

Supplementary Information

Indirect comparison of Topiramate and Monoclonal Antibodies for the prophylaxis of Episodic Migraine: A Systematic Review with Meta-Analysis

Lucas Hendrik Overeem¹, Bianca Raffaelli¹, Jasper Mecklenburg¹, Tim Kelderman², Lars Neeb¹, Uwe Reuter¹.

Corresponding author:

Prof. Dr. Uwe Reuter
Charité – Universitätsmedizin Berlin
Department of Neurology and Experimental Neurology
Charitéplatz 1 (Bonhoeffer-Weg 3)
10117 Berlin
Germany
uwe.reuter @charite.de

- 1 Department of Neurology and Experimental Neurology
Charité – Universitätsmedizin Berlin
Charitéplatz 1
10117 Berlin Germany.
- 2 Department of Neurology
Sint Vincentius Hospital
Sint-Vincentiusstraat 20
2018 Antwerp, Belgium.

Content:

Adverse events overview per category	4
Literature search	5
Databank search: PubMed.....	5
Databank search: The Cochrane Central Register of Controlled Trials (CENTRAL)	5
Register search: clinicaltrials.gov.....	6
PRISMA 2020 flow diagram.....	8
Monthly Migraine Days	9
Model 1 Mean Difference, Risk of Bias outcomes, and Funnel plot.....	9
Model 2 Mean Difference	10
Acute Medication Days	12
Model 1 Mean Difference, Risk of Bias outcomes, and Funnel plot.....	12
Model 2 Mean Difference	13
50% Response Rate	15
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	15
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	16
Model 2 Risk Ratio	17
Discontinuation due to Adverse Events	19
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	19
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	20
Model 2 Risk Ratio	21
Cognitive-Related Adverse Events	23
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	23
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	24
Model 2 Risk Ratio	25
Sensory or Pain-Related Adverse Events.....	27
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	27
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	28
Model 2 Risk Ratio	29
Gastrointestinal-Related Adverse Events.....	31
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	31
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	32
Model 2 Risk Ratio	33
Infections and Infestations-Related Adverse Events.....	35
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	35

Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	36
Model 2 Risk Ratio	37
Administration Site-Related Adverse Events	39
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	39
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	40
General-Related Adverse Events.....	41
Model 1 Risk Difference, Risk of Bias outcomes, and Funnel plot.....	41
Model 1 Risk Ratio, Risk of Bias outcomes, and Funnel plot.....	42
Model 2 Risk Ratio	43

Adverse events overview per category

Additional Table 1 | Adverse Events per category as used for safety analyses

Gastrointestinal-related AEs	General-related AEs	Sensory & pain-related AEs	Infection & infestation-related AEs	Cognitive-related AEs	Administration site-related AEs
Abdominal pain	AE not specified	Arthralgia	Bronchitis	Concentration difficulty	Injection-site bruising
Constipation	Anorexia	Back pain	Influenza	Confusion	Injection-site erythema
Diarrhea	Cough	Dry mouth	Nasopharyngitis	Depression	Injection-site hematoma
Dyspepsia	Dizziness	Headache	Pyrexia	Fatigue	Injection-site hemorrhage
Gastroenteritis	Dysmenorrhea	Hypoesthesia	Sinusitis	Insomnia	Injection-site induration
Nausea	Hypertension	Hypoesthesia	Upper respiratory tract infection	Language problems	Injection-site pain
	Injury	Migraine	Urinary tract infection	Memory difficulty	Injection-site pruritus
	Limb injury	Neck pain	Viral infection	Somnolence	Injection-site reaction
	Muscle spasms	Oropharyngeal pain			Injection-site swelling
	Nasal congestion	Pain in extremity			
	Tachycardia	Paresthesia			
	Tremor	Pruritus			
	Weight loss	Taste perversion			

AEs = Adverse events

Literature search

Databank search: PubMed

Search: (((((((erenumab) OR (AMG334)) OR (galcanezumab)) OR (LY2951742)) OR (fremanezumab)) OR (TEV-48125)) OR (eptinezumab)) OR (ALD403)) OR (topiramate)) OR (Topamax)) AND (episodic migraine)
Result: 332
Filter: Article type: Clinical Trial
Age: Adult: 19+ years
Results by year: 2000 - 2020
Result: 62

Databank search: The Cochrane Central Register of Controlled Trials (CENTRAL)

Search: (erenumab) OR (AMG334) AND (episodic migraine)
Result: 214
Filter: "Trials" and "Between 2000 and 2020"
Result: 204

Search: (galcanezumab) OR (LY2951742) AND (episodic migraine)
Result: 218
Filter: "Trials" and "Between 2000 and 2020"
Result: 199

Search: (fremanezumab) OR (TEV-48125) AND (episodic migraine)
Result: 313
Filter: "Trials" and "Between 2000 and 2020"
Result: 286

Search: (eptinezumab) OR (ALD403) AND (episodic migraine)
Result: 97
Filter: "Trials" and "Between 2000 and 2020"
Result: 89

Search: (topiramate) OR (Topamax) AND (episodic migraine)
Result: 1580
Filter: "Trials" and "Between 2000 and 2020"
Result: 1319

Total

Search: (((((((erenumab) OR (AMG334)) OR (galcanezumab)) OR (LY2951742)) OR (fremanezumab)) OR (TEV-48125)) OR (eptinezumab)) OR (ALD403)) OR (topiramate)) OR (Topamax)) AND (episodic migraine)
Result: 2422
Filter: "Trials" and "Between 2000 and 2020"
Result: 2097

Register search: clinicaltrials.gov

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: Erenumab

Result: 12

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 6

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: AMG334

Result: 9

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 6

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: Galcanezumab

Result: 7

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 3

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: LY2951742

Result: 6

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 3

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: Fremanezumab

Result: 4

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 1

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: TEV-48125

Result: 2

Filter: Study Phase: Phase 3 and Phase 4
Study Type: Interventional (Clinical Trial),
Age: Adult (18-64)
Status: Active, not recruiting, Completed, and Unknown status

Result: 2

Search: Status: "All studies", condition or disease: episodic migraine, and other terms: Eptinezumab

Result:	1
Filter:	Study Phase: Phase 3 and Phase 4 Study Type: Interventional (Clinical Trial), Age: Adult (18-64) Status: Active, not recruiting, Completed, and Unknown status
Result:	1

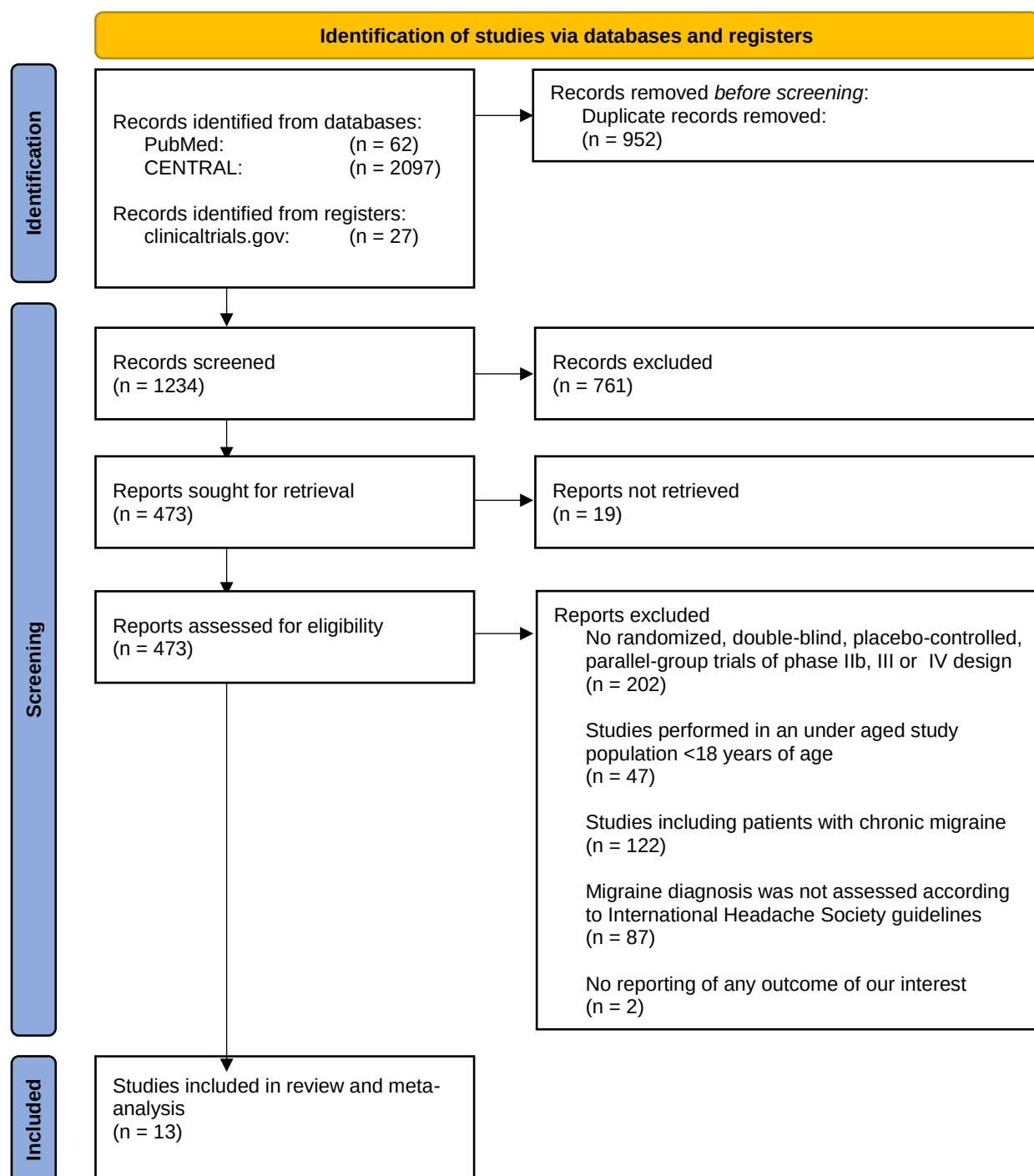
Search:	Status: "All studies", condition or disease: episodic migraine, and other terms: ALD403
Result:	2
Filter:	Study Phase: Phase 3 and Phase 4 Study Type: Interventional (Clinical Trial), Age: Adult (18-64) Status: Active, not recruiting, Completed, and Unknown status
Result:	1

Search:	Status: "All studies", condition or disease: episodic migraine, and other terms: Topiramate
Result:	4
Filter:	Study Phase: Phase 3 and Phase 4 Study Type: Interventional (Clinical Trial), Age: Adult (18-64) Status: Active, not recruiting, Completed, and Unknown status
Result:	2

Search:	Status: "All studies", condition or disease: episodic migraine, and other terms: Topamax
Result:	4
Filter:	Study Phase: Phase 3 and Phase 4 Study Type: Interventional (Clinical Trial), Age: Adult (18-64) Status: Active, not recruiting, Completed, and Unknown status
Result:	2

Total	
Search:	Status: "All studies", condition or disease: episodic migraine, and other terms: (((((((erenumab) OR (AMG334)) OR (galcanezumab)) OR (LY2951742)) OR (fremanezumab)) OR (TEV-48125)) OR (eptinezumab)) OR (ALD403)) OR (topiramate)) OR (Topamax))
Result:	51
Filter:	Study Phase: Phase 3 and Phase 4 Study Type: Interventional (Clinical Trial), Age: Adult (18-64) Status: Active, not recruiting, Completed, and Unknown status
Result:	27

PRISMA 2020 flow diagram



Additional Figure 1 | PRISMA 2020 flow diagram

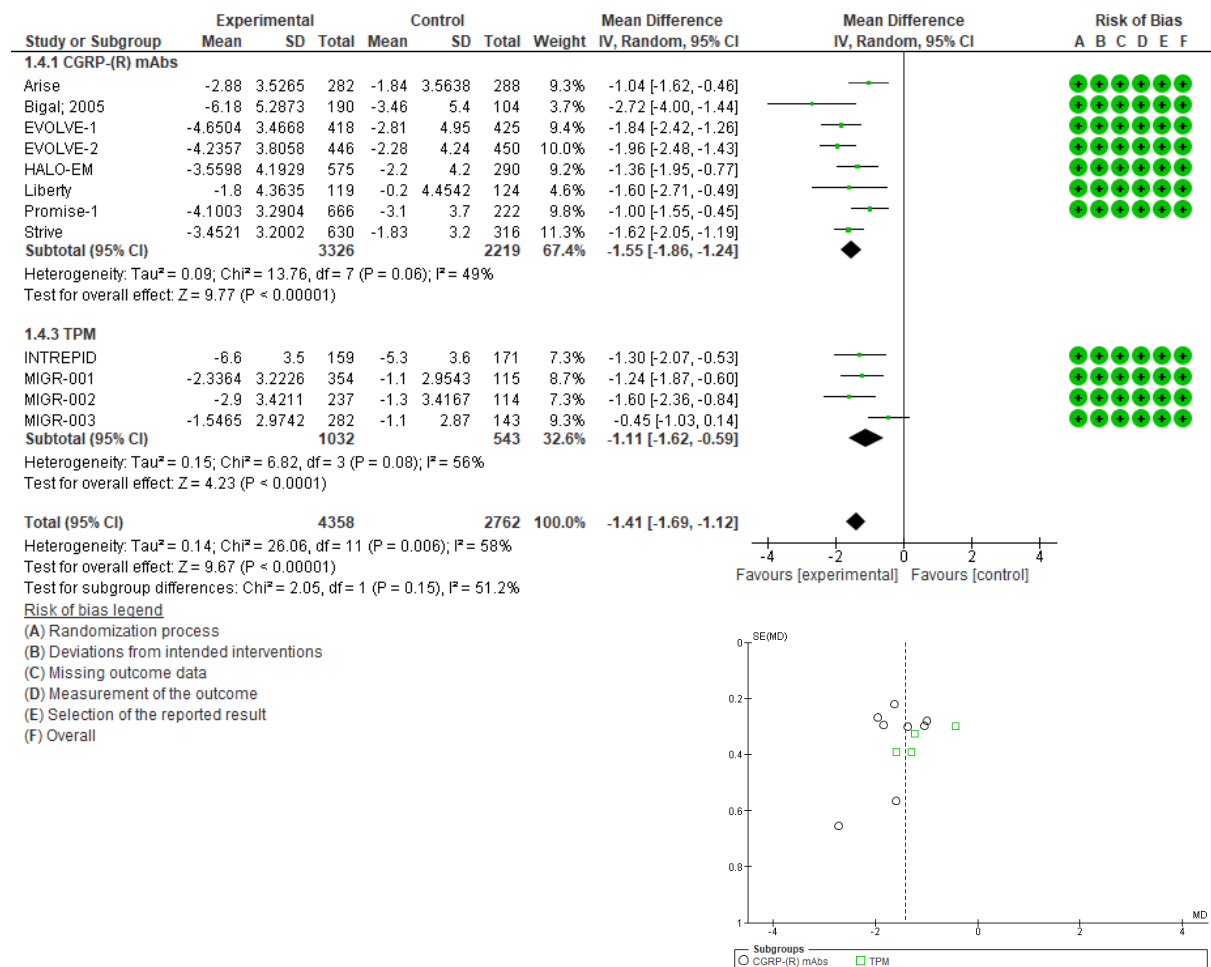
CENTRAL = Cochrane Central Register of Controlled Trials

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

Monthly Migraine Days

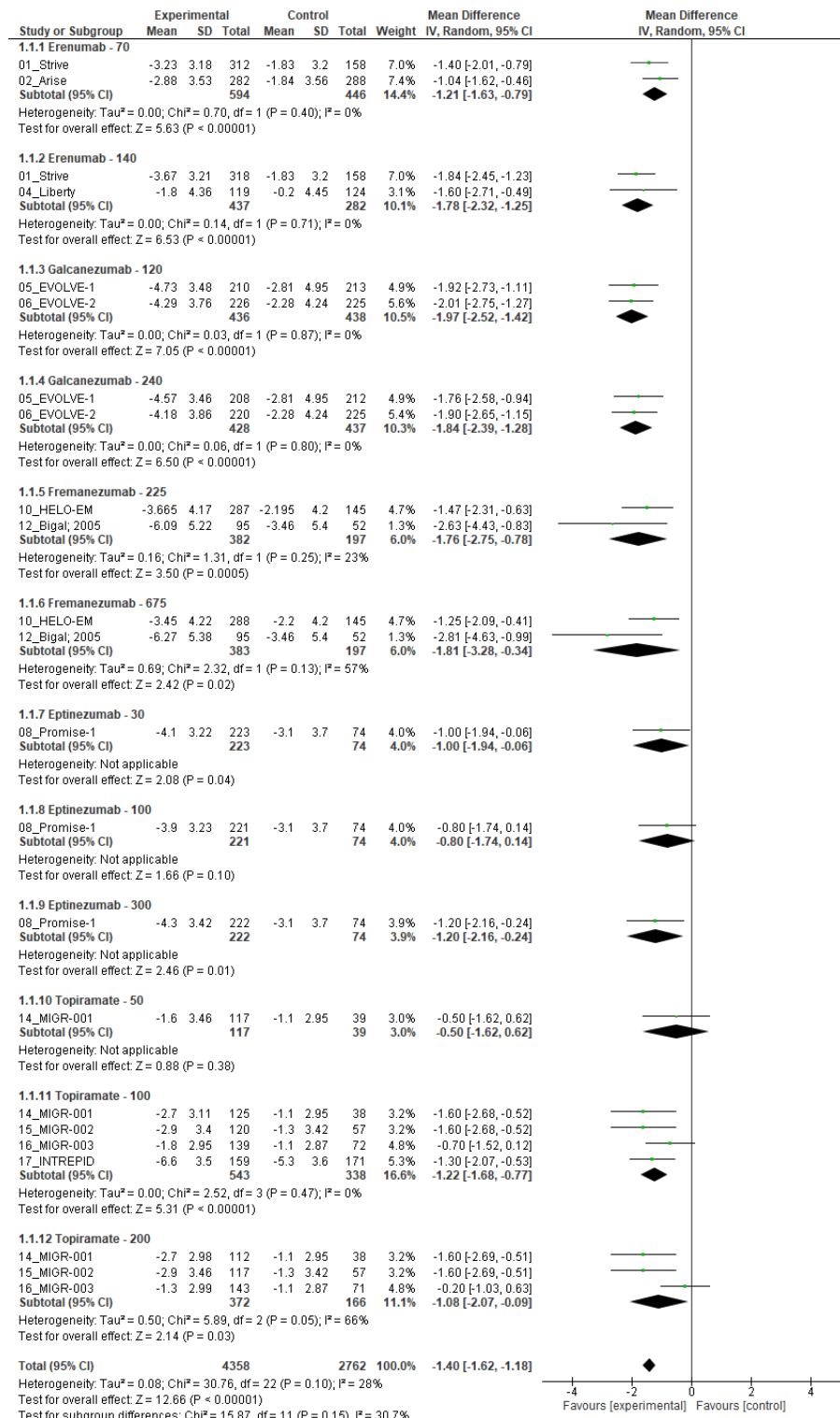
Model 1 | Mean Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 2 | Monthly migraine days model 1 [Mean Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Mean Difference



Additional Figure 3 | Monthly migraine days model 2 [Mean Difference] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

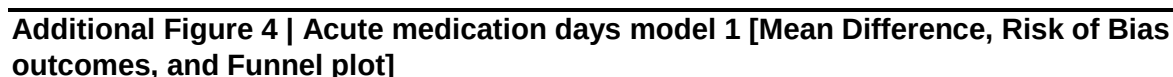
- Doses given in milligram (mg)

Additional Table 2 | Comparisons of monthly migraine days between the CGRP(R) mAbs and topiramate model 2 [Mean Difference]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.24	p = 0.04	p = 0.02	p = 0.04	p = 0.10	p = 0.16	p = 0.50	p = 0.69	p = 0.35
Topiramate 100 mg	p = 0.97	p = 0.12	p = 0.04	p = 0.09	p = 0.33	p = 0.45	p = 0.67	p = 0.43	p = 0.96
Topiramate 200 mg	p = 0.81	p = 0.22	p = 0.12	p = 0.19	p = 0.34	p = 0.41	p = 0.91	p = 0.69	p = 0.86

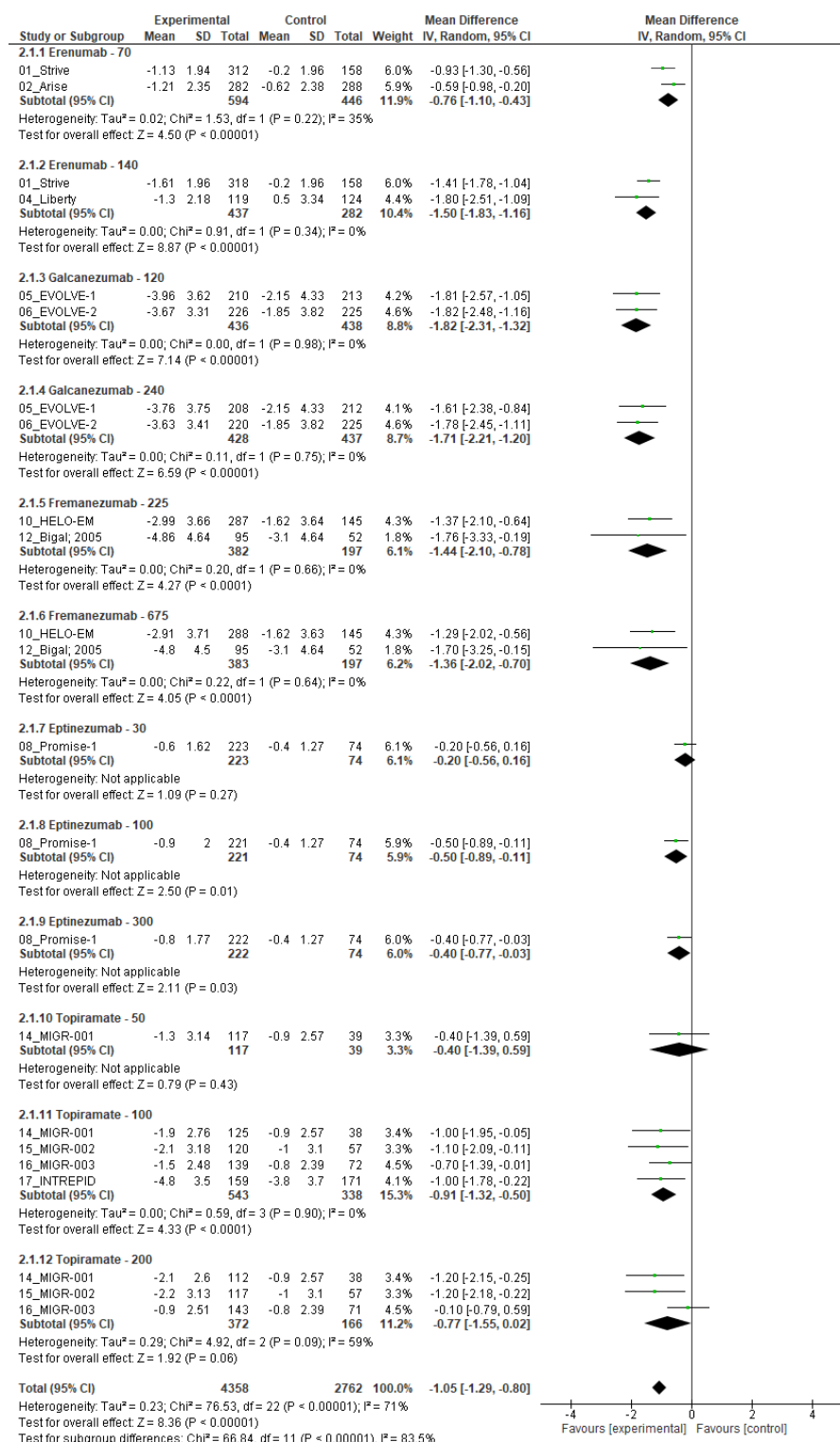
CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Model 1 | Mean Difference, Risk of Bias outcomes, and Funnel plot



12

Model 2 | Mean Difference



Additional Figure 5 | Acute medication days model 2 [Mean Difference] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

• Doses given in milligram (mg)

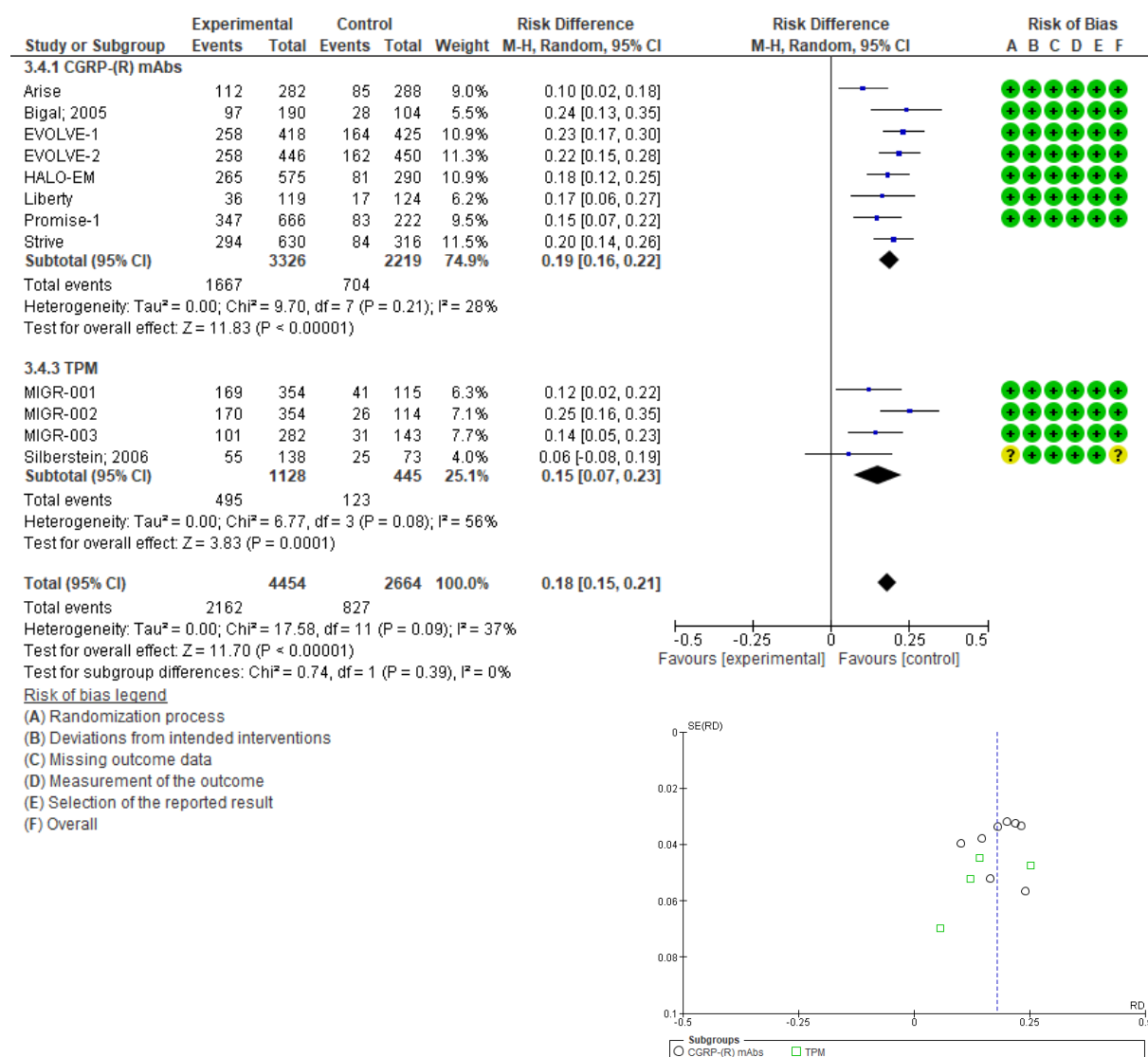
Additional Table 3 | Comparisons of acute medication days between the CGRP(R) mAbs and topiramate model 2 [Mean Difference]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.49	p = 0.04	p = 0.01	p = 0.02	p = 0.09	p = 0.11	p = 0.19	p = 0.85	p = 1.00
Topiramate 100 mg	p = 0.59	p = 0.03	p = 0.006	p = 0.02	p = 0.19	p = 0.25	p = 0.01	p = 0.16	p = 0.07
Topiramate 200 mg	p = 0.99	p = 0.09	p = 0.03	p = 0.05	p = 0.20	p = 0.26	p = 0.20	p = 0.55	p = 0.41

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

50% Response Rate

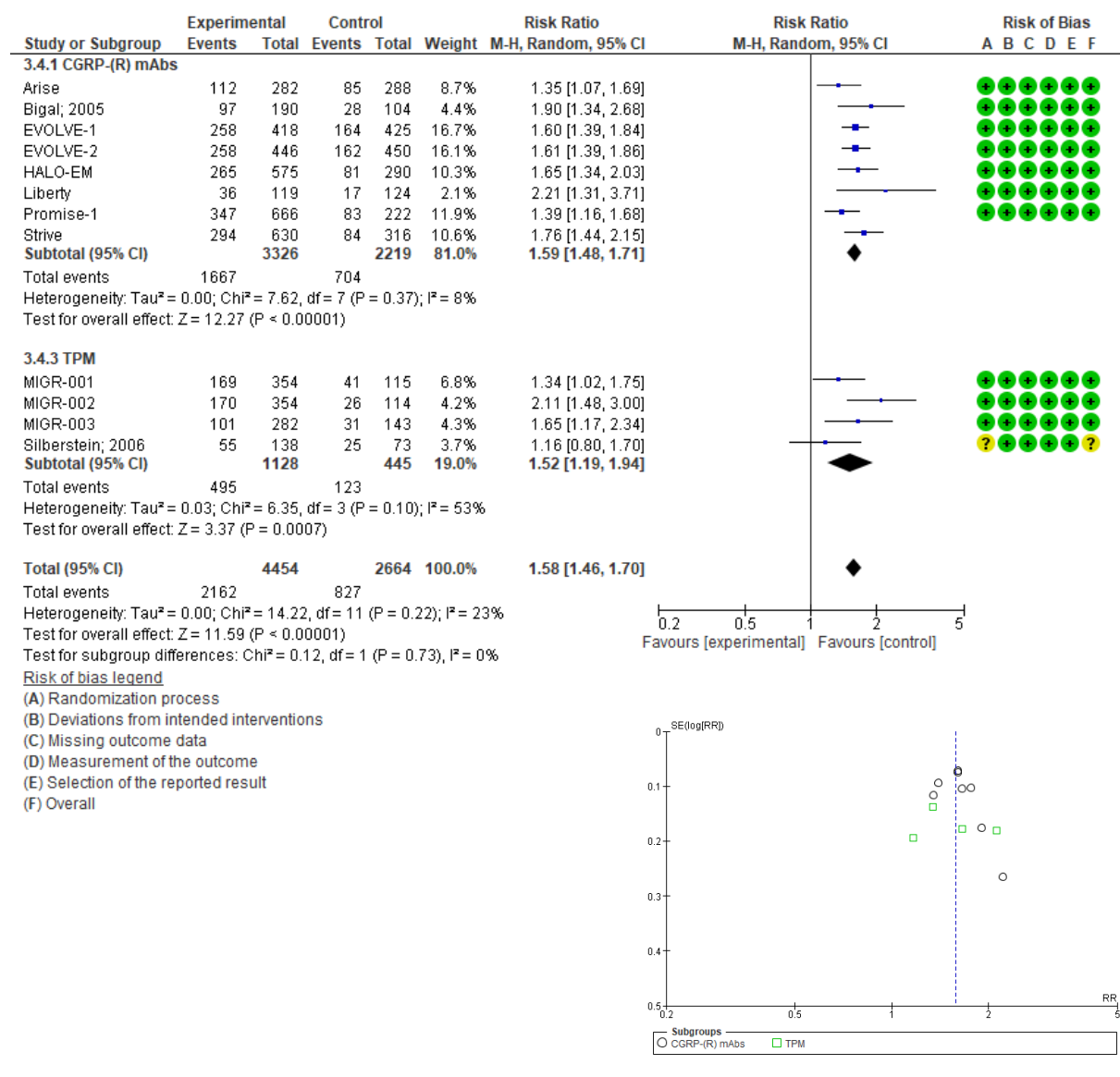
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 6 | 50% response rate model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

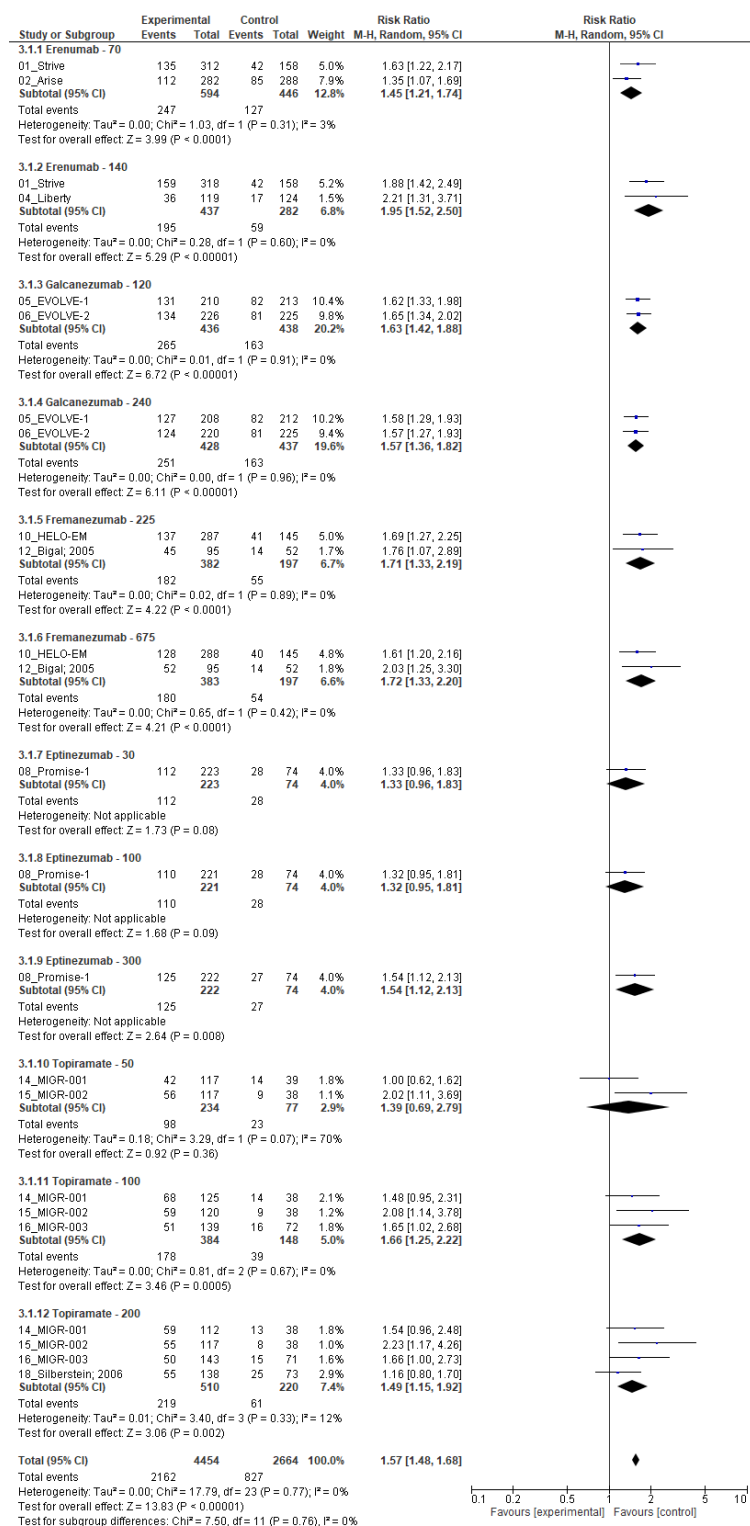
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 7 | 50% response rate model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 8 | 50% response rate model 1 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

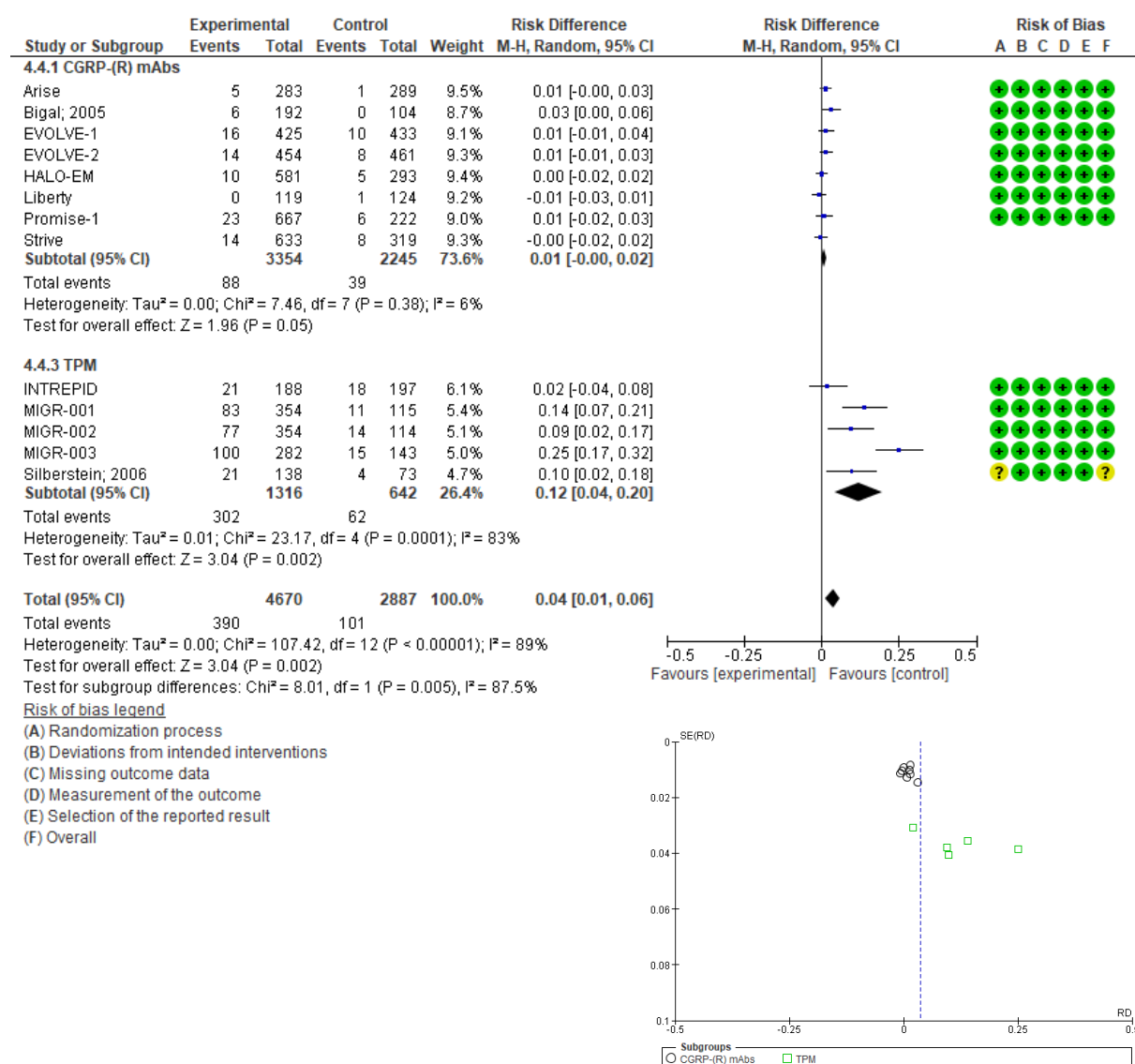
Additional Table 4 | Comparisons of 50% response rate between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.91	p = 0.37	p = 0.66	p = 0.73	p = 0.59	p = 0.58	p = 0.91	p = 0.89	p = 0.79
Topiramate 100 mg	p = 0.43	p = 0.41	p = 0.92	p = 0.74	p = 0.89	p = 0.87	p = 0.31	p = 0.29	p = 0.75
Topiramate 200 mg	p = 0.87	p = 0.55	p = 0.53	p = 0.71	p = 0.45	p = 0.44	p = 0.58	p = 0.55	p = 0.86

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Discontinuation due to Adverse Events

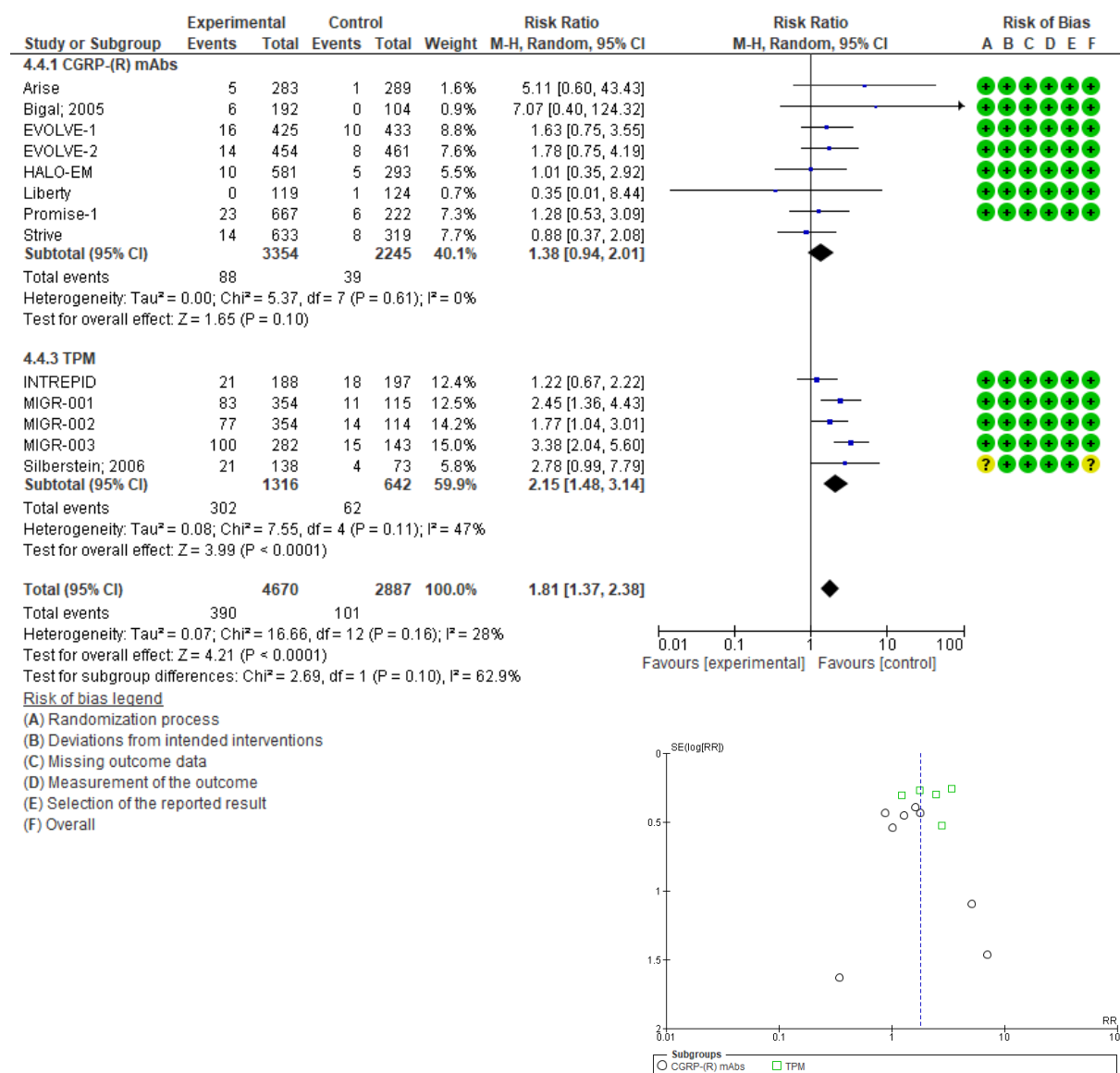
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 9 | Discontinuation due to adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

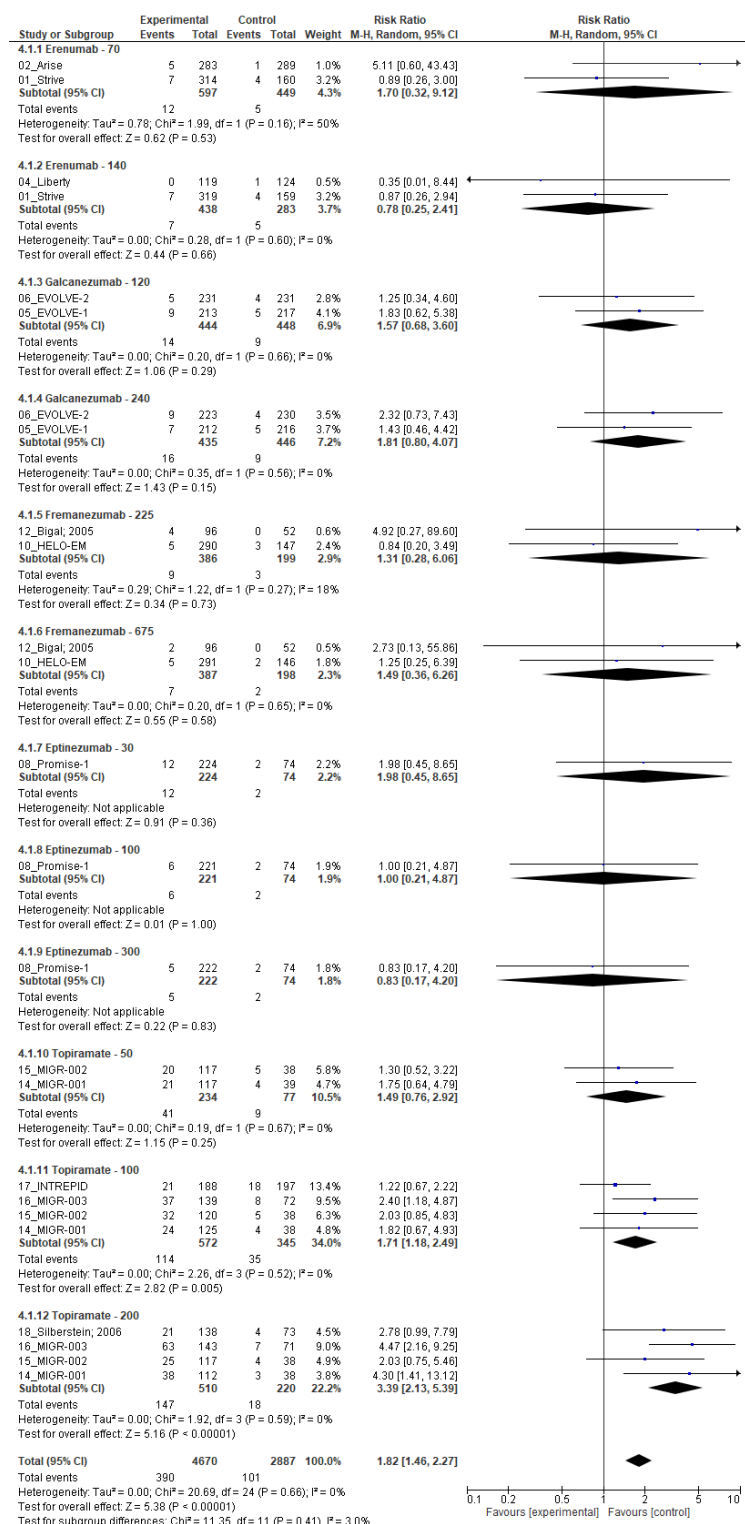
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 10 | Discontinuation due to adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 11 | Discontinuation due to adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

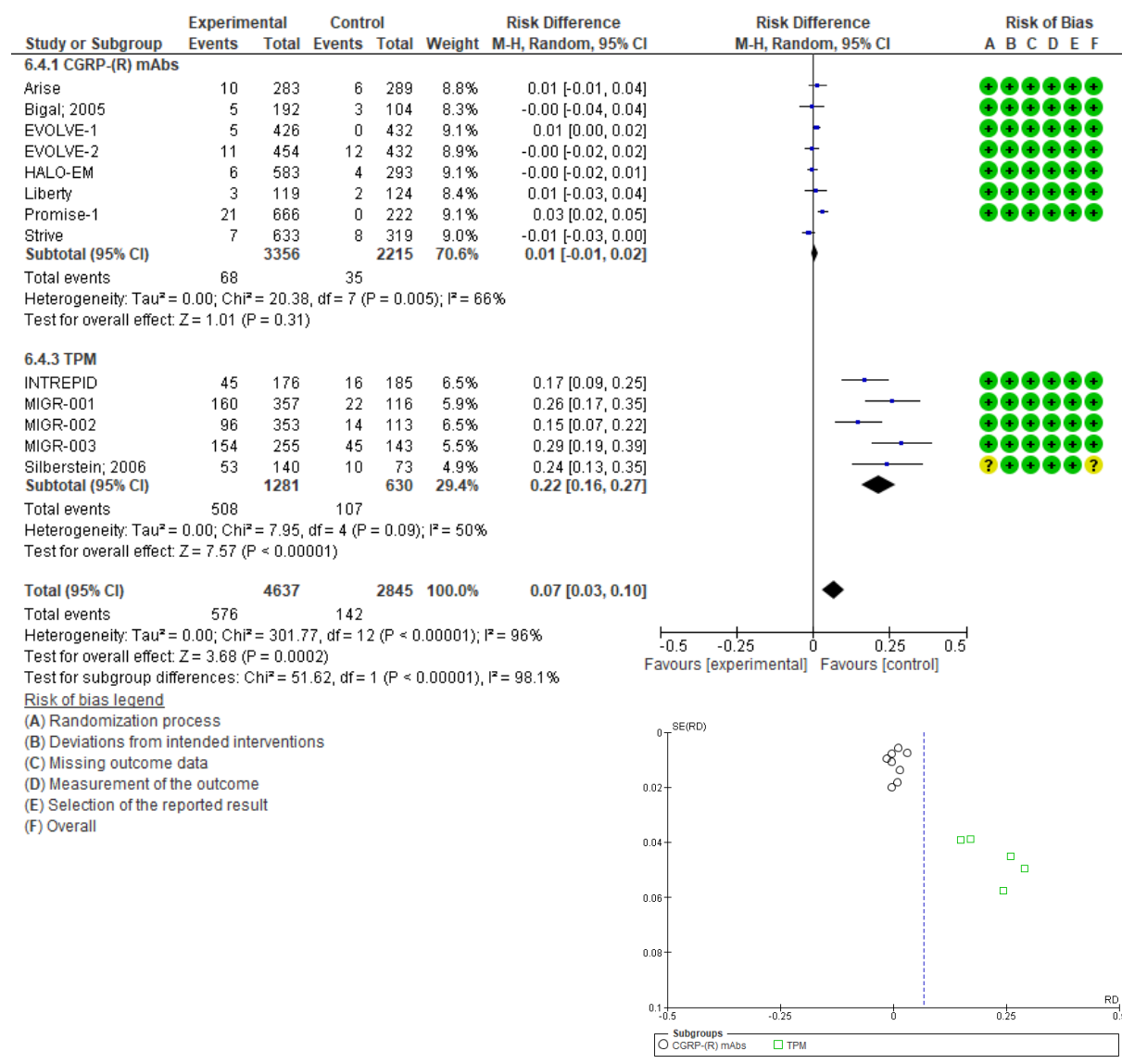
Additional Table 5 | Comparisons of discontinuation due to adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.88	p = 0.34	p = 0.92	p = 0.72	p = 0.88	p = 0.99	p = 0.73	p = 0.66	p = 0.52
Topiramate 100 mg	p = 0.99	p = 0.19	p = 0.85	p = 0.91	p = 0.59	p = 0.86	p = 0.85	p = 0.52	p = 0.39
Topiramate 200 mg	p = 0.44	p = 0.02	p = 0.11	p = 0.19	p = 0.24	p = 0.29	p = 0.50	p = 0.15	p = 0.33

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Cognitive-Related Adverse Events

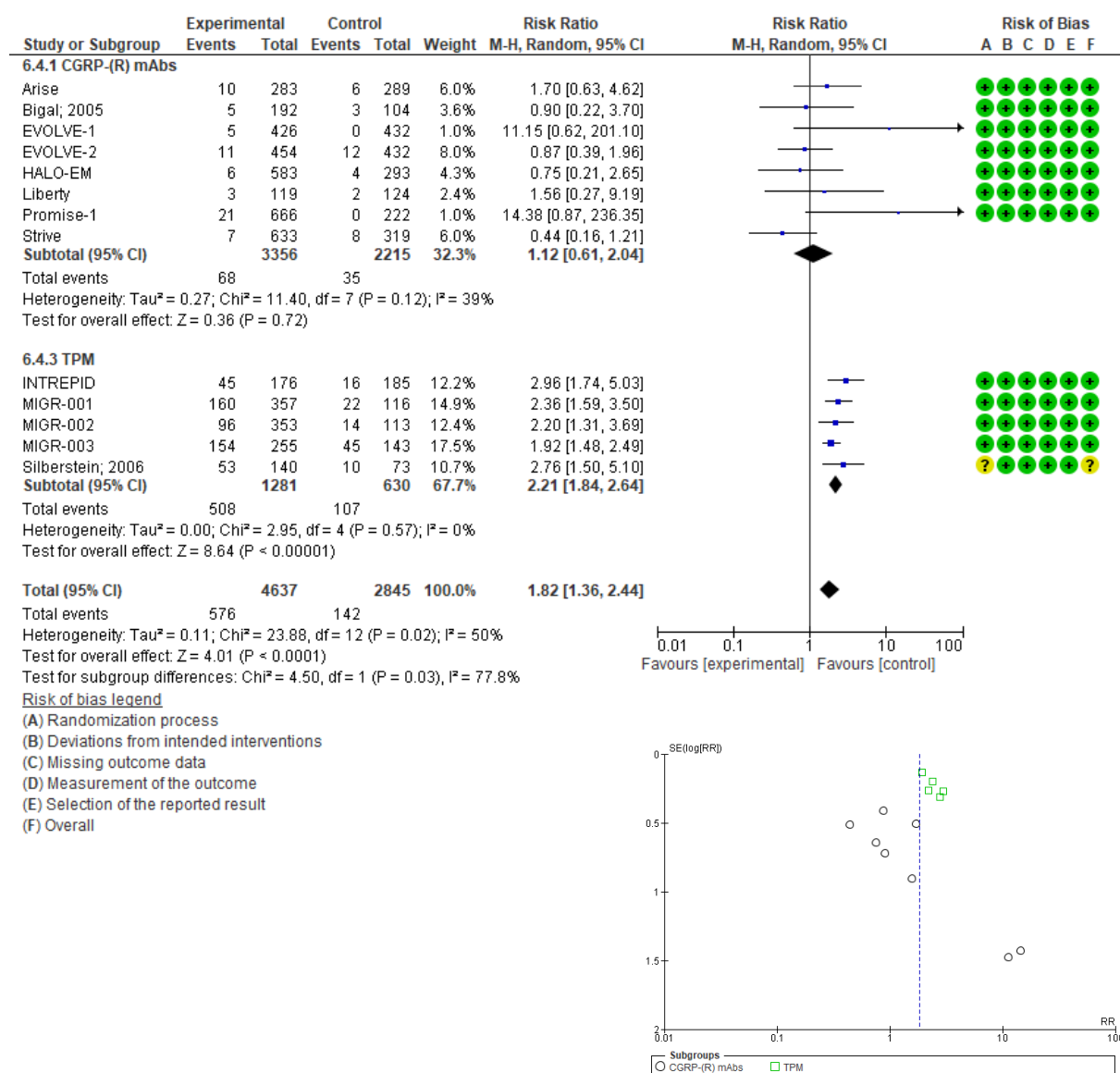
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 12 | Cognitive-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

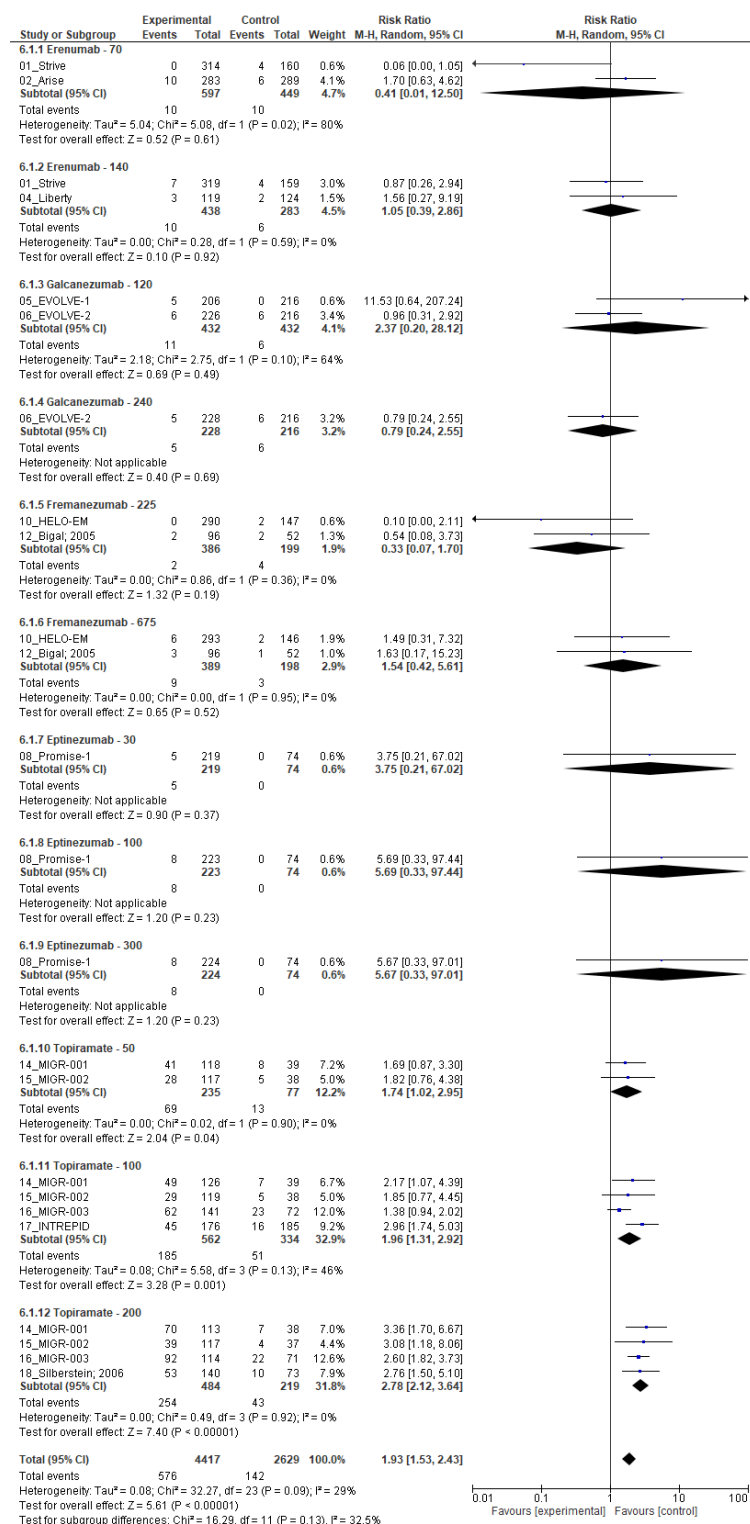
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 13 | Cognitive-related adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 14 | Cognitive-related adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

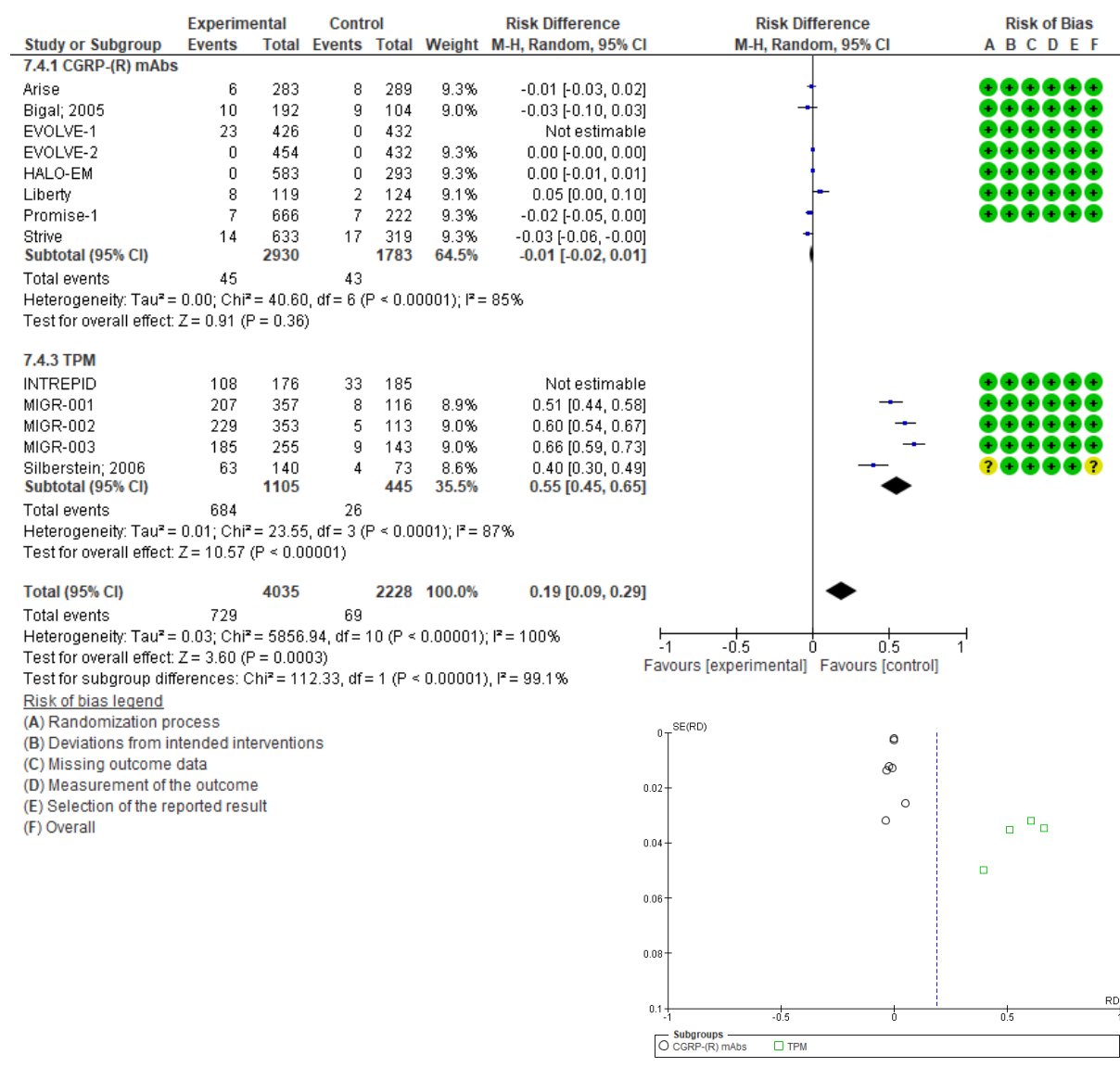
Additional Table 6 | Comparisons of cognitive-related adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.41	p = 0.38	p = 0.81	p = 0.23	p = 0.06	p = 0.86	p = 0.61	p = 0.42	p = 0.42
Topiramate 100 mg	p = 0.37	p = 0.26	p = 0.88	p = 0.15	p = 0.04	p = 0.73	p = 0.66	p = 0.47	p = 0.47
Topiramate 200 mg	p = 0.27	p = 0.07	p = 0.90	p = 0.04	p = 0.01	p = 0.38	p = 0.84	p = 0.62	p = 0.62

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Sensory or Pain-Related Adverse Events

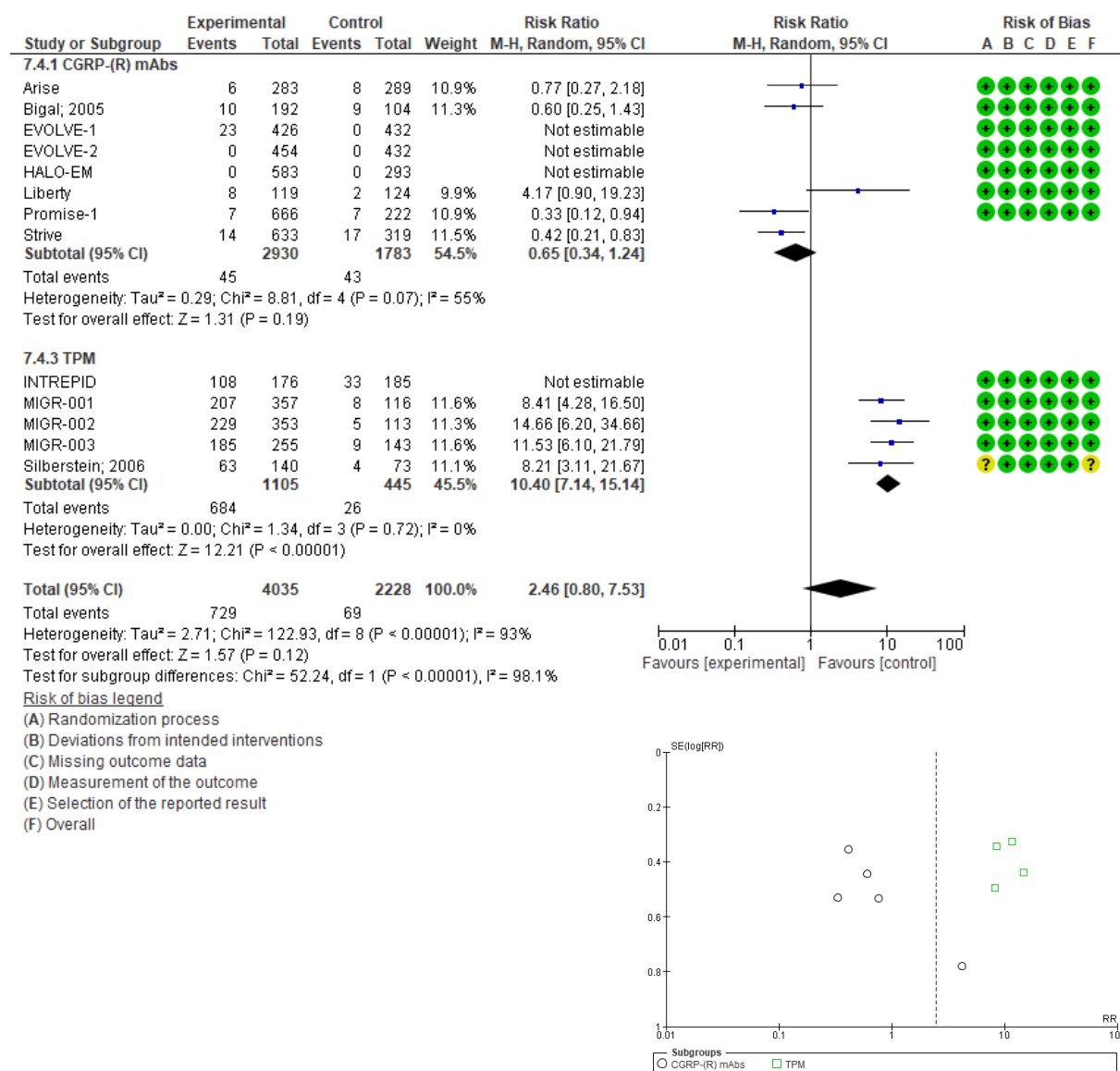
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 15 | Sensory or pain-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

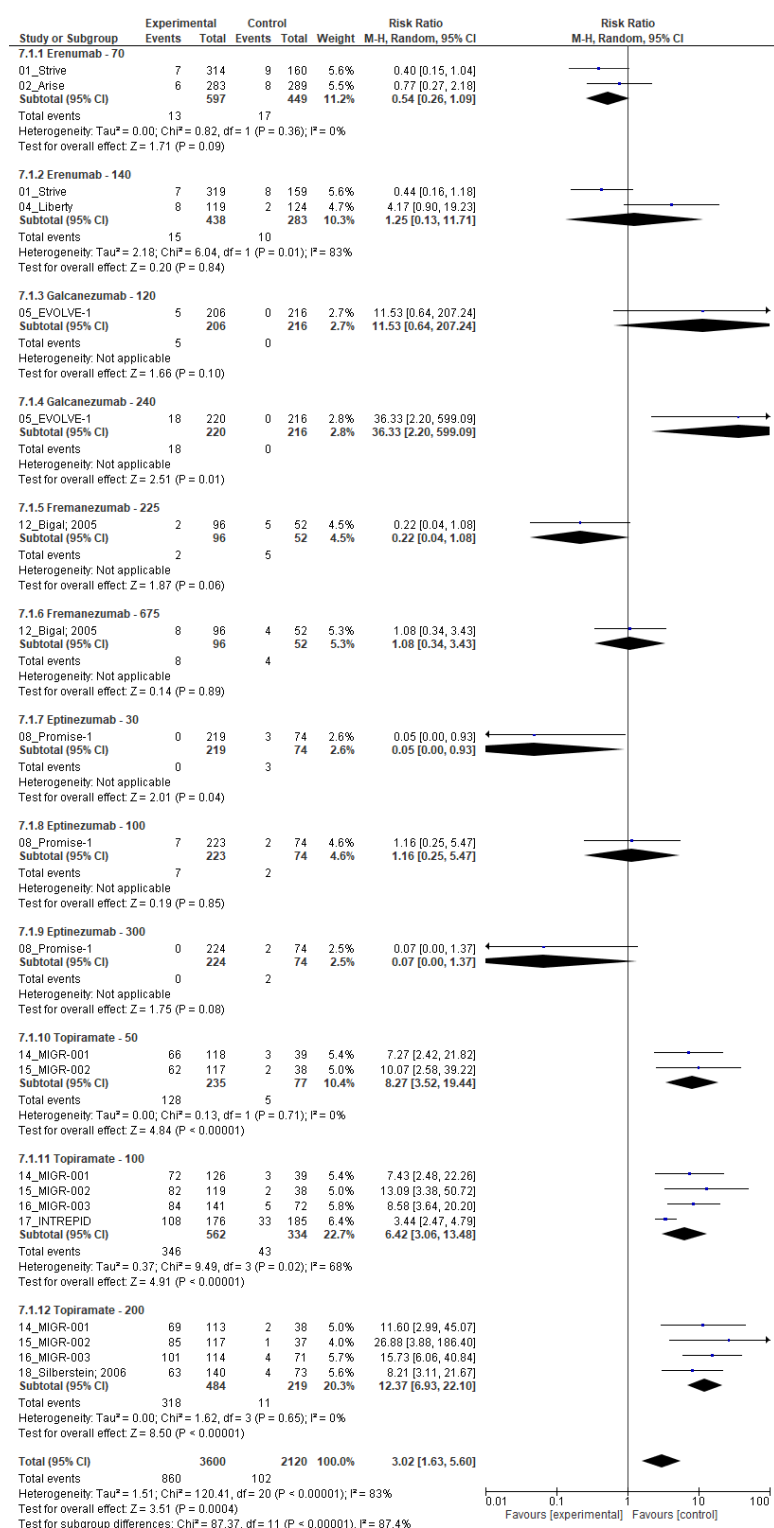
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 16 | Sensory or pain-related adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 17 | Sensory or pain-related adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

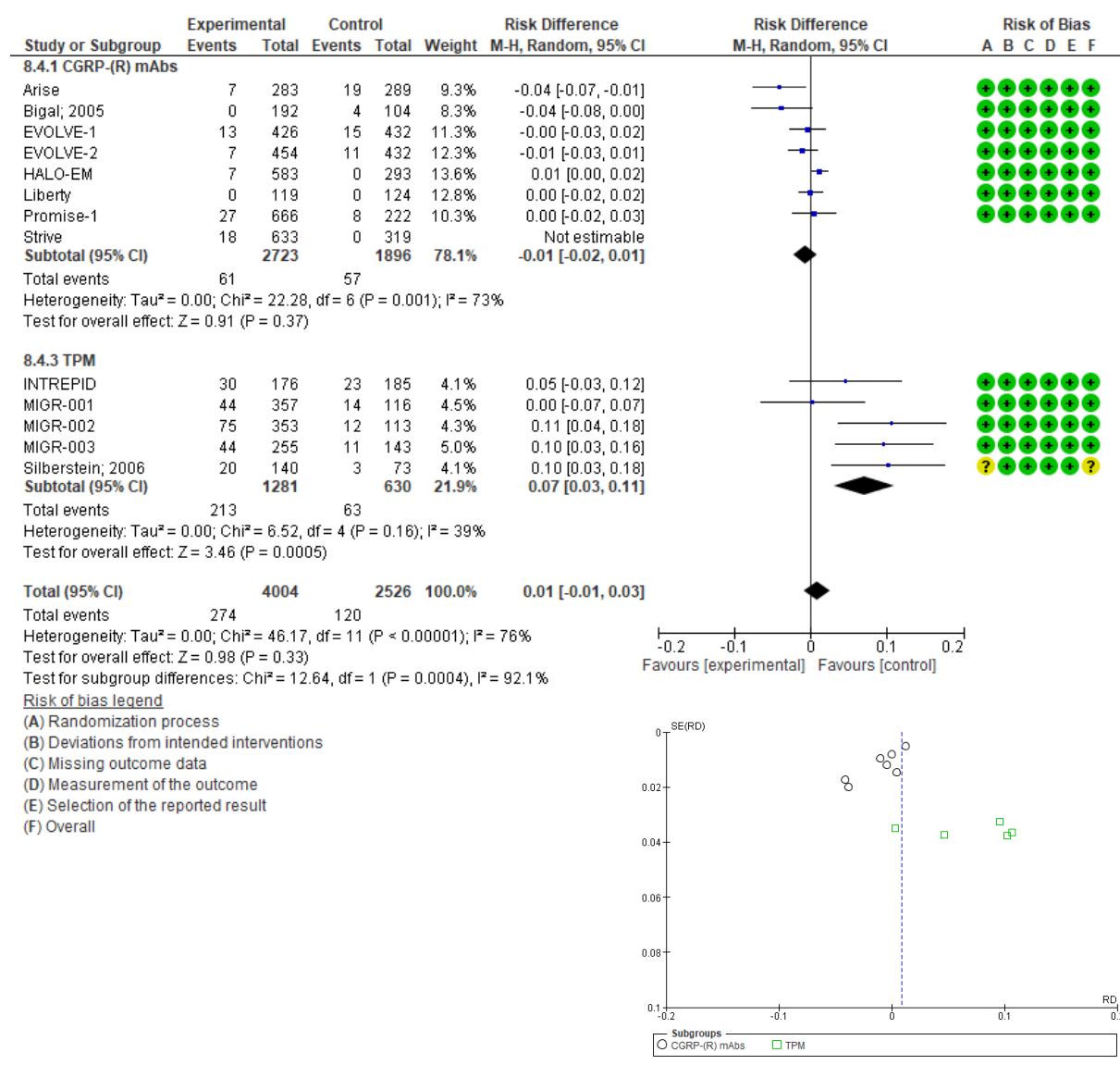
Additional Table 7 | Comparisons of sensory or pain-related adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.001	p = 0.12	p = 0.83	p = 0.32	p = 0.001	p = 0.005	p = 0.001	p = 0.03	p = 0.003
Topiramate 100 mg	p = 0.001	p = 0.17	p = 0.70	p = 0.24	p = 0.001	p = 0.01	p = 0.002	p = 0.05	p = 0.004
Topiramate 200 mg	p = 0.001	p = 0.05	p = 0.96	p = 0.46	p = 0.001	p = 0.001	p = 0.001	p = 0.005	p = 0.001

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Gastrointestinal-Related Adverse Events

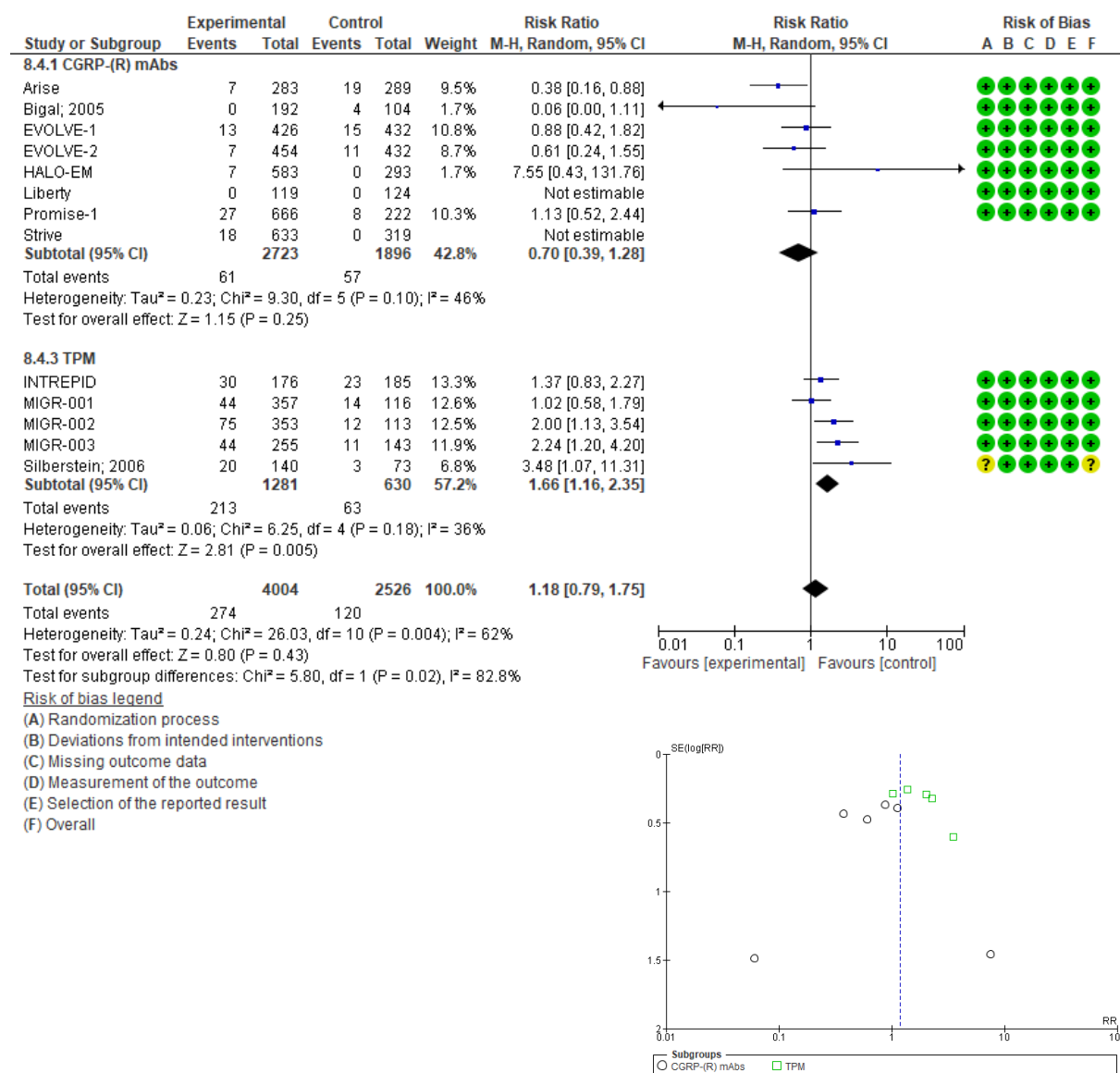
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 18 | Gastrointestinal-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

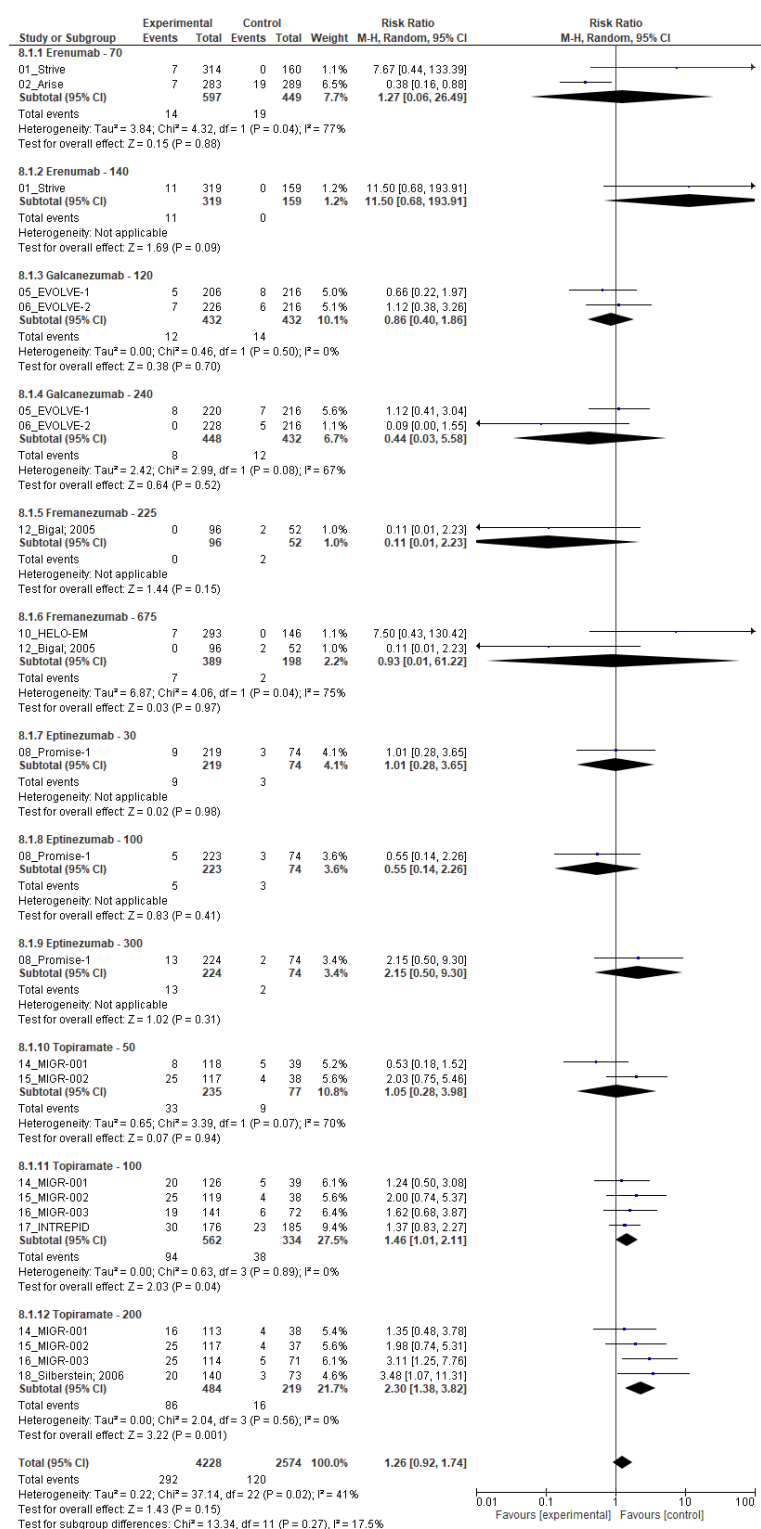
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 19 | Gastrointestinal-related adverse events adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 20 | Gastrointestinal-related adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

• Doses given in milligram (mg)

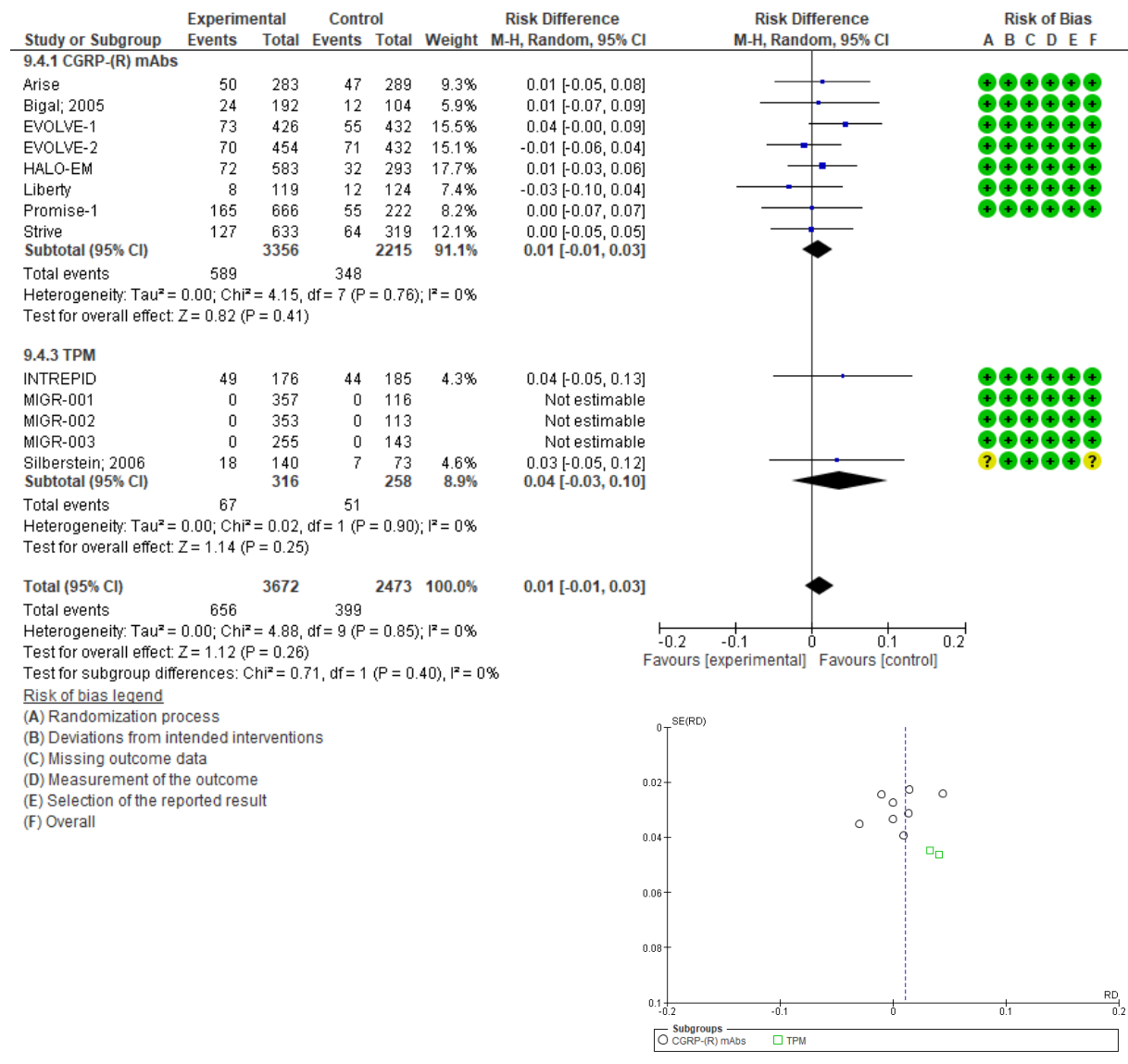
Additional Table 8 | Comparisons of gastrointestinal-related adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.91	p = 0.13	p = 0.8	p = 0.55	p = 0.18	p = 0.96	p = 0.97	p = 0.52	p = 0.48
Topiramate 100 mg	p = 0.93	p = 0.16	p = 0.22	p = 0.36	p = 0.09	p = 0.83	p = 0.59	p = 0.19	p = 0.62
Topiramate 200 mg	p = 0.70	p = 0.27	p = 0.04	p = 0.21	p = 0.05	p = 0.67	p = 0.24	p = 0.06	p = 0.93

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Infections and Infestations-Related Adverse Events

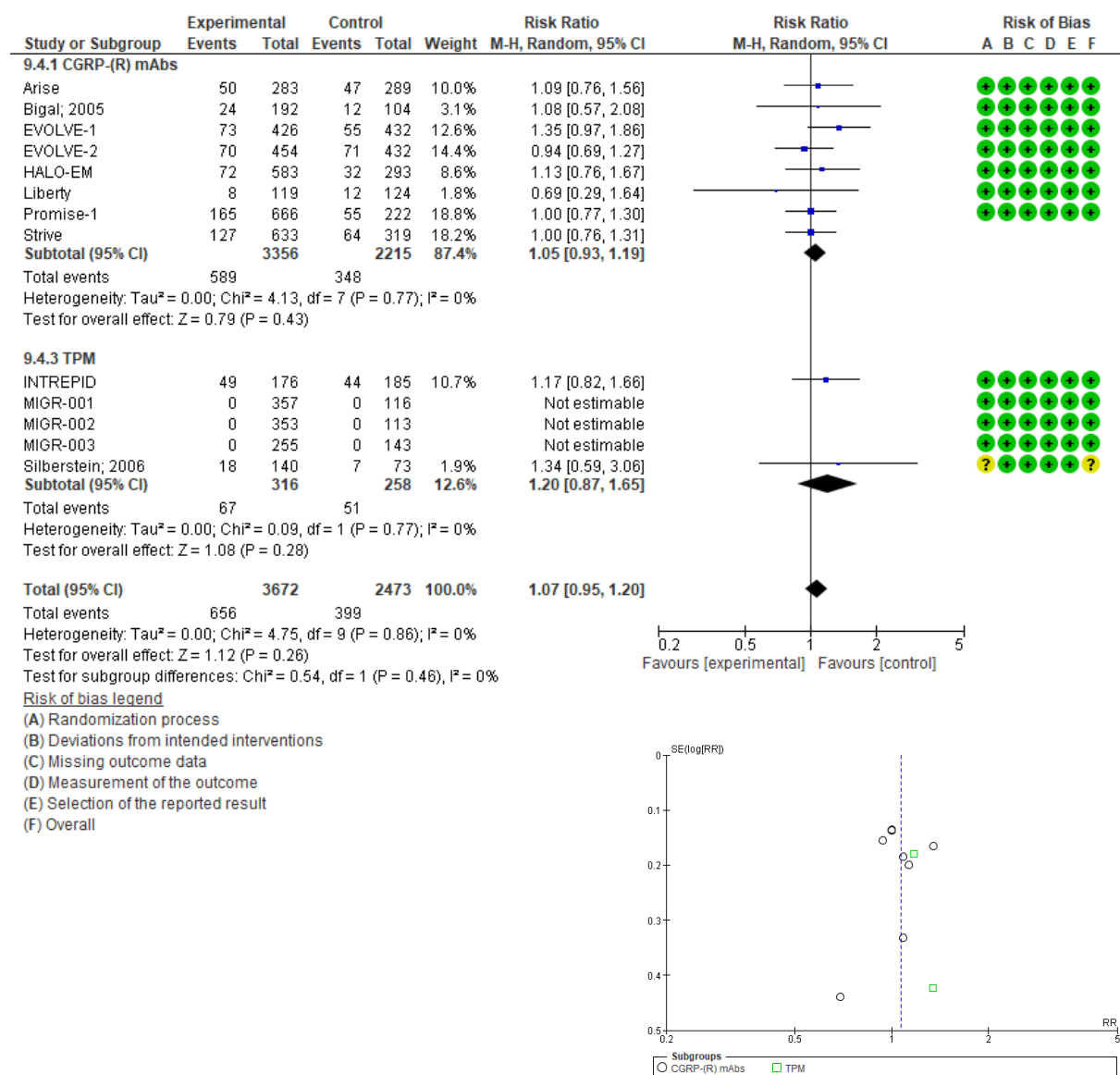
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 21 | Infections and infestations-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

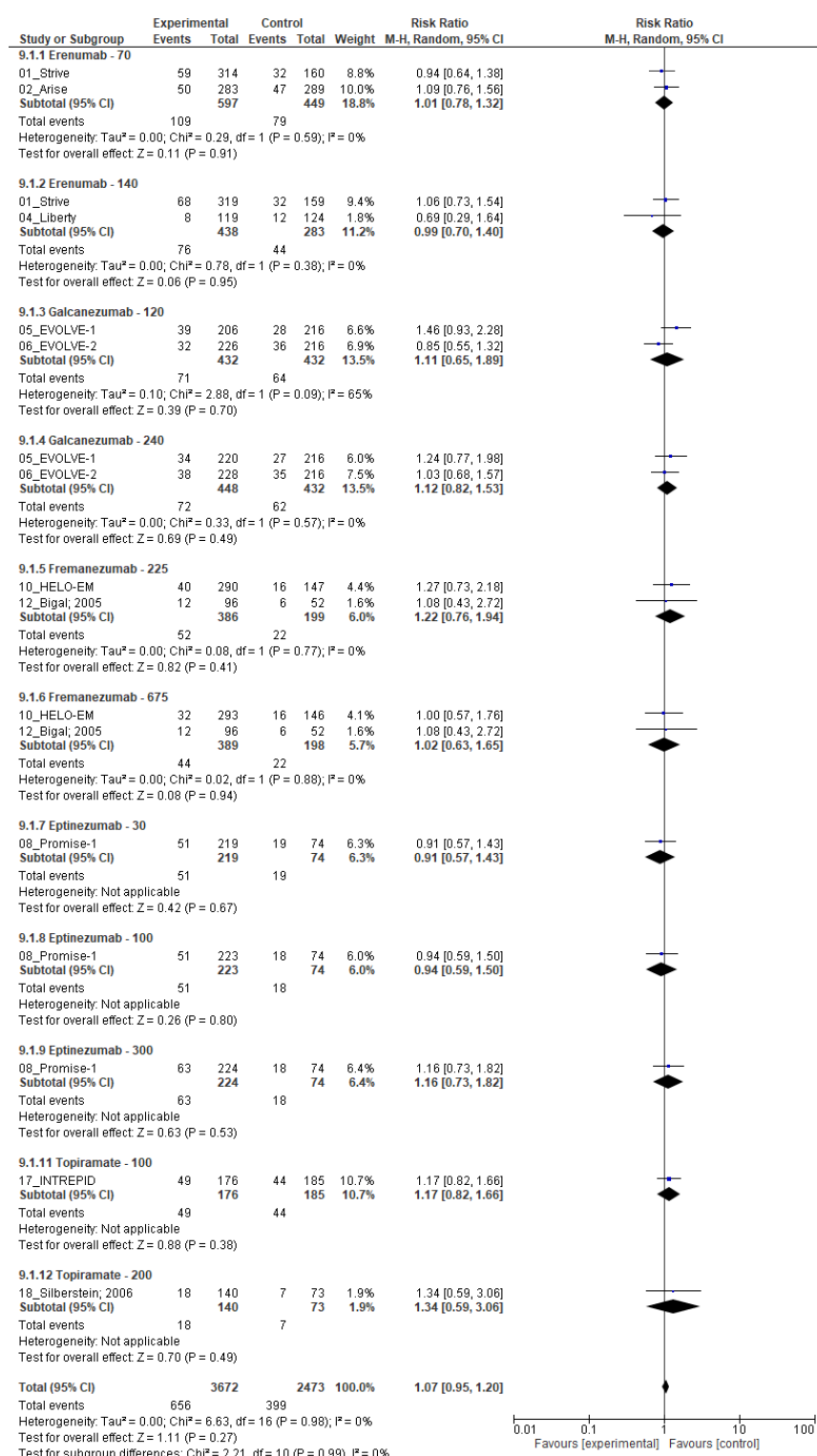
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 22 | Infections and infestations-related adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 23 | Infections and infestations-related adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

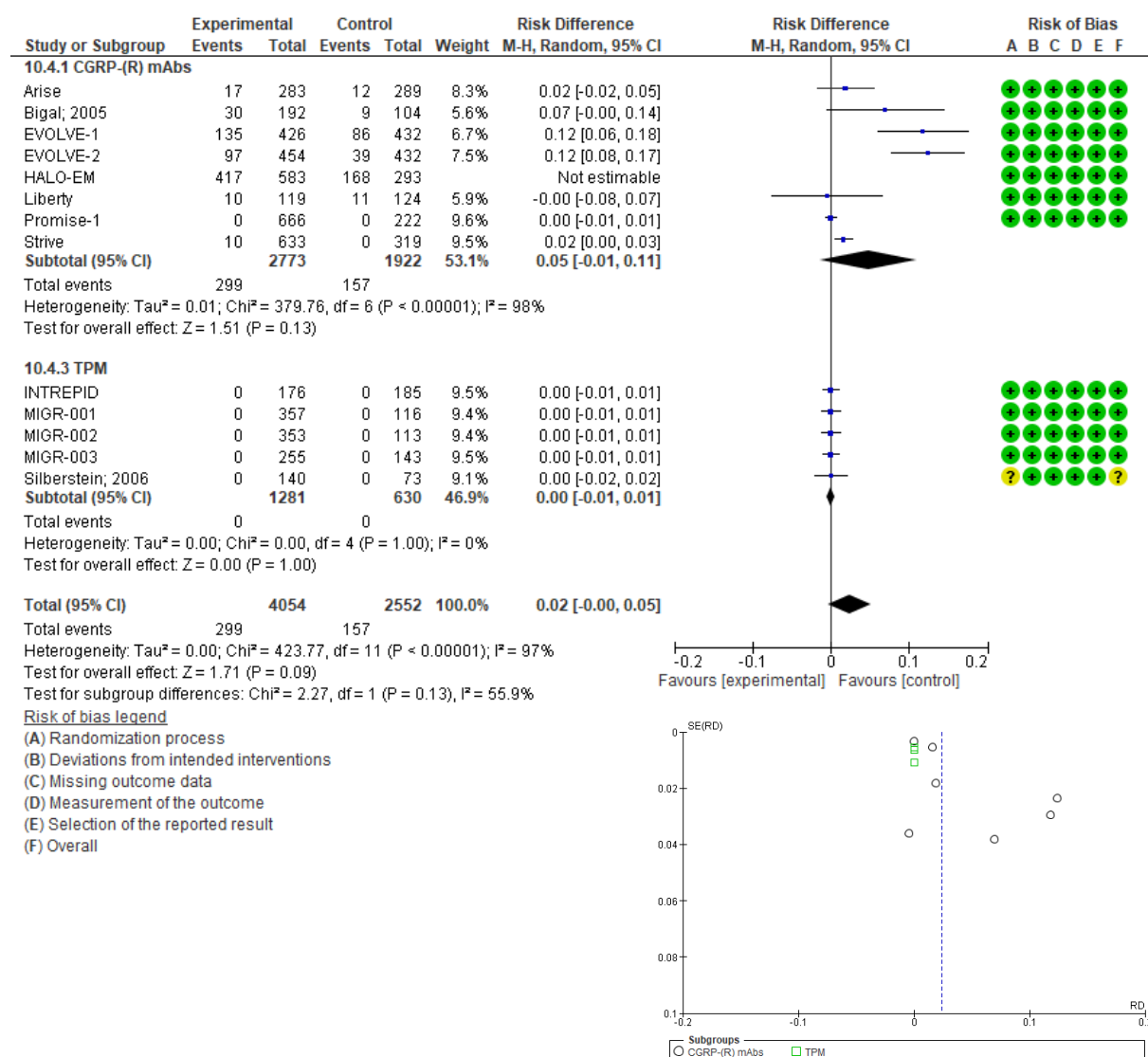
Additional Table 9 | Comparisons of infections and infestations-related adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	-	-	-	-	-	-	-	-	-
Topiramate 100 mg	p = 0.52	p = 0.50	p = 0.87	p = 0.84	p = 0.90	p = 0.65	p = 0.38	p = 0.46	p = 0.97
Topiramate 200 mg	p = 0.53	p = 0.51	p = 0.71	p = 0.68	p = 0.84	p = 0.57	p = 0.42	p = 0.46	p = 0.76

GRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

Administration Site-Related Adverse Events

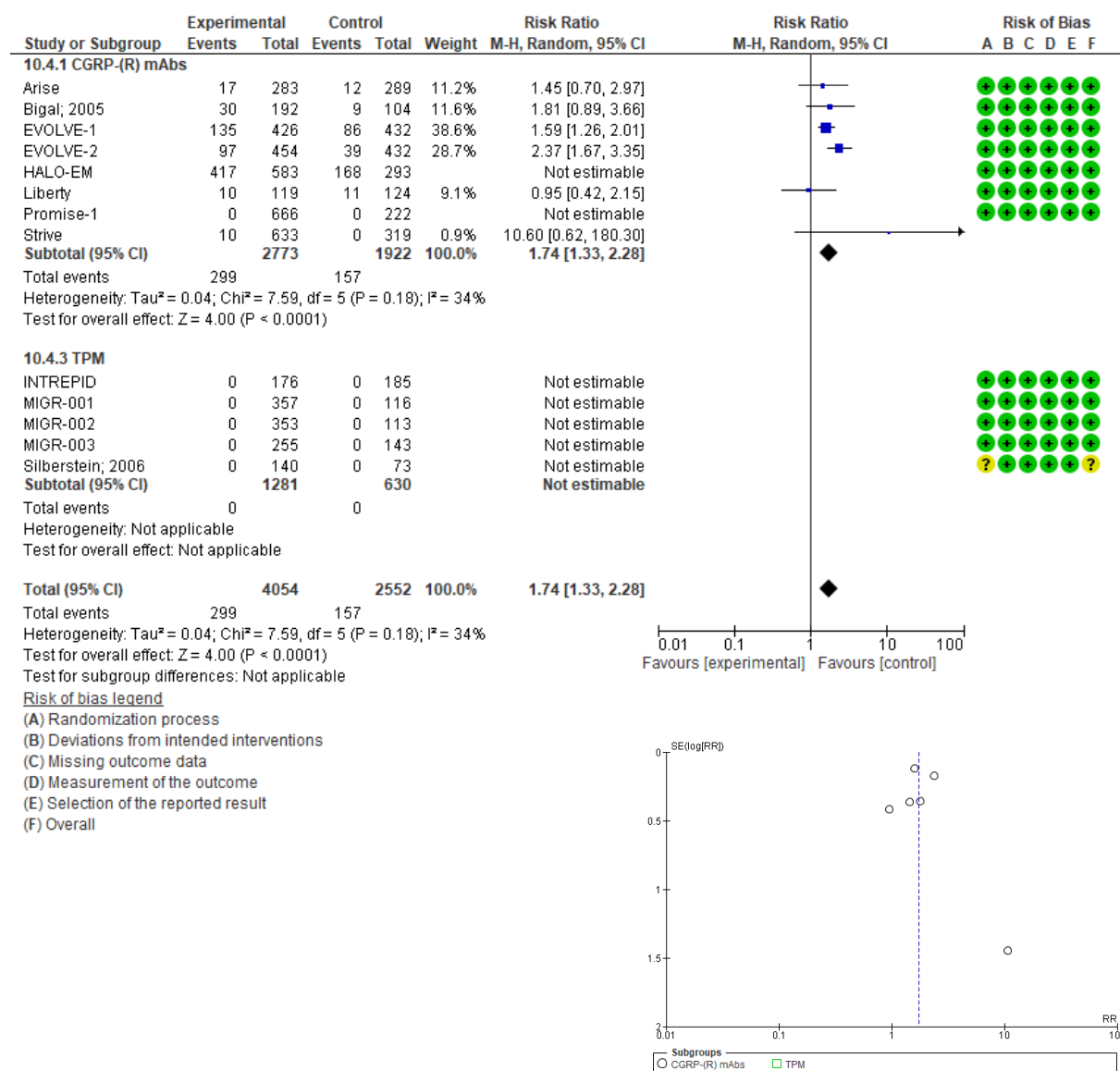
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 24 | Administration site-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot

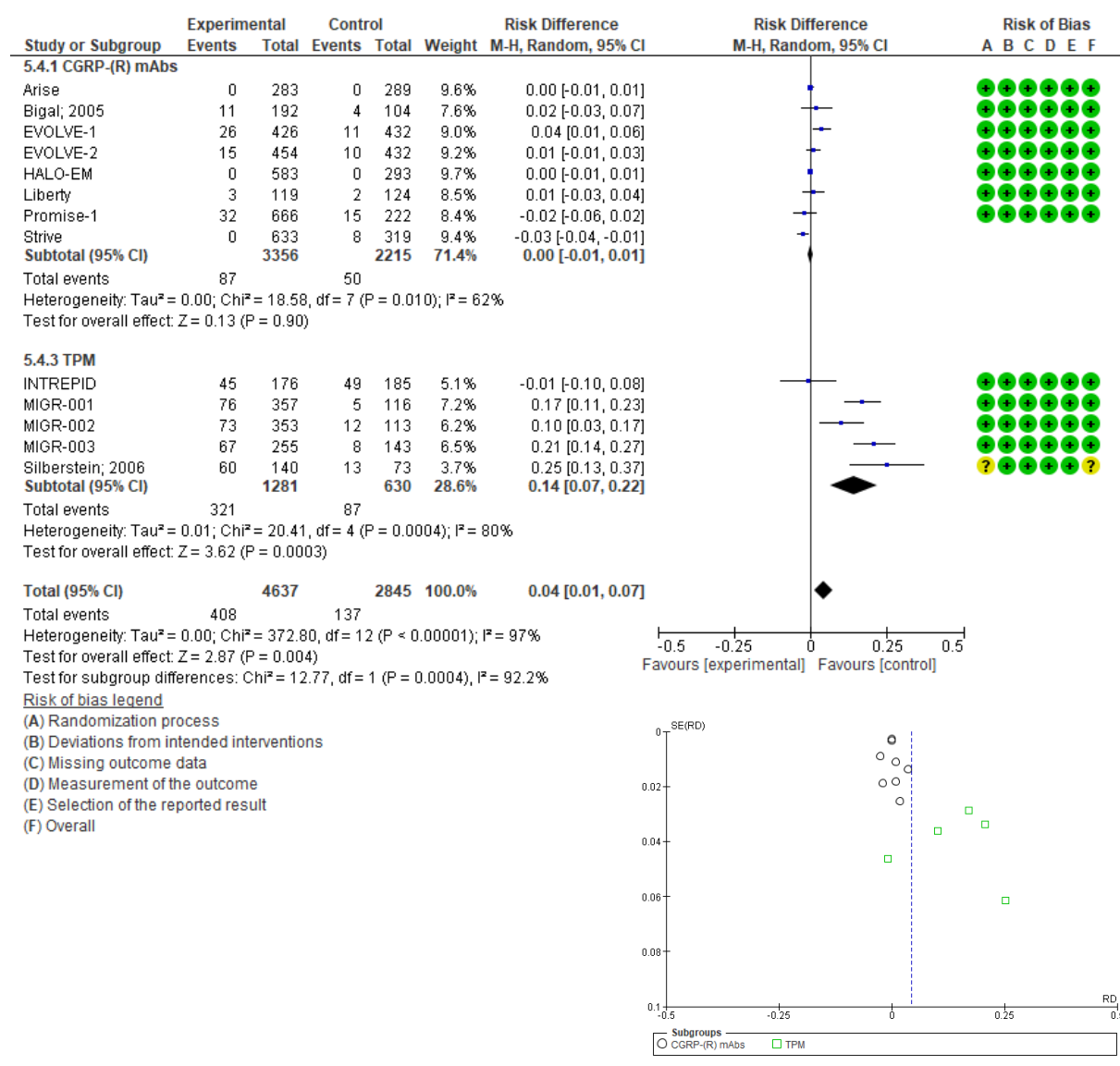


Additional Figure 25 | Administration site-related adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

General-Related Adverse Events

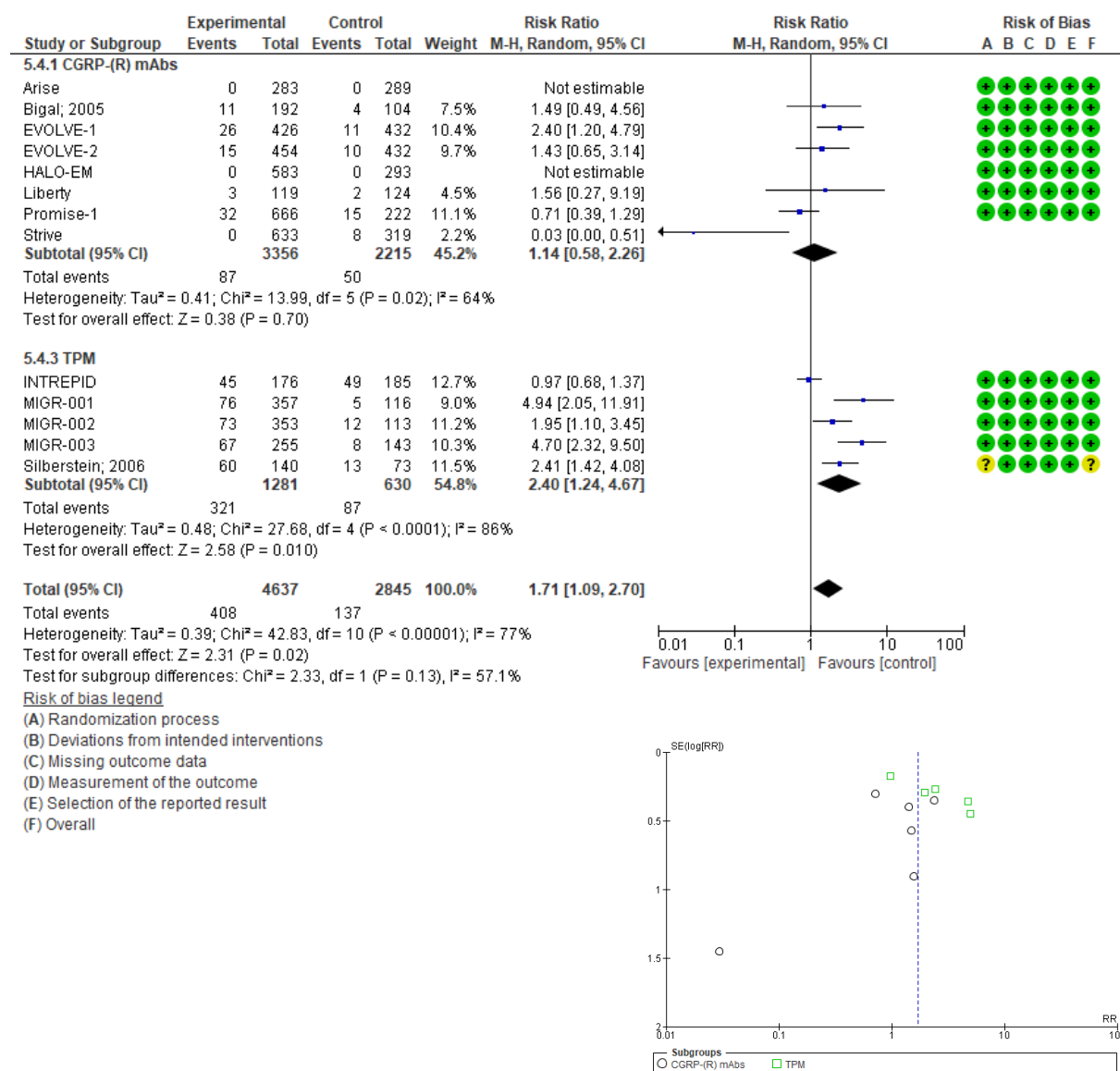
Model 1 | Risk Difference, Risk of Bias outcomes, and Funnel plot



Additional Figure 27 | General-related adverse events model 1 [Risk Difference, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

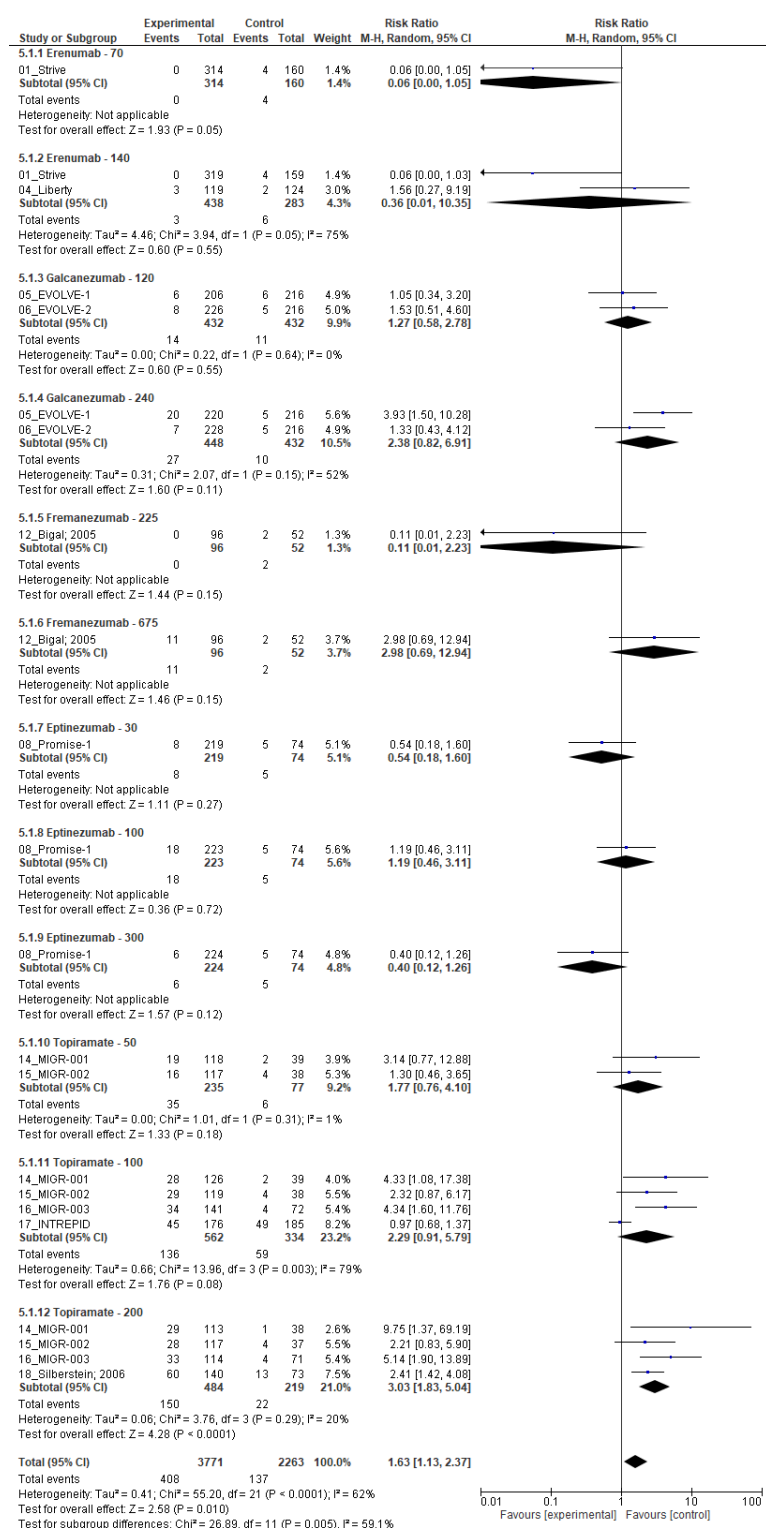
Model 1 | Risk Ratio, Risk of Bias outcomes, and Funnel plot



Additional Figure 28 | General-related adverse events model 1 [Risk Ratio, Risk of Bias outcomes, and Funnel plot]

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies; TPM = topiramate

Model 2 | Risk Ratio



Additional Figure 29 | General-related adverse events model 2 [Risk Ratio] •

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies

- Doses given in milligram (mg)

Additional Table 11 | Comparisons of general-related adverse events between the CGRP(R) mAbs and topiramate model 2 [Risk ratio]

	Erenumab 70 mg	Erenumab 140 mg	Galcanezumab 120 mg	Galcanezumab 240 mg	Fremanezumab 225	Fremanezumab 675	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Topiramate 50 mg	p = 0.03	p = 0.37	p = 0.57	p = 0.67	p = 0.08	p = 0.55	p = 0.09	p = 0.54	p = 0.04
Topiramate 100 mg	p = 0.02	p = 0.30	p = 0.34	p = 0.96	p = 0.06	p = 0.77	p = 0.05	p = 0.34	p = 0.02
Topiramate 200 mg	p = 0.008	p = 0.22	p = 0.07	p = 0.69	p = 0.03	p = 0.98	p = 0.005	p = 0.06	p = 0.002

CGRP(R) = calcitonin gene-related peptide or its' receptor; mAbs = monoclonal antibodies