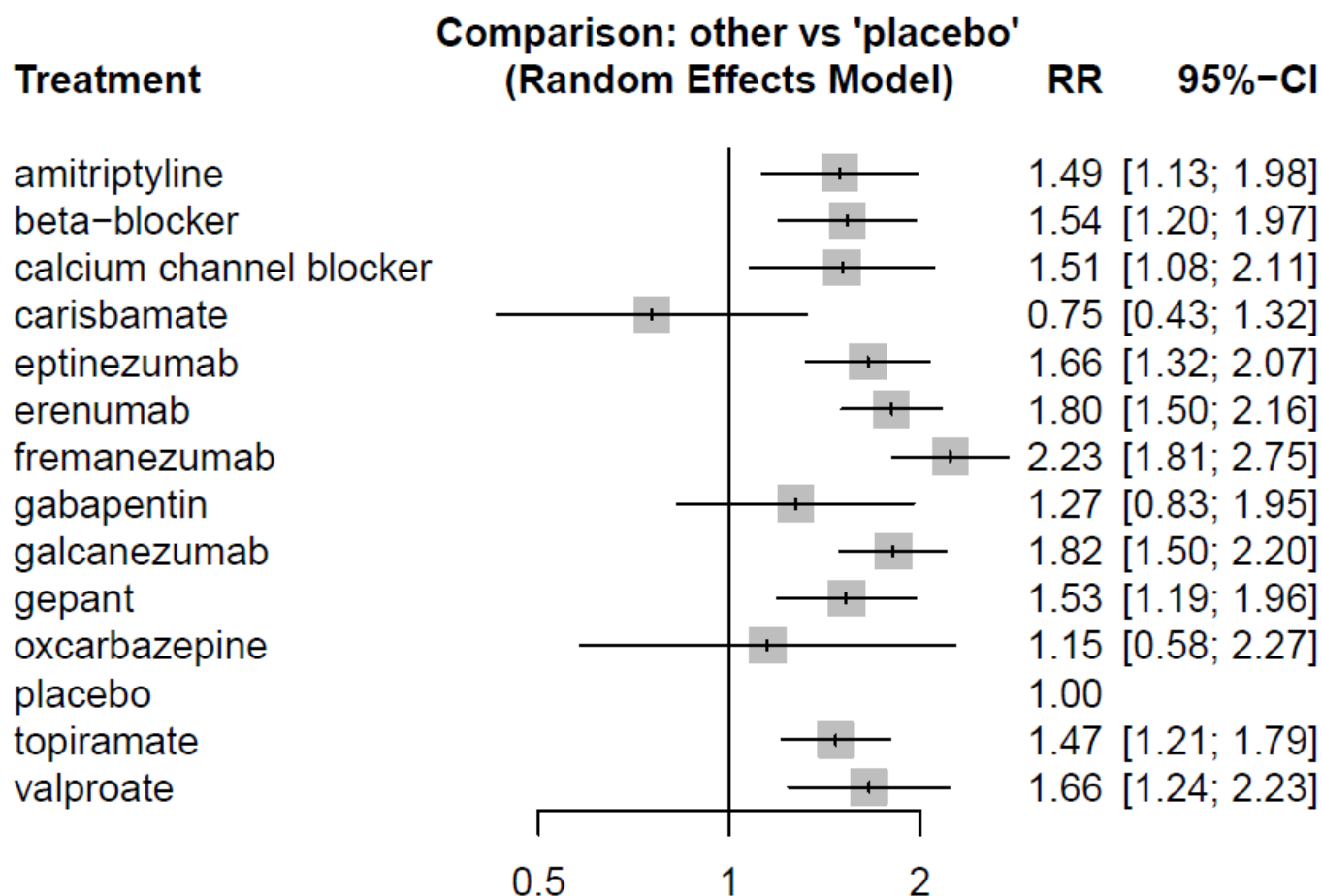


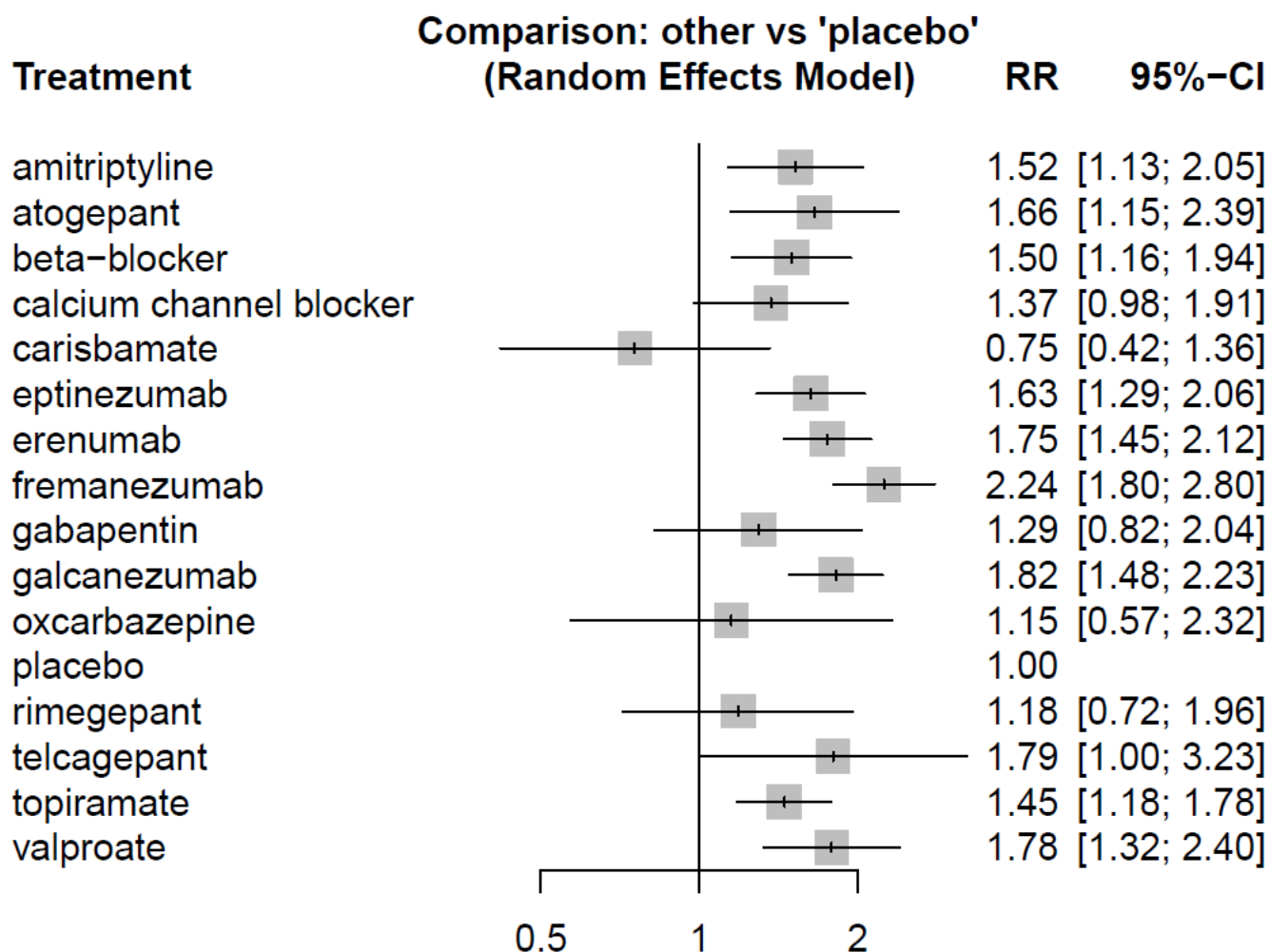
Supplement 9 – Node split plots for 50% or more reduction in monthly migraine days



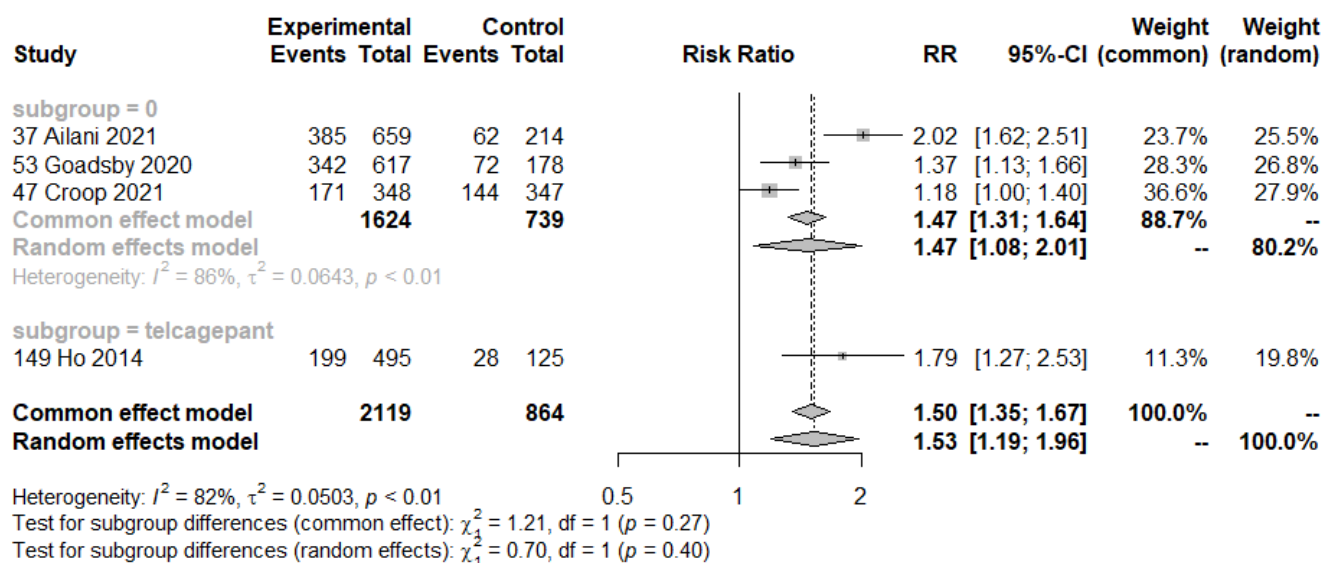


Supplement 11 – Secondary analysis for 50% or more reduction in monthly migraine days (restricted trials to those that investigated recommended therapeutic doses of drugs)





Supplement 13 – Secondary analysis comparing the effects of telcagepant with other gepants



Supplement 14 – Subgroup analyses for 50% or more reduction in monthly migraine days

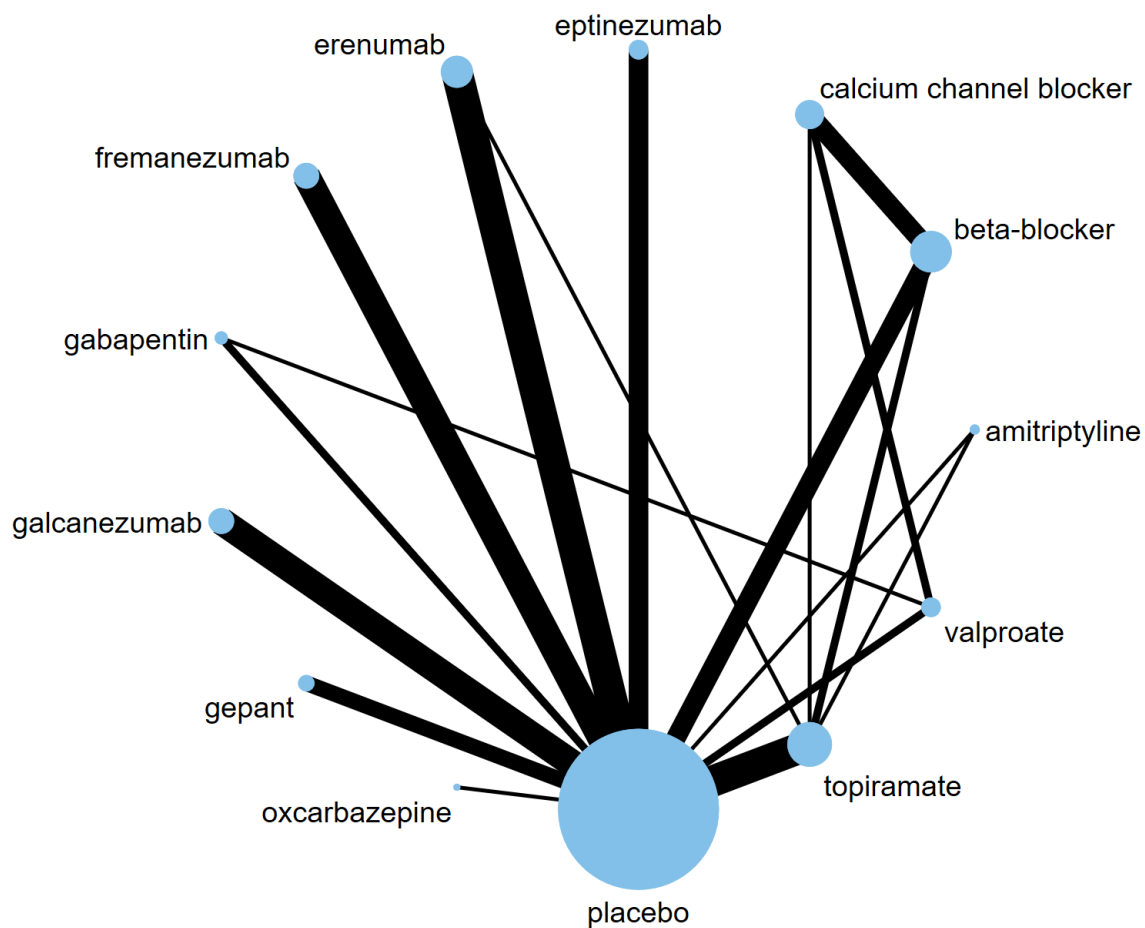
For subgroup analyses based on baseline monthly migraine days and proportion of patients that had previously used prophylactic drugs, for each comparison against placebo, we calculated the median monthly migraine days and median proportion of patients who had previously used prophylactic drugs across trials, and performed subgroup analyses comparing trials with mean baseline monthly migraine days or proportion of patients who had previously used prophylactic drugs above or equal to/below the median.

DRUG	RISK OF BIAS					
	Low			High		
	Number of trials (participants)	RR (95% CI)	I ² (%)	Number of trials (participants)	RR (95% CI)	I ² (%)
AMITRIPTYLINE	NA			3 (389)	1.60 (1.17, 2.19)	0
BETA-BLOCKER	1 (286)	1.97 (1.37, 2.83)	NA	2 (299)	1.23 (0.88, 1.72)	0
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	4 (3416)	1.59 (1.24, 2.05)	83	1 (143)	1.86 (1.28, 2.70)	NA
ERENUMAB	8 (4467)	1.62 (1.36, 1.92)	66	NA		
FREMANEZUMAB	6 (3973)	2.38 (1.79, 3.16)	76	1 (261)	1.72 (1.23, 2.41)	NA
GABAPENTIN	1 (474)	1.04 (0.86, 1.25)	NA	1 (87)	2.88 (1.23, 6.74)	NA
GALCANEZUMAB	7 (4043)	1.83 (1.46, 2.28)		NA		
GEPANT	3 (2363)	1.47 (1.08, 2.01)	86	1 (625)	1.79 (1.27, 2.53)	NA
TOPIRAMATE	3 (1361)	1.9 (1.55, 2.32)	0	2 (539)	1.24 (0.98, 1.58)	0
VALPROATE	1 (234)	1.48 (1.03, 2.13)	0	2 (276)	2.32 (1.33, 4.05)	26
Monthly migraine days						
	≤ median			> median		
	Number of trials (participants)	RR (95% CI)	I ² (%)	Number of trials (participants)	RR (95% CI)	I ² (%)
AMITRIPTYLINE	1 (118)	1.92 (1.05, 3.48)	28.1	NA		
BETA-BLOCKER	2 (419)	1.7 (1.19, 2.41)	30	1 (166)	1.1 (0.69, 1.77)	NA
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	3 (1899)	1.81 (1.31, 2.51)	85	2 (1660)	1.45 (1.27, 1.65)	12
ERENUMAB	4 (2429)	1.67 (1.15, 2.44)	76	4 (2038)	1.62 (1.29, 2.05)	61
FREMANEZUMAB	4 (2287)	2.55 (1.61, 4.03)	85	3 (1947)	2.05 (1.72, 2.43)	0
GABAPENTIN	1 (87)	2.88 (1.23, 6.74)	NA	1 (474)	1.04 (0.86, 1.25)	NA
GALCANEZUMAB	4 (1581)	1.76 (1.24, 2.49)	88	3 (2462)	1.92 (1.43, 2.59)	73
GEPANT	2 (1668)	1.66 (1.13, 2.42)	85	2 (1315)	1.42 (0.95, 2.12)	78

TOPIRAMATE	2 (636)	1.4 (0.99, 1.97)	44	2 (936)	2.04 (1.58, 2.62)	0
VALPROATE	1 (234)	1.48 (1.03, 2.13)	NA	1 (105)	3.44 (1.47, 8.06)	NA
Previous prophylactic drugs						
	≤ median			> median		
	Number of trials (participants)	RR (95% CI)	I² (%)	Number of trials (participants)	RR (95% CI)	I² (%)
AMITRIPTYLINE	NA			NA		
BETA-BLOCKER	NA			NA		
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	1 (588)	1.3 (1.03, 1.65)	NA	1 (868)	2.35 (1.89, 2.92)	NA
ERENUMAB	4 (3050)	1.5 (1.28, 1.76)	62	4 (1417)	1.96 (1.26, 3.03)	74
FREMANEZUMAB	4 (2840)	2.21 (1.64, 2.97)	70	3 (1394)	2.33 (1.39, 3.89)	82
GABAPENTIN	NA			NA		
GALCANEZUMAB	3 (1892)	2.02 (1.52, 2.7)	76	2 (1547)	2.17 (1.4, 3.37)	75
GEPANT	2 (1415)	1.51 (1.17, 1.94)	45	1 (873)	2.02 (1.62, 2.51)	NA
TOPIRAMATE	NA			NA		
VALPROATE	1 (234)	1.48 (1.03, 2.13)	NA	1 (171)	1.89 (1.11, 3.24)	NA

Supplement 15 – Network diagram for monthly migraine days

Each node represents a drug that has been tested in trials. The edges represent direct comparisons of the drugs in trials. The size of the nodes is proportional to the number of patients that have received that drug, and the thickness of the edges is proportional to the number of trials.

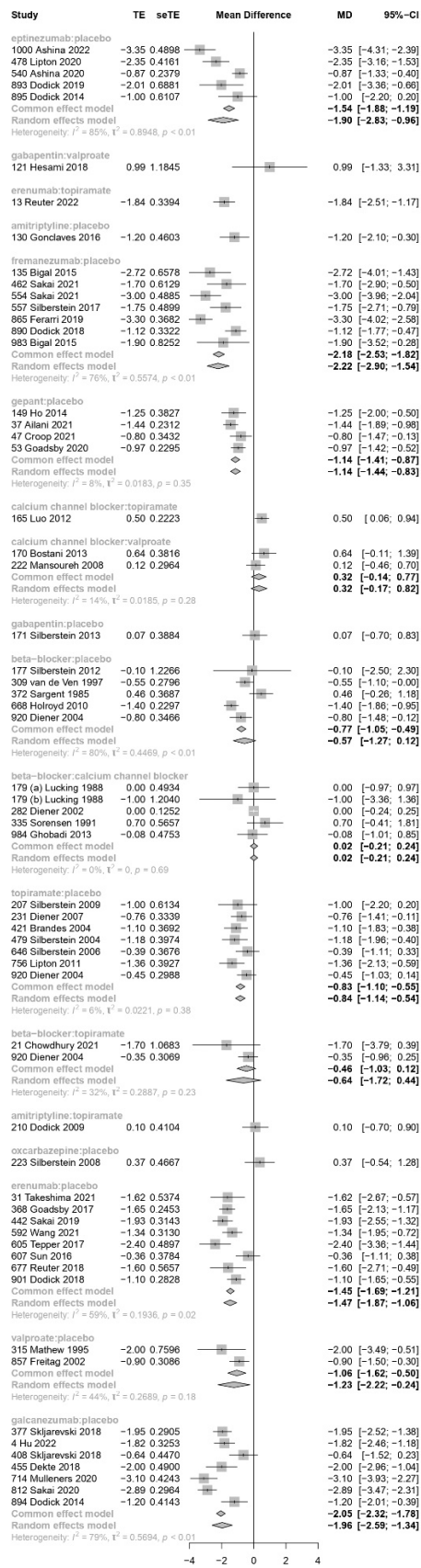


Supplemental Table 1 Comparisons and chi-square tests for categorical meta-analysis of individual studies.

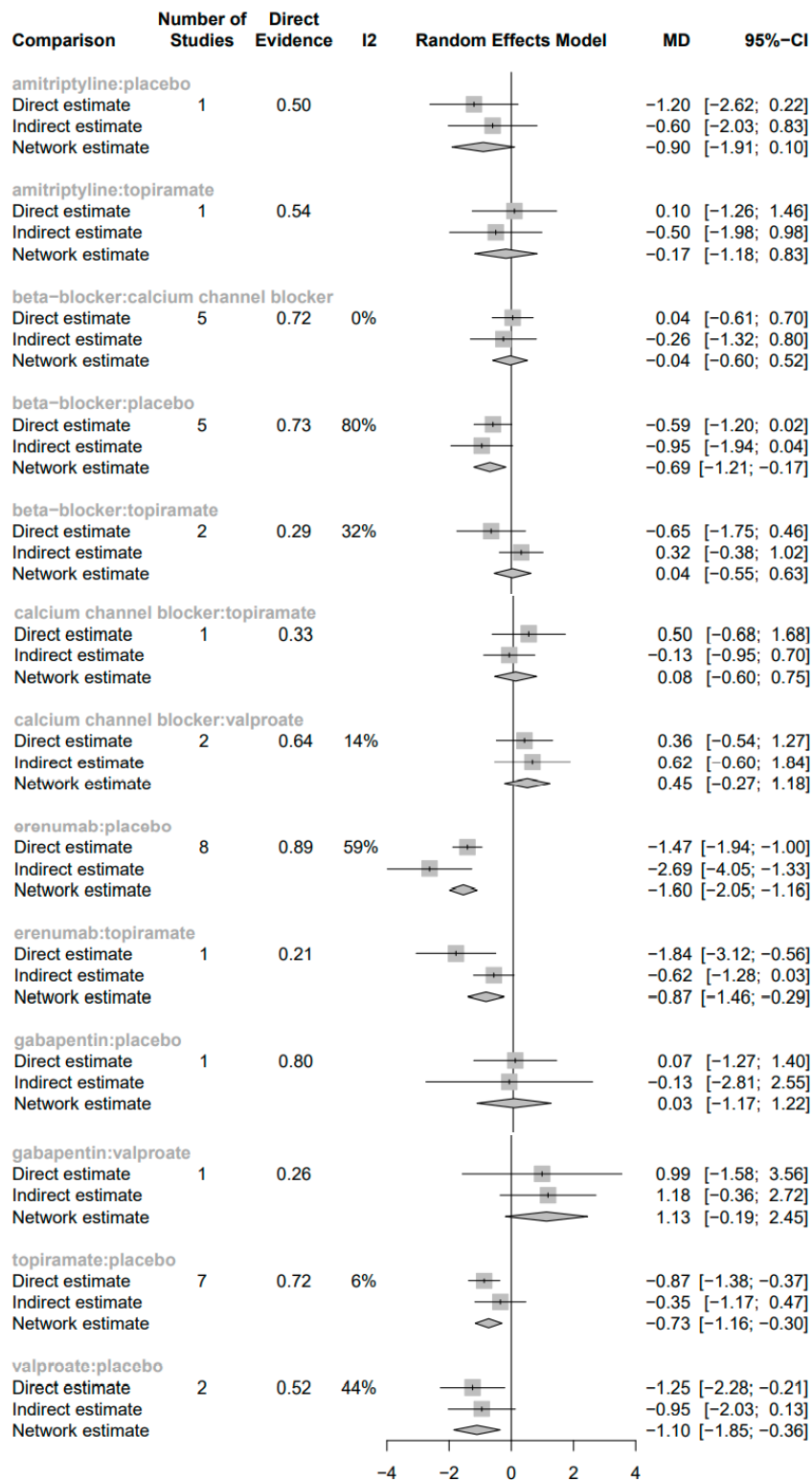
Comparison MD: 2 MM		Direct estimate		GRADE								Indirect estimate		Network estimate		GRADE						
		Relative estimate										Relative estimate		Relative estimate								
		Point estimate	CI lower limit	CI upper limit	Risk of bias	Inconsistency	Indirectness	Publication bias	Preliminary rating of direct evidence	Imprecision	Final rating of direct evidence	Point estimate	CI lower limit	CI upper limit	Preliminary rating of indirect evidence	Point estimate	CI lower limit	CI upper limit	Starting rating	Incoherence	Imprecision	Final rating
Treatment 1	Treatment 2																					
amitriptyline	beta-blocker															-0.2130229	-1.32096825	0.894922442	Moderate	No concerns	No concerns	Moderate
amitriptyline	calcium channel blocker															-0.25193445	-1.41330904	0.90944014	Moderate	No concerns	No concerns	Moderate
amitriptyline	epineuzumab															0.951959829	-0.24135119	2.14527085	Moderate	No concerns	Serious conc	Low
amitriptyline	erenumab															0.701388796	-0.38791147	1.790689066	Moderate	No concerns	No concerns	Moderate
amitriptyline	fremanezumab															1.314979536	0.16123583	2.46872324	Moderate	No concerns	No concerns	Moderate
amitriptyline	gabapentin															-0.92918077	-2.48741181	0.629505294	Moderate	No concerns	Serious conc	Low
amitriptyline	galcanezumab															1.071843596	-0.0321214	2.195790594	Moderate	No concerns	Serious conc	Low
amitriptyline	gepants															0.21604721	-0.96565056	1.39774977	Moderate	No concerns	No concerns	Moderate
amitriptyline	oxcarbazepine															-1.27204979	-3.01725366	0.475134085	Moderate	No concerns	Serious conc	Low
amitriptyline	placebo	-1.2	-2.61802366	0.21802366	Serious conc	No concerns	No concerns	No concerns	Moderate	Serious conc	Low	-0.600072644	-2.0276468	0.827501462	Moderate	0.90204979	-1.90810353	0.104003952	Moderate	No concerns	No concerns	Moderate
amitriptyline	topiramate	0.1	-1.25786288	1.45786288	Serious conc	No concerns	No concerns	No concerns	Moderate	No concerns	Moderate	-0.499927356	-1.9848406	0.984985883	Moderate	-0.17320496	-1.17527029	0.828860369	Moderate	No concerns	No concerns	Moderate
amitriptyline	valproate															0.201473051	-1.03587497	1.438821068	Moderate	No concerns	No concerns	Moderate
beta-blocker	calcium channel blocker	0.044556139	-0.61356712	0.7026794	Serious conc	No concerns	No concerns	No concerns	Moderate	No concerns	Moderate	-0.255547176	-1.3158087	0.804714329	Moderate	-0.03891155	-0.59807244	0.520249341	Moderate	No concerns	No concerns	Moderate
beta-blocker	epineuzumab															1.164982732	0.34028227	1.989683189	High	No concerns	No concerns	High
beta-blocker	erenumab															0.914411699	0.24092648	1.587896919	High	No concerns	No concerns	High
beta-blocker	fremanezumab															1.528002439	0.7616708	2.294334081	High	No concerns	No concerns	High
beta-blocker	gabapentin															-0.71615786	-2.00102387	0.568708146	High	No concerns	Serious conc	Moderate
beta-blocker	galcanezumab															1.284857499	0.56415178	2.005563211	High	No concerns	No concerns	High
beta-blocker	gepants															0.429070113	-0.3787351	1.236875327	High	No concerns	No concerns	High
beta-blocker	oxcarbazepine															-1.05902688	-2.57622041	0.458166646	High	No concerns	Serious conc	Moderate
beta-blocker	placebo	-0.590911611	-1.9831875	0.01649553	No concerns	No concerns	No concerns	No concerns	High	No concerns	High	-0.950529232	-1.9421586	0.041100134	High	-0.68902688	-1.20698806	-0.17106571	High	No concerns	No concerns	High
beta-blocker	topiramate	-0.647498281	-1.75133694	0.45634038	No concerns	No concerns	No concerns	No concerns	High	No concerns	High	0.318783764	-0.384455	1.022022526	High	0.039817944	-0.55328372	0.632919609	High	No concerns	No concerns	High
beta-blocker	valproate															0.414495954	-0.37934917	1.208341083	Moderate	No concerns	No concerns	Moderate
calcium channel blo	epineuzumab															1.203894279	0.29772604	2.110062514	Moderate	No concerns	No concerns	Moderate
calcium channel blo	erenumab															0.953323246	0.18514831	1.721498181	Moderate	No concerns	No concerns	Moderate
calcium channel blo	fremanezumab															1.566913867	0.71552415	2.420360382	Moderate	No concerns	No concerns	Moderate
calcium channel blo	gabapentin															-0.67724632	-1.9863879	0.641895365	Moderate	No concerns	No concerns	Moderate
calcium channel blo	galcanezumab															1.323769047	0.5111026	2.136435498	Moderate	No concerns	No concerns	Moderate
calcium channel blo	gepants															0.467981661	-0.42283779	1.358801108	Moderate	No concerns	No concerns	Moderate
calcium channel blo	oxcarbazepine															-1.02011534	-2.58308886	0.542858186	Moderate	No concerns	Serious conc	Low
calcium channel blo	placebo															-0.65011534	-1.28987607	0.0103546	Moderate	No concerns	No concerns	Moderate
calcium channel blo	topiramate	0.5	-0.677635	1.677635	Serious conc	No concerns	No concerns	No concerns	Moderate	No concerns	Moderate	-0.126903148	-0.9496689	0.695862593	Moderate	0.078729492	-0.59573098	0.753189965	Moderate	No concerns	No concerns	Moderate
calcium channel blo	valproate	0.362644309	-0.54246178	1.2673904	Serious conc	No concerns	No concerns	No concerns	Moderate	No concerns	Moderate	-0.618067369	-0.599581	1.83571574	Moderate	0.453407502	-0.27290575	1.179720749	Moderate	No concerns	No concerns	Moderate
gepants	oxcarbazepine															-1.488097	-3.04304327	0.066849277	High	No concerns	Serious conc	Moderate
gepants	placebo	-1.118096997	-1.73798851	-0.49820548	No concerns	No concerns	No concerns	No concerns	High	No concerns	High					-1.118097	-1.73798851	-0.49820548	High	No concerns	No concerns	High
gepants	topiramate															-0.38925217	-1.14563865	0.365154311	High	No concerns	No concerns	High
gepants	valproate															-0.01457416	-0.98522888	0.956080957	Moderate	No concerns	No concerns	Moderate
epineuzumab	erenumab															-0.25057103	-1.03107543	0.529933362	High	No concerns	No concerns	High
epineuzumab	fremanezumab															0.363019707	-0.49186477	1.217904189	High	No concerns	No concerns	High
epineuzumab	gabapentin															-1.88114059	-3.23615896	-0.52612223	High	No concerns	No concerns	High
epineuzumab	galcanezumab															0.119874768	-0.69436109	0.934110623	High	No concerns	No concerns	High
epineuzumab	gepants															-0.73591262	-1.62816402	0.156338779	High	No concerns	No concerns	High
epineuzumab	oxcarbazepine															-2.22400962	-3.78779972	0.66021951	High	No concerns	No concerns	High
epineuzumab	placebo	-1.854009615	-2.49576274	-1.21225649	No concerns	No concerns	No concerns	No concerns	High	No concerns	High					-1.85400962	-2.49576274	-1.21225649	High	No concerns	No concerns	High
epineuzumab	topiramate															-1.12516479	-1.89763532	-0.35269426	High	No concerns	No concerns	High
epineuzumab	valproate															-0.750488678	-1.73524673	0.234273172	Moderate	No concerns	No concerns	Moderate
erenumab	fremanezumab															0.61359074	-0.10496368	1.332145157	High	No concerns	No concerns	High
erenumab	gabapentin															-1.63056956	-2.90323632	-0.3579026	High	No concerns	No concerns	High
erenumab	galcanezumab															0.370455801	-0.29923547	1.04012707	High	No concerns	No concerns	High
erenumab	gepants															-0.48534159	-1.24797225	0.277289078	High	No concerns	No concerns	High
erenumab	oxcarbazepine															-1.97343858	-3.46706922	-0.47980795	High	No concerns	No concerns	High
erenumab	placebo	-1.473313339	-1.94339788	-1.00322879	No concerns	No concerns	No concerns	No concerns	High	No concerns	High	-2.689713187	-0.40479172	-1.331509175	High	-1.60343858	-2.0476683	-1.15920886	High	No concerns	No concerns	High
erenumab	topiramate	-1.84	-3.12041351	-0.55958649	No concerns	No concerns	No concerns	No concerns	High	No concerns	High	-0.623600152	-1.2764699	0.02926956	High	-0.87459375	-1.4562192	-0.29296831	High	No concerns	No concerns	High
erenumab	valproate															-0.49991574	-1.36383751	0.364006016	Moderate	No concerns	No concerns	Moderate
fremanezumab	gabapentin															-2.2411603	-3.56446637	-0.92385423	High	No concerns	No concerns	High
fremanezumab	galcanezumab															-0.2431494	-0.99820346	0.51191398	High	No concerns	No concerns	High
fremanezumab	gepants															-1.08932426	-1.93729902	-0.260397478	High	No concerns	No concerns	High
fremanezumab	oxcarbazepine															-2.98702933	-4.12883932	1.053219413	High	No concerns	No concerns	High
fremanezumab	placebo	-2.217029323	-2.781812829	-1.652245817	No concerns	No concerns	No concerns	No concerns	High	No concerns	High					-2.217029323	-2.781812829	-1.652245817	High	No concerns	No concerns	High
fremanezumab	topiramate															-1.488184495	-2.198004232	-0.778364758	High	No concerns	No concerns	High
fremanezumab	valproate															-1.113506485	-2.049928131	-0.177084839	Moderate	No concerns	No concerns	Moderate
gabapentin	galcanezumab															2.001015362	0.706658122	3.295372602	High	No concerns	No concerns	High
gabapentin	gepants															1.145227976	-0.199574311	2.490030263	High	No concerns	Serious conc	Moderate
gabapentin	oxcarbazepine															-0.342869021	-2.022390501	1.516565249	High	No concerns	Serious conc	Moderate
gabapentin	placebo	0.065062391	-1.267739556	1.397866138	No concerns	No concerns	No concerns	No concerns	High	No concerns	High	-0.126287847	-2.806693855	2.554118161	Moderate	0.027130979	-1.166279136	1.220541095	High	No concerns	No concerns	High
gabapentin	topiramate															0.759797907	-0.506246077	2.018197691	High	No concerns	Serious conc	Moderate
gabapentin	valproate	0.99	-1.576474867	3.556474867	Serious conc	No concerns	No concerns	No concerns	Moderate	No concerns	Moderate	1.181351138	-0.359475443	2.72217772	Moderate	1.130636917	-0.196398017	2.451168782	Moderate	No concerns	Serious conc	Low
galcanezumab	gepants															-0.855787386	-1.652296227	-0.068685454	High	No concerns	No concerns	High
galcanezumab	oxcarbazepine															-2.343884383	-3.855415193	-0.832353573	High	No concerns	No concerns	High
galcanezumab	placebo	-1.973884383	-2.475016063	-1.472752703	No concerns	No concerns	No concerns	No concerns	High	No concerns	High					-1.973884383	-2.475016063	-1.472752703	High	No concerns	No concerns	High
galcanezumab	topiramate															-1.245039555	-1.90533995	-0.584739161	High	No concerns	No concerns	High
galcanezumab	valproate															-0.870361545	-1.769826971	0.02910388	Moderate	No concerns	No concerns	Moderate
oxcarbazepine	placebo	0.37	-1.056040823	1.796040823	No concerns	No concerns	No concerns	No concerns	High	No concerns	High					0.37	-1.056040823	1.79604				

Full table also available at: <https://osf.io/g3u26>

Supplement 17 – Pairwise meta-analyses for monthly migraine days

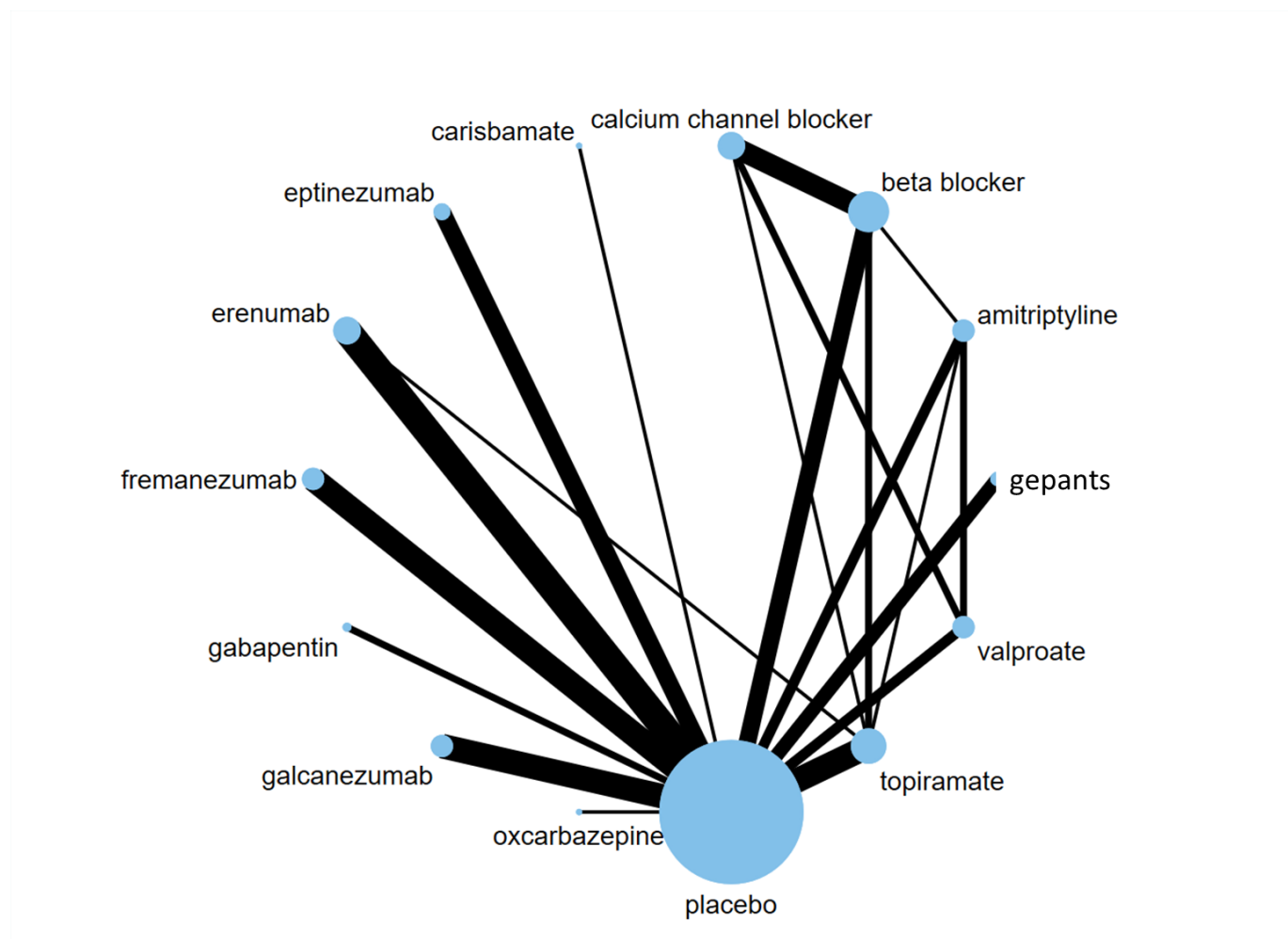


Supplement 18 – Node split plots for monthly migraine days

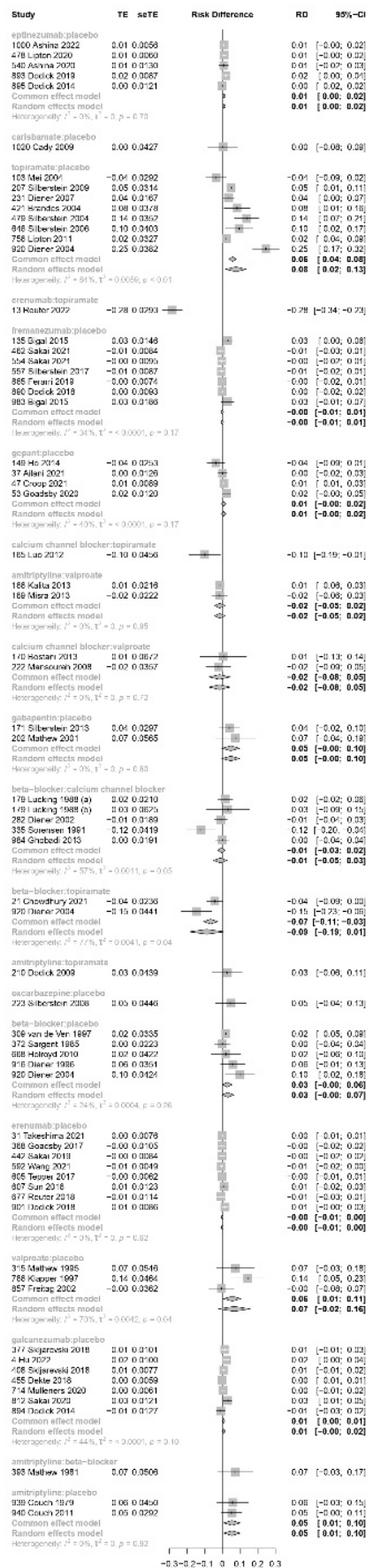


Supplement 19 – Network diagram for adverse events leading to discontinuation

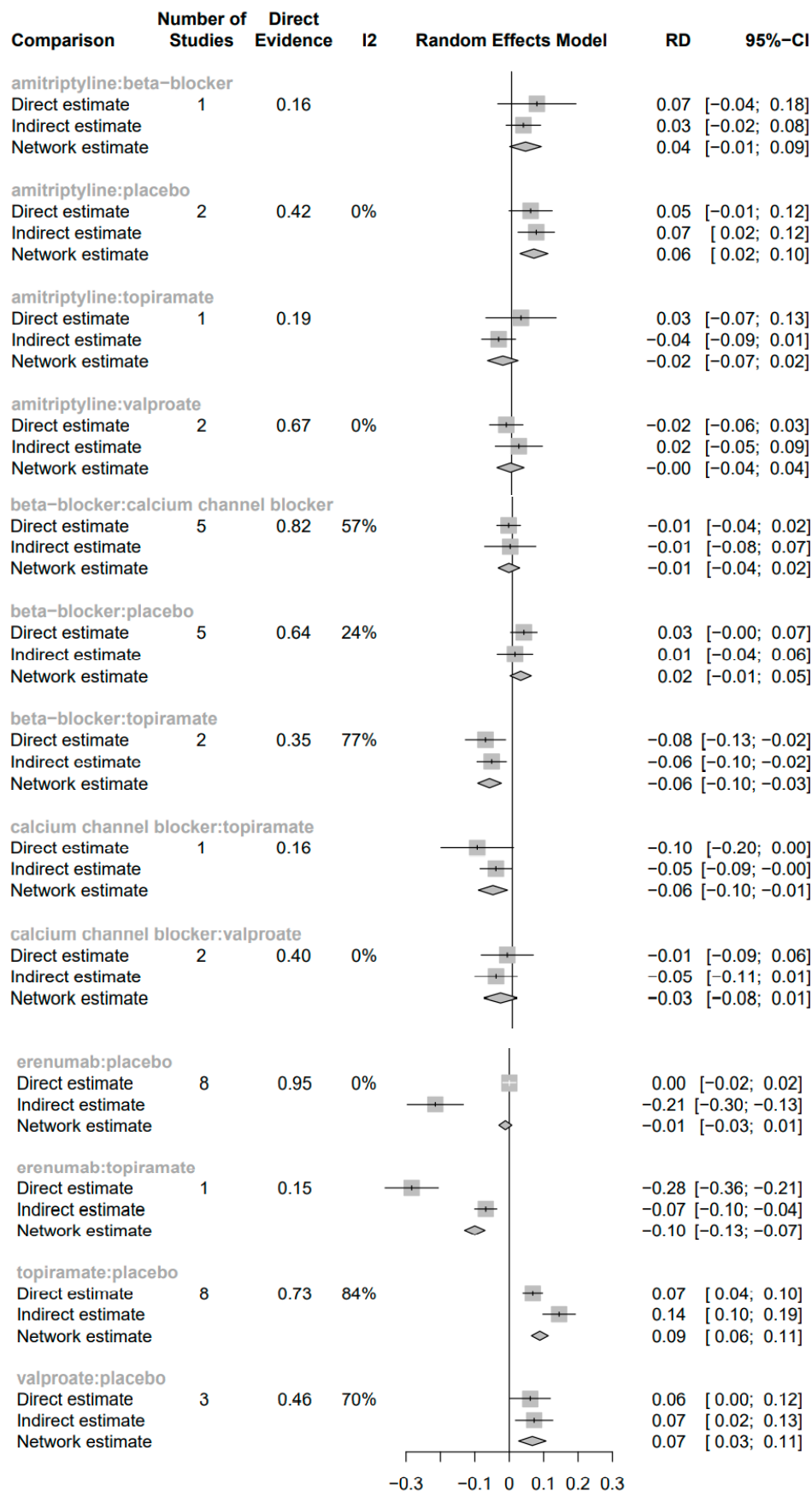
Each node represents a drug that has been tested in trials. The edges represent direct comparisons of the drugs in trials. The size of the nodes is proportional to the number of patients that have received that drug, and the thickness of the edges is proportional to the number of trials.

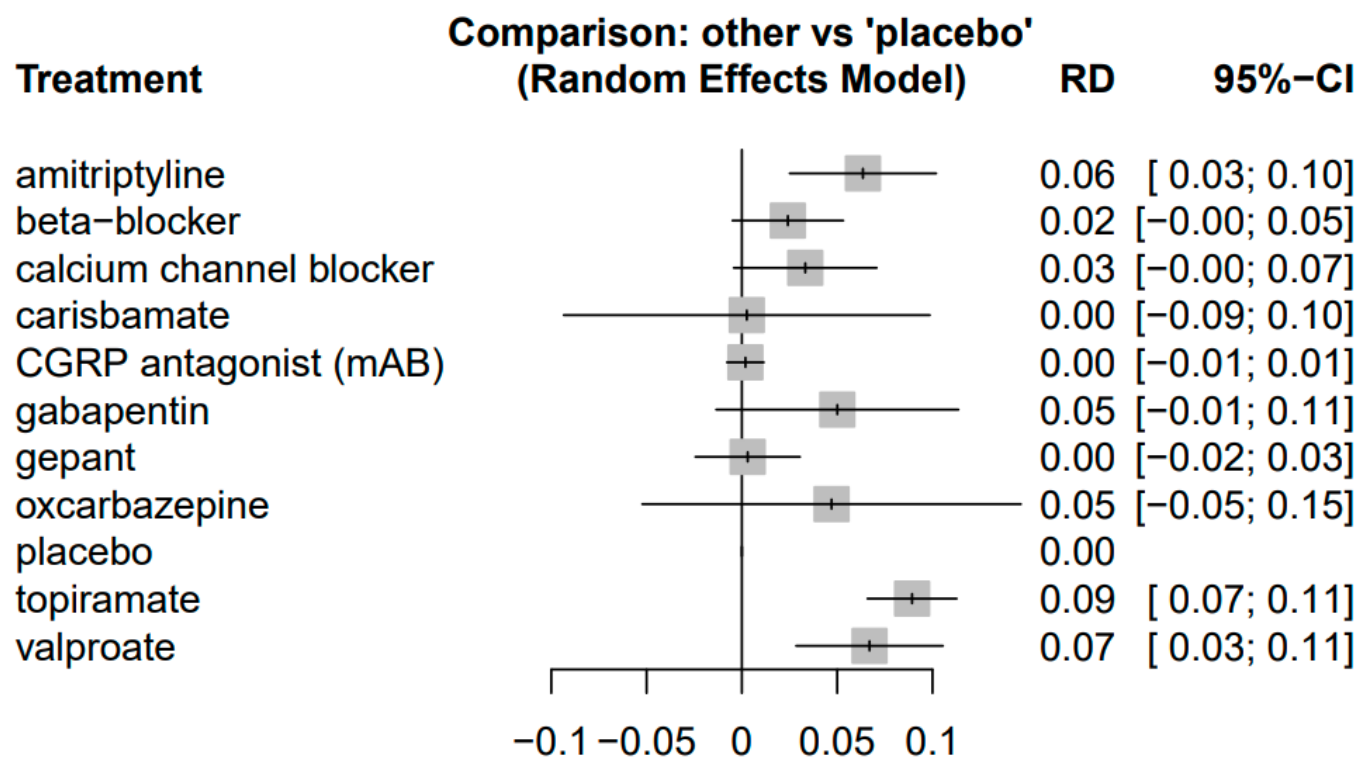


Supplement 21 – Pairwise meta-analyses for adverse events leading to discontinuation

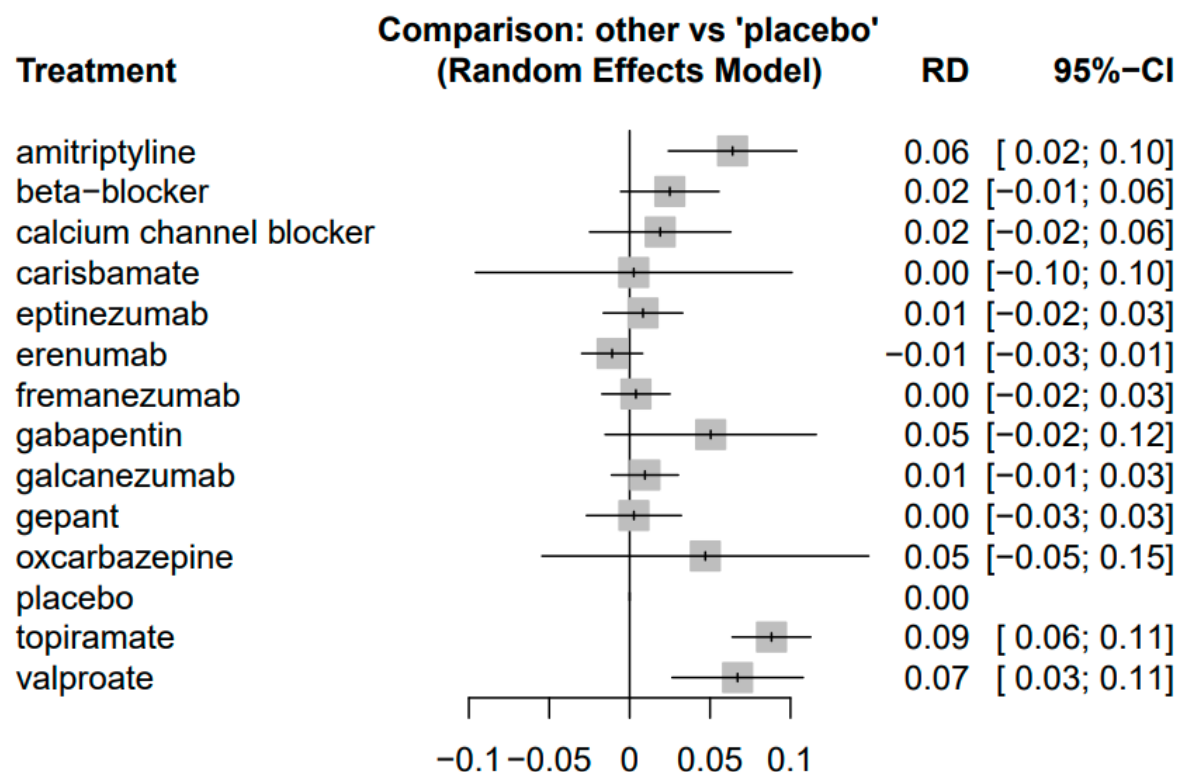


Supplement 22 – Node split plots for adverse events leading to discontinuation

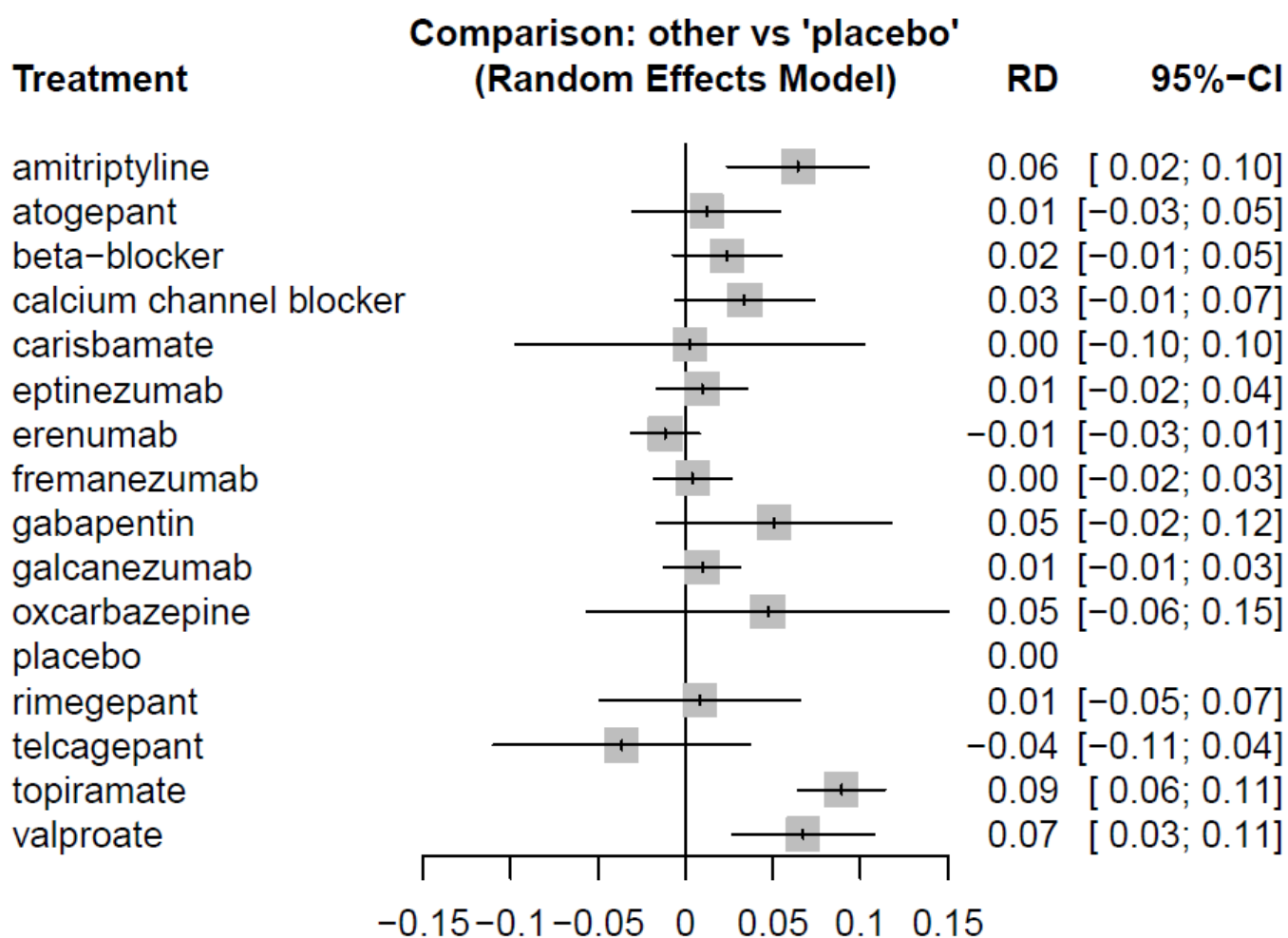




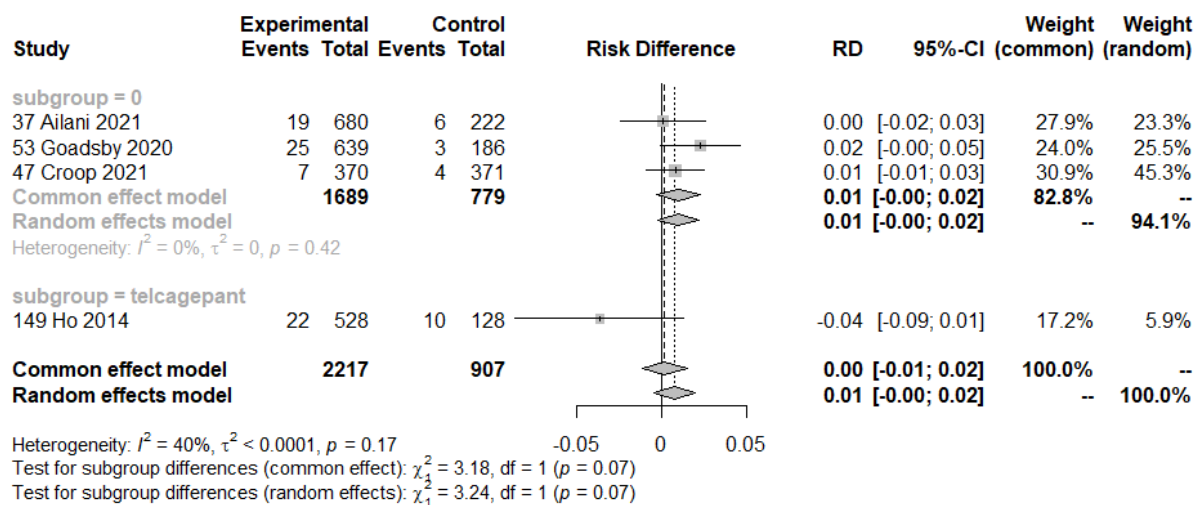
Supplement 24 – Secondary analysis for adverse events leading to discontinuation (restricted trials to those that investigated recommended therapeutic doses of drugs)



Supplement 25 – Secondary analysis for adverse events leading to discontinuation (each gepant grouped in a separate node)



Supplement 26 – Secondary analysis comparing the effects of telcagepant with other gepnts



Supplement 27 – Subgroup analyses for adverse events leading to discontinuation

For subgroup analyses based on baseline monthly migraine days and proportion of patients that had previously used prophylactic drugs, for each comparison against placebo, we calculated the median monthly migraine days and median proportion of patients who had previously used prophylactic drugs across trials, and performed subgroup analyses comparing trials with mean baseline monthly migraine days or proportion of patients who had previously used prophylactic drugs above or equal to/below the median.

DRUG	RISK OF BIAS					
	Low			High		
	Number of trials (participants)	RD (95% CI)	I ² (%)	Number of trials (participants)	RD (95% CI)	I ² (%)
AMITRIPTYLINE	1 (391)	0.05 (0.00, 0.11)	NA	1 (116)	0.06 (-0.03, 0.15)	NA
BETA-BLOCKER	2 (511)	0.06 (-0.02, 0.13)	54	2 (220)	0.02 (-0.03, 0.08)	50
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	5 (3630)	0.01 (0.00, 0.02)	0	NA		
ERENUMAB	8 (4528)	0.00 (-0.01, 0.00)	0	NA		
FREMANEZUMAB	7 (4327)	0.00 (-0.01, 0.01)	34	NA		
GABAPENTIN	2 (669)	0.05 (0.00, 0.10)	0	NA		
GALCANEZUMAB	7 (4097)	0.01 (0.00, 0.02)	44	NA		
GEPANT	3 (2468)	0.01 (0.00, 0.02)	0	1 (656)	-0.04 (-0.09, 0.01)	NA
TOPIRAMATE	5 (2092)	0.12(0.05, 0.19)	86	3 (797)	0.01 (-0.04, 0.06)	52
VALPROATE	2 (413)	0.07 (-0.08, 0.21)	84	1 (107)	0.07 (-0.03, 0.18)	NA
	Monthly migraine days					
	≤ median			> median		
	Number of trials (participants)	RD (95% CI)	I ² (%)	Number of trials (participants)	RD (95% CI)	I ² (%)
AMITRIPTYLINE	NA			NA		
BETA-BLOCKER	2 (359)	0.04 (-0.01, 0.09)	0	1 (285)	0.1 (0.02, 0.18)	NA
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	3 (1942)	0.01 (0.00, 0.02)	0	2 (1688)	0.01 (0.00, 0.02)	0
ERENUMAB	4 (2470)	0.00 (-0.00, 0.01)	0	4 (2058)	0.00 (-0.01, 0.00)	0
FREMANEZUMAB	4 (2365)	0.00 (-0.01, 0.01)	37	3 (1962)	0.00 (-0.02, 0.01)	47
GABAPENTIN	1 (143)	0.07 (-0.04, 0.19)	NA	1 (526)	0.04 (-0.02, 0.10)	NA
GALCANEZUMAB	4 (1607)	0.01 (0.00, 0.03)	56	3 (2490)	0.00 (0.00, 0.01)	0
GEPANT	2 (1727)	0.01 (-0.01, 0.03)	38	2 (1397)	-0.01 (-0.05, 0.03)	64
TOPIRAMATE	4 (1229)	0.11 (-0.11, 0.22)	92	3 (1339)	0.04 (0.01, 0.07)	0

VALPROATE	1 (237)	0.00 (-0.08, 0.07)	NA	1 (107)	0.07 (-0.03, 0.18)	NA
	Previous prophylactic drugs					
	≤ median			> median		
	Number of trials (participants)	RD (95% CI)	I ² (%)	Number of trials (participants)	RD (95% CI)	I ² (%)
AMITRIPTYLINE	NA			NA		
BETA-BLOCKER	NA			NA		
CALCIUM CHANNEL BLOCKERS	NA			NA		
EPTINEZUMAB	1 (616)	0.02 (0.00, 0.04)	NA	1 (891)	0.01 (0.00, 0.02)	NA
ERENUMAB	4 (3078)	0.00 (-0.01, 0.01)	29	4 (1450)	0.00 (-0.01, 0.01)	0
FREMANEZUMAB	3 (2929)	-0.01 (-0.01, 0.00)	0	3 (1398)	0.02 (-0.01, 0.04)	64
GABAPENTIN	NA			NA		
GALCANEZUMAB	3 (1894)	0.02 (0.01, 0.03)	0	2 (1575)	0.00 (-0.01, 0.01)	0
GEPANT	2 (1481)	0.00 (-0.06, 0.06)	78	1 (902)	0.00 (-0.02, 0.03)	NA
TOPIRAMATE	NA			NA		
VALPROATE	1 (237)	0.00 (-0.08, 0.07)	NA	1 (176)	0.14 (0.05, 0.23)	NA

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