APPENDIX F. ADVERSE EFFECTS

For all studies reporting between group data for adverse effects, we calculated baseline risk, relative risk, pooled relative risk, and absolute risk difference using the following equations.

- Absolute risk difference = $|((Baseline\ Risk) * (Relative\ Risk - 1))|$
- Baseline Risk = $\frac{Total\ \#\ Events\ in\ Control\ Group}{Total\ \#\ people\ in\ control\ group}$
- Relative Risk = $\frac{\frac{Total\ \#\ Events\ in\ Intervention\ Group}{Total\ \#\ People\ in\ Intervention\ Group}}{\frac{Total\ \#\ Events\ in\ Control\ Group}{Total\ \#\ People\ in\ Control\ Group}}$

Our 3 member technical expert panel (TEP) identified key adverse effects for each intervention (see Table D-1 below). We extracted data for each adverse effect (when reported by group) from each study. Absolute risk difference between intervention vs. placebo/sham may be found in the map by hovering over the orange dots for "Adverse Effects" on Map 1.

Table D-1. Key Adverse Events by Intervention

Intervention	Adverse Events (AEs) Identified for Extraction* (additional synonyms extracted in parentheses)	Number of Studies Reporting AE data
Candesartan	Dizziness, hypotension, increased creatinine/impaired kidney function, lightheadedness, syncope (tendency to faint)	1
Lisinopril	Dizziness, hypotension, lightheadedness	1
Topiramate	Acute angle glaucoma, cognitive impairment (cognitive difficulties, difficulty with concentration/ attention, difficulty with memory), decreased appetite (anorexia), kidney stones, paresthesias/tingling (distal paresthesias), teratogenicity, weight loss (slight weight loss), worsened mood (depression, emotional lability)	13
Valproate/ Valproic acid	Dizziness, fatigue (asthenia, tiredness), general adverse events, hair loss, liver problems, teratogenicity, tremor, weight gain	6
Metoprolol/ Propanolol	Bradycardia (low heart rate at exercise), dizziness, erectile dysfunction, exercise intolerance, fatigue (asthenia, tiredness), general adverse events, hypotension, lightheadedness, serious adverse events	Metoprolol – 3 Propranolol – 6

Intervention	Adverse Events (AEs) Identified for Extraction* (additional synonyms extracted in parentheses)	Number of Studies Reporting AE data
OnabotulinumtoxinA	Difficulty breathing, double vision, eyelid droop (transient frontalis muscle asymmetry, upper eyelid ptosis), general adverse events, neck pain, neck weakness, serious adverse events, trouble swallowing/ dysphagia, worsened headache	15
CGRP antagonists (atogepant, eptinezumab, erenumab, fremanezumab, galcanezumab)	Constipation, flu-like symptoms, general adverse events, injection-site reactions**, joint or muscle aches, new onset hypertension, rhinorrhea, serious adverse events	Atogepant – 1 Eptinezumab – 3 Erenumab – 6 Fremanezumab – 5 Galcanezumab – 7
Non-invasive vagus nerve stimulator (Gammacore)	Coughing or tickling (oropharyngeal pain), dizziness, tingling in neck	1
Transcutaneous supraorbital nerve stimulation (Cefaly)	Fatigue, paresthesias/tingling, worsened headache	1
Venlafaxine	Anxiety, constipation, dizziness, fatigue (asthenia, tiredness), hypertension, insomnia, nausea (gastric intolerance), weight gain, withdrawal syndrome, worsened mood	1
Amitriptyline/ Nortryptiline	Blurred vision, cardiac arrhythmia, constipation, dry eyes, dry mouth, nightmares, somnolence (drowsiness), tachycardia, urinary retention, weight gain	Amitriptyline - 2 Nortryptiline - 0

*Specified by 3 members of the TEP as key adverse effect for clinical decision-making

** If multiple adverse events at the injection site reported, most frequent adverse event was extracted