

SEPTEMBER 2024

SYSTEMATIC REVIEW AND META-ANALYSIS

Behavioral Interventions for Migraine Prevention

In Partnership with



Behavioral Interventions for Migraine Prevention

Prepared for:

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

and

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Contract No. 75Q80120D00002

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This report is based on research conducted by the ECRI-Penn Evidence-based Practice Center under Contract No. 75Q80120D00002 from the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD. The work was funded by the Patient-Centered Outcomes Research Institute (PCORI®) through a Memorandum of Agreement Amendment, number 20-603M-23. This report is PCORI Publication No. 2024-SR-01. Funders were kept informed throughout the review process regarding the scope and the findings. The findings and conclusions are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ or PCORI, its Board of Governors, or Methodology Committee. Therefore, no statement in this report should be construed as an official position of PCORI, AHRQ, or the U.S. Department of Health and Human Services.

Six authors (Treadwell, Tsou, Rouse, Ivlev, Fricke, and Mull) do not have any affiliations or financial involvement that conflicts with the material presented in this report. Four authors (Buse, Powers, Minen, and Szperka) have declarations that could constitute potential intellectual and/or financial conflicts of interest. Dr. Buse has been a consultant to Amgen, AbbVie, Biohaven, Collegium, Lilly, Lundbeck, Theranica, and Teva. Dr. Powers provides scientific consultation to Theranica. Dr. Minen is a co-developer of the RELAXaHEAD application, co-owned by NYU and Irody, Inc. Dr. Szperka or her institution have received compensation for serving as a consultant for Teva, Lundbeck, AbbVie, and Impel Neuropharma. She has received personal compensation for serving on a data safety monitoring board for Eli Lilly, Upsher-Smith, and Lundbeck. Mitigation plan: In this review, these four investigators were not involved in the selection of studies for inclusion (title, abstract, and full-text screening); the risk of bias assessment for any publications; data extraction; meta-analysis or any data synthesis; or strength-of-evidence rating.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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A representative from AHRQ served as a Contracting Officer's Representative and reviewed the contract deliverables for adherence to contract requirements and quality. AHRQ did not directly participate in the literature search, determination of study eligibility criteria, data analysis, interpretation of data, or preparation or drafting of this report.

AHRQ and PCORI appreciate appropriate acknowledgment and citation of their work. Suggested language for acknowledgment: This work was based on an evidence report, Behavioral Interventions for Migraine Prevention, by the Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ) and funded by the Patient-Centered Outcomes Research Institute (PCORI®).

Suggested citation: Treadwell JR, Tsou AY, Rouse B, Ivlev I, Fricke J, Buse D, Powers S, Minen M, Szperka C, Mull NK. Behavioral Interventions for Migraine Prevention. Comparative Effectiveness Review No. 270. (Prepared by the ECRI-Penn Evidence-based Practice Center under Contract No. 75Q80120D00002.) AHRQ Publication No. 24-EHC015. PCORI Publication No. 2024-SR-01. Rockville, MD: Agency for Healthcare Research and Quality; September 2024. DOI: <https://doi.org/10.23970/AHRQEPCCER270>. Posted final reports are located on the Effective Health Care Program [search page](#).

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The Patient-Centered Outcomes Research Institute® (PCORI®) requested this report from the EPC Program at AHRQ. AHRQ assigned this report to the EPC (ECRI-Penn Evidence-based Practice Center, Contract No. 75Q80120D00002).

AHRQ EPC reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

The Patient-Centered Outcomes Research Institute® (PCORI®) was established to fund research that helps patients and caregivers make better informed healthcare choices. To fulfill its authorizing mandate, PCORI partners with AHRQ to generate evidence synthesis products and make comparative effectiveness research more available to patients and providers.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see <https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis>.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve healthcare quality. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Acknowledgments

We greatly appreciate the assistance of ECRI employees Lindsey Miller (project management), Kristy McShea (literature searches), Helen Dunn (database management), Katherine Donahue (references and document procurement), Michael Phillips (copyediting), and Britney Hall (formatting and 508 compliance).

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In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Behavioral Interventions for Migraine Prevention

Structured Abstract

Objectives. Behavioral interventions for migraine prevention can offer an important alternative or complement to medications. An updated systematic review is needed to support evidence-based guidance for clinicians and identify evidence gaps for future research.

Data Sources. MEDLINE, Embase, PsycINFO, PubMed, the Cochrane Database of Systematic Reviews, clinicaltrials.gov, and grey literature sources for randomized trials published from January 1, 1975, to August 24, 2023.

Review Methods. A multidisciplinary expert panel including adult and pediatric clinical psychologists, adult and pediatric neurologists, primary care physicians, researchers, funders, children and adults with migraine and their caregivers provided input on scope and methods. We included randomized trials enrolling at least 80% participants with migraine (or outcomes for migraine participants reported separately) and reporting a primary outcome at 4 weeks or more after the start of treatment. Primary outcomes were migraine/headache attack frequency, migraine disability, and migraine-related quality of life. We did not require a formal diagnosis of migraine (i.e., International Classification of Headache Disorders criteria). The review team tabulated information from included trials, rated risk of bias, conducted pairwise meta-analyses, and rated the strength of evidence (SOE). The SOE is a formal rating of the reviewer's confidence in the estimated effects.

Results. For adults, we included 50 trials published since 1978. Most preventive interventions were multicomponent, using one or more of five primary components (cognitive behavioral therapy [CBT], biofeedback, relaxation training, mindfulness-based therapies, and/or education). Most trials were at high risk of bias, primarily due to measurement bias and incomplete data. Given the small amount of evidence on any given intervention/comparator/outcome combination, data were often insufficient to permit conclusions. For adults, we found that any of three components (CBT, relaxation training, mindfulness-based therapies) may reduce migraine/headache attack frequency (SOE: low). Education alone that targets behavior may improve migraine-related disability (SOE: low). For three other interventions (biofeedback, acceptance and commitment therapy, and hypnotherapy), evidence was insufficient to permit conclusions. We also found that mindfulness-based therapy may improve migraine disability more than education, and relaxation + education may improve migraine-related quality of life more than propranolol (SOE: low). For children/adolescents, we included 13 trials published since 1984 (average age 14.5), but the evidence was only sufficient to conclude that CBT + biofeedback + relaxation training may reduce migraine attack frequency and disability more than education alone (SOE: low).

Conclusion. Several behavioral interventions appear to reduce migraine/headache attack frequency in adults. Evidence consisted primarily of underpowered trials of multicomponent interventions compared with various types of control groups. Future research should enroll children and adolescents, standardize intervention components to improve reproducibility, use comparison groups that control for expectation confounds, enroll larger samples, consider digital and telehealth modes of care delivery, and improve the completeness of data collection.

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Executive Summary

Main Points

- Adults: Interventions including cognitive behavioral therapy (CBT), relaxation training, or mindfulness-based treatment (alone or combined with other components) may lower migraine/headache attack frequency, and education alone may also improve migraine-related disability (strength of evidence [SOE]: All low).
- Evidence regarding adverse effects among individuals of any age, effectiveness for children and adolescents, and biopsychosocial factors is inconclusive.
- Adults: Mindfulness-based stress reduction (MBSR) may offer greater benefit for disability than education; CBT + relaxation training might result in higher migraine attack frequency but also higher quality of life (QOL) than propranolol; relaxation training may outperform CBT + relaxation + education in QOL; MBSR + education may reduce attack frequency compared with stress management training + education; and biofeedback may reduce attack frequency compared with CBT + relaxation training (SOE: All low).
- Children/adolescents: a combination of CBT, biofeedback, and relaxation training may lead to lower migraine attack frequency and disability compared with education alone (SOE: low).
- Evidence is insufficient to address the effects of individual behavioral components.
- In adults with chronic migraine, behavioral sleep modification may reduce headache frequency at 6 weeks (SOE: low); no studies were included for children.

Background and Purpose

Migraine affects one in six Americans and constitutes the second leading global cause of disability, often limiting activities during crucial life stages (e.g., schooling, parenting).¹ Migraine prevention strategies are aimed at lowering the frequency, severity, and life-affecting repercussions of migraine attacks. Behavioral interventions, including CBT, biofeedback, relaxation training, mindfulness-based therapies, and education, present a potentially beneficial alternative or adjunct to pharmacoprevention, which may be associated with adverse effects, drug interactions, and contraindications.

Existing guidance on behavioral interventions from professional societies is relatively limited and requires updating. The latest clinical practice guidelines, from 2012, exclude certain newer therapies such as mindfulness-based cognitive therapy.² Consensus statements from the American Headache Society (AHS) and the American Academy of Family Physicians (AAFP) regarding nonpharmacologic prevention for migraine were not developed from systematic reviews and did not provide guidance for prevention in pediatric and adolescent populations.³⁻⁶ Existing systematic reviews on behavioral therapies are notably outdated and do not evaluate all available preventive behavioral therapy options.⁷⁻⁹

Due to the absence of a recent, comprehensive systematic review and the accumulation of new evidence, **we conducted a systematic review to evaluate the effects of behavioral interventions for migraine prevention among children, adolescents, and adults.** Our focus included the effectiveness and comparative effectiveness of migraine-specific behavioral interventions, comparisons with pharmacotherapy, potential harms, effects of non-migraine-focused behavioral interventions, and associations between effectiveness and biopsychosocial

factors. For this review, behavioral interventions were defined as nonpharmacologic strategies intended to enhance outcomes by modifying behavior and/or ways of thinking. The Agency for Healthcare Research and Quality (AHRQ), AHS, and the Patient-Centered Outcome Research Institute (PCORI) collaborated to conceive this systematic review. The review will be used by members of AHS to inform decisions about a clinical practice guideline.

Methods

Our methods were consistent with guidance from the AHRQ Evidence-based Practice Center Program Methods Guidance (<https://effectivehealthcare.ahrq.gov/topics/ebp-methods-guide/overview>). Five Key Questions determined the scope, after consulting with a wide range of experts and incorporating perspectives from patients and caregivers. We searched MEDLINE®, Embase®, PsycINFO®, PubMed®, the Cochrane Database of Systematic Reviews, and grey literature sources for English-language randomized trials published from 1975 to August 24, 2023. We included trials conducted in countries rated as “very high” on the 2022 Human Development Index (as defined by the United Nations Development Programme). The team systematically screened trials, extracted data, assessed the risk of bias, conducted meta-analyses, and rated the strength of evidence in duplicate. We registered the protocol on PROSPERO CRD42023397752.

Results

We included 63 randomized trials published since 1978. Most evidence was inconclusive, and this section describes only our analyses that resulted in strength of evidence (SOE) ratings of low, moderate, or high.

Adults may experience a reduction in headache frequency following interventions that included a CBT component (pooled effect from 10 trials, -1.1 migraine days/month, 95% confidence interval [CI] -0.4 to -1.8, SOE: low), or relaxation training (pooled effect from 13 trials, -1 migraine day/month, 95% CI -0.4 to -1.7; SOE: low), or mindfulness-based treatment (pooled effect from 5 trials, -1 migraine day/month, 95% CI -0.2 to -1.8 SOE: low). An improvement in migraine-related disability may follow education-only interventions (pooled effect not estimable; SOE: low).

Regarding comparative effectiveness in adults, MBSR may result in clinically important lower migraine disability and higher migraine-specific quality of life (MSQOL) compared with education (1 trial, for disability the impact was 18 points on the Migraine Disability Assessment [MIDAS] scale, 95% CI 7 to 30; SOE: low). CBT + relaxation training may result in higher migraine attack frequency than propranolol (1 trial, 1.40 migraine days/month, 95% CI: 0.16 to 2.63; SOE: low), but a clinically important advantage in MSQOL (1 trial, difference of -12 points on the MSQOL, 95% CI from -18 to -7; SOE: low). Biofeedback may result in lower migraine attack frequency than a combination of CBT and relaxation training (1 trial, difference in migraine days/month of -2.2, 95% CI -4.4 to -0.1; SOE: low).

Among children and adolescents, combined CBT, biofeedback, and relaxation training are likely to result in lower migraine attack frequency (one trial, -1.6 migraine days/month, 95% CI -2.7 to -0.4) and lower disability (one trial, pediatric MIDAS [PedMIDAS] difference -11, 95% CI -20 to -2) than education alone (SOE: low). Other evidence for children and adolescents was inconclusive.

We included five studies examining the specific impact of adding a behavioral component to other behavioral components, but none of the data were sufficient to permit conclusions.

A small body of evidence explored behavioral interventions aimed at sleep in adults with chronic migraine, with one trial suggesting potential benefits of behavioral sleep modification in reducing headache frequency at 6-week followup (about 7 fewer migraine attacks/month, SOE: low). No studies assessed behavioral interventions for anxiety or depression in migraine or for children with migraine addressing behavioral interventions for sleep, anxiety, or depression.

Adverse events were often not ascertained systematically, and the extent to which behavioral interventions are associated with any adverse events remains understudied (though rarely reported), as was delivery of interventions via digital technology or telehealth.

Limitations

Intervention complexity, with much evidence coming from older trials and variations in the labeling and implementation of treatment components, introduced subjectivity to our analyses and the applicability of results. The incomplete data reporting and underpowered studies resulted in wide confidence intervals, undermining the precision of our meta-analyses. Outcome measurement inconsistencies and lack of uniform metrics across studies posed another major limitation.

Implications and Conclusions

A limited body of evidence suggests some behavioral interventions possibly offer reductions in headache frequency and disability to adults. However, the extent to which behavioral interventions offer similar or greater benefit than pharmacoprevention remains unknown. The effect of behavioral interventions in children/adolescents is mostly uncertain. Adverse events are rarely reported, although this appears understudied. Future research needs to standardize treatment components and adopt standardized outcome measures to enable better comparability across studies. Future research should also address the potential variance in treatment effectiveness across patient biopsychosocial factors, such as gender, race, and comorbidities.

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1. Introduction

1.1 Background

One in six Americans experience migraine disease, a condition that globally stands as the second leading cause of disability. Migraine often impacts individuals during crucial periods of their lives, including years of education, career progression, and child-rearing.¹ Migraine interventions aim to decrease the frequency, severity, and negative life impact of migraine attacks. Behavioral interventions (e.g., cognitive behavioral therapy [CBT], relaxation training, mindfulness-based therapies, biofeedback) can offer an important alternative or complement to drug therapies, which can be associated with side-effects, drug-drug interactions, contraindications (e.g., pregnancy, cardiac history), and limited efficacy. For this report, we defined behavioral interventions as nonpharmacologic strategies intended to enhance outcomes by modifying behavior and/or ways of thinking.

Despite interest in behavioral interventions, current guidance from headache societies is limited and requires updating. The latest adult clinical practice guidelines from 2012 overlook therapies that have been more recently applied to migraine, such as mindfulness-based cognitive therapy (MBCT),² and the pediatric headache preventive guidelines were limited to studies which included pharmacologic agents.³ Consensus statements issued by the American Headache Society (AHS) and American Academy of Family Physicians (AAFP) about nonpharmacologic prevention for migraine were not based on systematic reviews of the evidence and did not fully address the unique treatment needs of children and adolescents.⁴⁻⁷ A recent topic brief and rapid scoping review of the literature suggested existing systematic reviews on behavioral therapies were outdated.⁸ The most recent reviews were published several years ago (2018, 2019) and covered psychological interventions, biofeedback, CBT, and progressive muscle relaxation for migraine prevention in adults but did not comprehensively assess all preventive behavioral therapy options.⁹⁻¹¹ Two recent reviews^{12,13} of children and adolescents provided evidence summaries for headache, but did not specifically address migraine. Although a recently published network meta-analysis assessed nonpharmacologic interventions for episodic migraine in children and adolescents, the literature search was completed in 2019.¹⁴

Given the lack of a recent and comprehensive systematic review and accumulation of newer evidence, we performed a systematic review to identify and assess evidence for behavioral interventions for migraine prevention in children, adolescents, and adults. This review addresses effectiveness, comparative effectiveness of migraine-focused behavioral interventions and pharmacotherapy, and harms. We also examined the effects of particular non-migraine-focused behavioral interventions. Furthermore, we examine the extent to which the effects of these interventions vary among individuals characterized by biopsychosocial factors (e.g., sex, socioeconomic status, co-occurring mental health conditions). In this project, we pragmatically define behavioral interventions as nonpharmacologic interventions that aim to improve outcomes through changing behavior and/or ways of thinking.

1.2 Purpose and Scope of the Systematic Review

This systematic review is intended to serve as the basis for development of AHS clinical practice guidelines. The intended audience includes guideline developers, health system administrators, and clinicians who provide care to individuals with migraine (e.g., primary care providers, advanced practice practitioners, neurologists, psychologists).

1. Introduction

1.3 Organization of This Report

In the remaining chapters of this report, we describe methods for this systematic review, present results, and discuss overall findings. After the Methods section, we provide a summary of the literature searches and screening. Within each Results section, we describe included studies, key points, detailed syntheses of the studies, and strength-of-evidence tables. The Discussion chapter reviews key findings and strength of evidence, discusses two Contextual Questions, examines the general applicability of studies, describes limitations of the systematic review process and the evidence base, and identifies knowledge gaps that require further research. The main body of the report is followed by Appendix A: Search Strategies, Appendix B: Excluded Publications, Appendix C: Evidence Tables. Appendix D: Appendix References, Appendix E: Patient-Centered Outcomes Research Institute (PCORI) Methodology Standards, Appendix F: Meta-Analyses of Any Behavioral Intervention for Key Question 1, and Appendix G: Network Meta-Analyses for Key Questions 1, 2, and 3.

2. Methods

2.1 Review Approach

This Systematic Review follows methods outlined in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews. We have reported the results of the systematic review in accordance with the Preferred Items for Reporting in Systematic Reviews and Meta-Analyses (PRISMA).¹⁵ We recruited Key Informants (KIs) to refine the topic and Key Questions (KQs) and provide input on the scope. We recruited a Technical Expert Panel (TEP) to provide input on all details of the protocol, including outcomes. The KIs and TEP included primary care physicians, adult and pediatric neurologists, clinical psychologists, researchers, funders, pediatric and adult migraine patients, and caregiver representatives. With feedback from the TEP, KIs, AHRQ, the Patient-Centered Outcomes Research Institute (PCORI) and our partners, we finalized the protocol and posted it on the AHRQ Effective Health Care Program's website (www.effectivehealthcare.ahrq.gov) for public comment from July 19, 2022, to August 9, 2022. The protocol was registered on [PROSPERO CRD42023397752](https://www.prospero.com/CRD42023397752). We also made available an online portal for the submission of additional data (Supplemental Evidence and Data for Systematic Reviews, SEADS)..

2.2 Role of the Technical Expert Panel

We identified experts in the field of behavioral interventions for migraine prevention to serve as members of the project's TEP. We selected individuals to represent a broad range of perspectives, including behavioral psychologists, adult and pediatric neurologists, and pain medicine specialists. Panel members had experience in both academic and government environments. We convened a conference call with the TEP before finalizing the protocol to obtain key input for methodologic aspects of the review, including KQs, inclusion criteria, and minimal important differences. TEP members are listed in the front matter of this report.

2.3 Key Questions

Key Question 1: What are the benefits and harms of behavioral interventions, either alone or in combination with other preventive strategies (including pharmacologic therapy), for migraine prevention compared to inactive control for children and adults?

Key Question 1a: What are the benefits and harms of behavioral interventions delivered via telehealth and digital health (e/mHealth) technology compared to inactive control?

Key Question 2: What are the comparative effectiveness and harms of a behavioral intervention for migraine prevention compared to either (a) a pharmacologic preventive agent or (b) another behavioral intervention for children and adults?

Key Question 2a: What are the comparative effectiveness and harms of behavioral interventions delivered via telehealth and digital health

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(e/mHealth) technology compared to (a) pharmacologic prevention or (b) other behavioral interventions?

Key Question 3: For multicomponent or combined behavioral interventions, what are the effects of individual behavioral intervention components?

Key Question 4: What are the benefits and harms of non-headache focused behavioral interventions (e.g., cognitive behavioral therapy [CBT] for insomnia, CBT for depression/anxiety, parent training) for migraine prevention in children and adults with migraine?

Key Question 5: For Key Questions 1–4, how do the findings vary by baseline biopsychosocial factors (e.g., sex, socioeconomic status, co-occurring mental health conditions)?

In brief:

- KQ 1 involves *treatment effectiveness* (treatment vs. no treatment), with 1a specifically about digital and telehealth implementations.
- KQ 2 involves *comparative effectiveness* (treatment A vs. B), with 2a specifically about telehealth and eHealth implementations.
- KQ 3 involves *dismantling* (treatment A with component 1 vs. treatment A without component 1) to determine the impact of each specific component.
- KQ 4 involves *interventions that do not primarily target headaches*, and whether they help prevent migraine.
- KQ 5 involves *interactions or subgroup analyses* investigating whether effects vary by patient characteristics.

We also explored two Contextual Questions, discussed in the Discussion section:

Contextual Question 1: What evidence is available on the benefits of behavioral preventive treatments for children and adults with migraine that include intervention components targeting caregivers (e.g., parents, spouses, other key support people)?

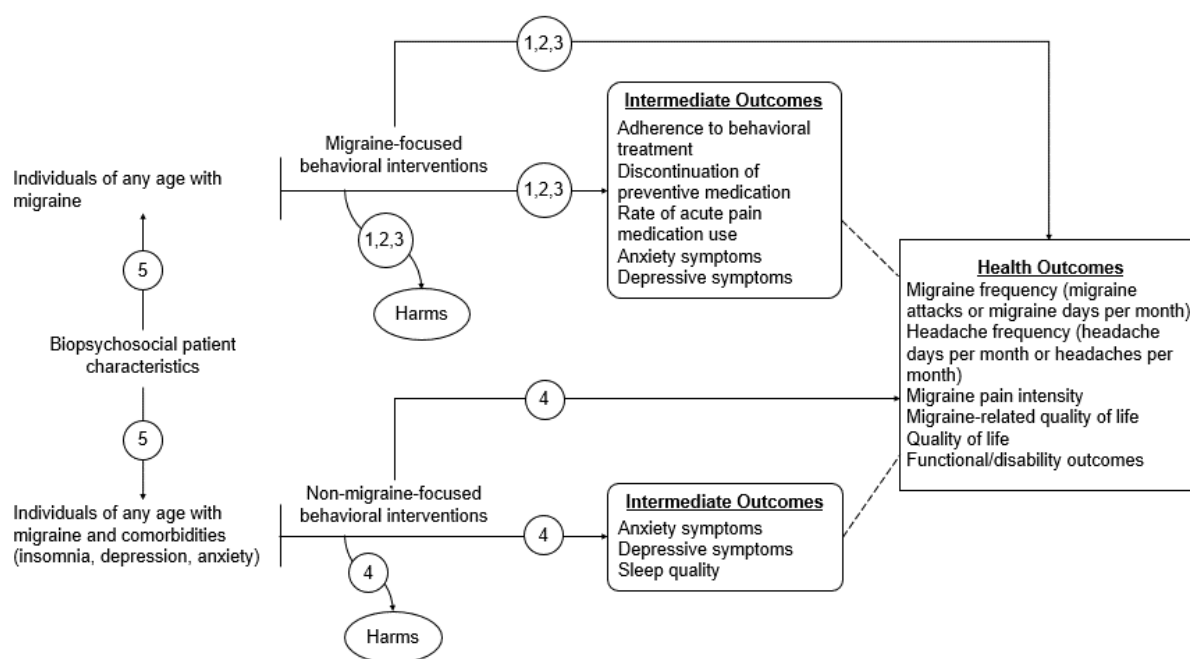
Contextual Question 2: What are patient and provider perceptions of the benefits, harms, and barriers to engaging with behavioral treatments for migraine prevention in children and adults?

2.4 Logic Model

A graphical depiction of the scope appears in Figure 1.

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Figure 1. Logic model



Circled numbers denote KQs; KQs 1a and 2a are not represented explicitly because they specifically targeted digital/telehealth interventions for KQs 1 and 2, respectively

2.5 Literature Searches

The full search strategies and gray literature resources are included in Appendix A. An Evidence-based Practice Center (EPC) research librarian conducted a comprehensive literature search following established systematic review protocols. The research librarian searched MEDLINE® and Embase® (via Embase.com), PsycINFO® (via Ovid), PubMed® (in process citations, to capture items not yet indexed in Medline), and the Cochrane Database of Systematic Reviews for randomized controlled trials, systematic reviews, and meta-analyses published from 1975 to August 24, 2023 (**Appendix A**). We chose January 1, 1975, as a starting point because recent systematic reviews covering adult and pediatric populations identified no relevant studies published before 1975. A second librarian independently peer reviewed the search strategy using the PRESS [Checklist](#). We also reviewed reference lists of other systematic reviews for inclusion in the current review. Gray literature was searched only for background and contextual information, not evidence, as we required that studies be published for inclusion.

The research librarian also conducted a gray literature search of relevant stakeholder organizations (e.g., American Headache Society, American Academy of Neurology), clinical trial registries (e.g., ClinicalTrials.gov), government agencies (e.g., National Institutes of Health, AHRQ), PCORI, and additional resources identified by team members, KIs, and the TEP. To inform the Contextual Questions, we searched for pertinent survey and qualitative studies, in addition to any pertinent data from the search results from the KQs. Contextual Questions are addressed in the Discussion section.

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2.6 Study Selection

Our study selection criteria appear in Table 1, with inclusion criteria in the middle column and exclusion criteria in the rightmost column. We employed dual screening of both abstracts and full-text articles using a team of six analysts, with discrepancies resolved by discussion. We used DistillerSR software for screening, data extraction, and risk-of-bias assessment.

Table 1. PICOTS (population, intervention, comparator, outcome, timing, setting)

PICOTS	Inclusion	Exclusion
Patients	<p>All KQs:</p> <ul style="list-style-type: none"> Children (age 6 to 11), adolescents (12 to 17), and adults (18 or older) with migraine headache (episodic or chronic). <p>We did not require studies to include only individuals with an International Classification of Headache Disorders diagnosis of migraine headache.</p> <ul style="list-style-type: none"> ≥80% of study participants had migraine headache, or the study reports a subgroup analysis composed of at least 80% migraine patients. For studies with participants with other headache types (e.g., medication overuse headache, tension type headache, cluster headache) in addition to migraine, we included the study if at least 80% of participants had migraine. 	<p>All KQs:</p> <p>Studies conducted exclusively</p> <ul style="list-style-type: none"> Among individuals in institutions (e.g., psychiatric inpatients, long-term care facilities, incarcerated populations) Parents, for studies with interventions targeting children and adolescents Individuals with psychotic disorders
Interventions	<p>KQs 1–3</p> <p>Migraine-focused behavioral interventions used for prevention, administered either alone or with pharmacotherapy, delivered in-person, via telehealth, or with e- or mHealth</p> <p>1. Cognitive behavioral therapy (CBT)</p> <ul style="list-style-type: none"> CBT Cognitive therapy Mindfulness-based cognitive therapy (MBCT)* Behavioral therapy Stress management training (SMT) Coping skills training “Learning to cope with triggers” Parent/caregiver operant training (parent or caregiver reinforces coping behaviors) Problem-solving training <p>2. Biofeedback</p> <ul style="list-style-type: none"> Thermal/temperature biofeedback (Hand warming/Thermal biofeedback) (often feedback of skin temperature from finger) Electromyographic biofeedback (feedback of electrical activity from muscles of scalp, neck, or upper body) Heart rate variability biofeedback Electrocardio biofeedback Pulse Blood volume pulse Respiratory Electroencephalography/Neurofeedback <p>3. Relaxation training</p> <ul style="list-style-type: none"> Diaphragmatic breathing 	<p>We excluded studies focused solely on the following interventions:</p> <ul style="list-style-type: none"> Physical therapy Exercise Catharsis therapy (e.g., written emotional disclosure) Occupational therapy Creative arts therapy (art therapy, music therapy, dance therapy) Massage

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PICOTS	Inclusion	Exclusion
	<ul style="list-style-type: none"> Progressive muscle relaxation (alternatively tensing/relaxing selected muscles) Autogenic feedback (use of calm, self-soothing statements to promote a state of deep relaxation) Autogenic training Guided imagery/guided visual imagery (children/adolescents) <p>4. Mindfulness-based stress reduction</p> <ul style="list-style-type: none"> Meditation (use of silently repeated word or sound to promote mental calm and relaxation) MBCT* Transcendental meditation Guided imagery/Guided visual imagery (adults) <p>5. Third-wave CBT</p> <ul style="list-style-type: none"> Acceptance and commitment therapy <p>6. Education</p> <ul style="list-style-type: none"> Education (skills, lifestyle, exercise, nutrition, hydration, stress management, sleep hygiene) Neuroscience education therapy Healthy lifestyle counseling Sleep counseling Trigger avoidance Weight management (informational) Diary/tracking <p>7. Hypnotherapy</p> <p>8. Trauma-informed therapy</p> <ul style="list-style-type: none"> Eye movement desensitization and reprocessing Trauma-focused therapy <p>9. Dialectical behavioral therapy</p> <p>10. Motivational interviewing and stages of change</p> <p>11. Professionally led support groups/peer support</p> <p>12. Combination therapies</p> <p>KQ1a and KQ2a: The above interventions delivered via telehealth or with e- or mHealth.</p> <p>KQ 4 Non-headache-focused behavioral interventions</p> <ul style="list-style-type: none"> CBT for insomnia or depression/anxiety Sleep hygiene counseling Parent/caregiver operant training (parent or caregiver reinforces adaptive sleep behaviors) Healthy lifestyle counseling <p>KQ5 Interventions included for KQs 1–4</p>	
Comparisons	<p>KQs 1</p> <ul style="list-style-type: none"> No intervention (e.g., waitlist, usual care) Minimal intervention (e.g., educational materials without skills training) Most active: Attention control, sham, or placebo <p>KQs 2–4 A different eligible behavioral intervention</p>	Comparators not listed as included.

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PICOTS	Inclusion	Exclusion
	<p>KQ 2–4 Medications from the following drug classes (see Table 2):</p> <ul style="list-style-type: none"> • Alpha agonists • Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers • Antiepileptics • Antihistamines (for child and adolescents only) • Beta-blockers • Botulinum toxin type A • Calcitonin gene–related peptide antagonists • Calcium channel blockers • Other antidepressants • Serotonin norepinephrine reuptake inhibitors • Tricyclic antidepressants <p>KQ5 Comparators in KQs 1–4, comparisons among patients with different biopsychosocial factors (e.g., sex, socioeconomic status, co-occurring mental health conditions)</p>	
<p>Outcomes</p>	<p>All KQs</p> <p>Migraine/Headache attack frequency:</p> <ul style="list-style-type: none"> • Migraine/headache count: Migraine days per month, migraine attacks per month, headache days per month, or headaches per month. • Responder rate: 50% or more reduction in 1 of the above quantities <p>Functional Status/Disability</p> <ul style="list-style-type: none"> • Migraine Disability Assessment (MIDAS), Pediatric MIDAS (PedMIDAS), Headache Impact Test (HIT-6), Headache Needs Assessment, Headache Disability Inventory, Migraine Interictal Burden Scale, Functional Impairment Scale, Functional Disability Inventory (FDI)-Parent form, FDI-Child and adolescent, Functional Status Questionnaire, Impact of Migraine on Partners and Adolescent Children, Pain Disability Inventory <p>Quality of Life (QOL)</p> <ul style="list-style-type: none"> • Migraine-specific: Migraine-Specific Quality of Life Questionnaire (MSQoL) v2.1, other MSQOL instruments • General: 36-Item Short Form Survey (SF-36), EuroQol-5D (EQ-5), 12-Item Short Form Survey (SF-12), Pediatric Quality of Life Inventory (PedsQL) <p>Adverse effects such as dropouts due to adverse events and any reported specific adverse effects.</p> <p>Emotional Status</p> <ul style="list-style-type: none"> • Anxiety symptoms (e.g., General Anxiety Disorder-7 [GAD-7], Patient-Reported Outcomes Measurement Information System [PROMIS] Pediatric – Anxiety, Hospital Anxiety and Depression Scale [HADS]) • Depression symptoms (e.g., Patient Health Questionnaire [PHQ] 4, PHQ 9, Children's Depression Inventory [CDI], PROMIS Pediatric-Depression, HADS) <p>Other:</p>	<p>Outcomes not listed as included</p>

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PICOTS	Inclusion	Exclusion
	<ul style="list-style-type: none"> Most bothersome symptoms Headache pain intensity (visual analog scale, numeric rating scale) Acute headache medication use Discontinuation of preventive medication <p>KQ 4. Additional outcomes:</p> <ul style="list-style-type: none"> Anxiety (e.g., GAD-7, PROMIS Pediatric - Anxiety) Depression (e.g., PHQ 4, PHQ 9, CDI, PROMIS Pediatric-Depression) Sleep outcomes (sleep onset latency, wake after sleep onset, total sleep time, sleep efficiency) 	
Study Design Criteria	<p>All KQs:</p> <ul style="list-style-type: none"> Randomized controlled trials (RCTs) reporting outcomes for ≥10 participants per treatment arm Period 1 data from crossover RCTs Published in English Published 1975 or after Subgroup analyses addressing KQ5 must have reported outcomes on at least 10 patients per subgroup <p>For KQ1-4, we required studies to report at least 1 of 3 primary outcomes: migraine/headache attack frequency, migraine-related disability, migraine-specific quality of life.</p>	<p>All KQs:</p> <ul style="list-style-type: none"> Excluded crossover trials not reporting period 1 data separately Excluded reviews, letters, guidelines, position statements, and commentaries Excluded single-arm or non-randomized controlled studies Unpublished studies/Not published as a full-length article (e.g., conference abstract) <p>SRs were used only to identify potential RCTs for inclusion</p>
Setting	<ul style="list-style-type: none"> Any non-inpatient setting Trials conducted in countries rated as “very high” on the 2022 Human Development Index (as defined by the United Nations Development Programme). This was to focus our efforts on treatment settings relatively similar to US settings. 	<p>Hospitalized patients</p> <p>Trials conducted in other countries</p>
Timing	Studies must have reported 1 of our primary outcomes at 4 weeks or longer after treatment initiation.	Earlier timepoints

Abbreviations: ; CBT- Cognitive Behavioral Therapy; CDI - Children's Depression Inventory; EQ-5 - EuroQoL-5D; FDI - Functional Disability Inventory; GAD-7 – General Anxiety Disorder-7; HADS – Hospital Anxiety and Depression Scale; HIT-6 - Headache Impact Test; KQ – Key Question; ; MCBT – Mindfulness-based cognitive therapy; MIDAS – Migraine Disability Assessment; MSQoL - Migraine-specific quality of life; PedMIDAS – Pediatric Migraine-Specific Disability Assessment; PedQOL – Pediatric Quality of Life Inventory; PHQ - Patient Health Questionnaire; PROMIS – Patient-Reported Outcomes Measurement Information System; QOL – Quality of life; RCT – Randomized controlled trial; SF-12 – Short Form 12; SF-36 – Short Form 36; SMT – Stress Management Training; SR – Systematic Review

*MBCT is a combination of cognitive therapy and MBSR, so it appears in both categories.

2.7 Data Extraction

For each included article (or secondary publications reporting additional outcomes or later timepoints), we extracted which KQ(s) the study addressed, the age group, relevance to Contextual Questions, type of randomized trial, country, trial purpose, funding, whether single center or multicenter, trial duration, setting, patient eligibility criteria, how the trial measured migraine attack frequency at both baseline and followup, concomitant interventions (e.g., medications), the arm names used by trial investigators, details of active interventions including

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each separate component, the types of practitioners who delivered the interventions, how it was delivered (i.e., in-person or digital/telehealth), details of control group(s) including level of attention, whether any measures were used to ensure therapist fidelity to the intervention (if so, what they were), whether patients' adherence to intervention was measured (if so, how), the number of patients randomly assigned, the number of patients at baseline, age, percentage female, race, ethnicity, criteria for migraine diagnosis, comorbid headache disorders, type of migraine experienced at baseline (episodic/chronic/mixed), and how long patients have had migraine.

We extracted data on all included outcomes, listed in the logic model in Figure 1 above and the PICOTS (population, intervention, comparator, outcome, timing, setting) shown in Table 1 above. One person extracted data from each study. For data appearing only in figures, we used a Web digitizer (<https://automeris.io/WebPlotDigitizer/>) to estimate the numbers. If a study reported multiple metrics of migraine/headache attack frequency (e.g., both migraine days per month and migraine attacks per month), we extracted only one metric, using the following prioritization:

1. Migraine days per month
2. Headache days per month
3. Migraine attacks per month
4. Headaches per month
5. Percentage of patients experiencing 50 percent or more reduction in one of the above metrics

We defined timepoints from the beginning of the intervention. We used 3 timepoint categories: at least 8 weeks but <12 weeks, 12 weeks to <6 months, and 6 months or more. If a study reported multiple measures within the same time category, we chose the shorter timepoint to minimize the time between intervention and outcome measurement. If a study reported change-from-baseline data in addition to at-followup data, we prioritized the former. We prioritized the mean over the median in studies reporting both for dispersion, and we chose the standard deviation or standard error or confidence interval over the range or interquartile range. These decisions were based on our planned calculation of effect sizes for quantitative meta-analysis, if appropriate.

2.8 Risk of Bias Assessment

To assess each study's risk of bias, we used the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2).¹⁶ This instrument has five domains:

- Bias arising from the randomization process
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

For the domain missing outcome data, we considered a study at high risk of bias if fewer than 80 percent of enrolled patients had provided to that timepoint. Because the EPC strength of evidence (SOE) system employs reporting bias as its own domain (see the section below on Grading the Strength of the Body of Evidence), the fifth domain above did not influence our risk-of-bias ratings, but rather we used it to inform the SOE reporting bias domain.

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The Cochrane instrument uses several “signaling questions” that are intended to improve fidelity to the instrument’s intent. For each of the first four domains above, the analyst categorized the risk of bias as “Low,” “Some Concerns,” or “High.” For overall risk of bias, based on the first four domains listed above, the analyst categorized the study as “Low,” “Some Concerns,” or “High.” Typically, each study received only a single risk-of-bias rating, but for some cases we judged that risk of bias varied by treatment comparison (e.g., treatment versus waitlist at higher risk of bias than treatment vs attention control) or outcome (e.g., measurement concerns with one but not another), or timepoint (e.g., more missing data at later timepoints). Two analysts independently rated each study using the instrument in DistillerSR, with discrepancies resolved by consensus.

2.9 Data Synthesis and Analysis

2.9.1 Intervention Categorization

Behavioral interventions can be delivered as single component interventions (e.g., relaxation training) or multicomponent intervention that includes a variety of other behavioral or non-behavioral interventions. Our evidence base included studies published since 1978; given insights from our subject matter experts (SMEs) regarding shifts in practice, we anticipated older studies were more likely to assess single-component interventions (e.g., biofeedback), while newer studies would often comprise multiple interventions. For example, CBT may be delivered as a “treatment package” that also includes relaxation training and/or biofeedback. Adding further complexity, studies might describe a “relaxation” intervention as providing written materials on relaxation training, providing a virtual training session on relaxation training, or providing in-person relaxation training sessions.

Given these considerations, to facilitate comparisons across single and multiple component interventions, we used the following approach to categorize interventions. First, regardless of how study authors named the intervention, we considered the descriptions of interventions provided and considered whether a study intervention included one or more of the behavioral interventions of interest. For example, a study that described itself as a “CBT” intervention, but for which a narrative description demonstrated that study participants also received relaxation training and biofeedback, was considered a combination intervention with three components: CBT, relaxation training, and biofeedback. Second, if studies mentioned incorporating an intervention, we considered this to be an intervention, regardless of the “intensity” of how the intervention was delivered. For example, a study providing written materials describing relaxation techniques was considered a relaxation training intervention. Likewise, a study in which participants attended in-person weekly relaxation training sessions was also categorized as a relaxation training intervention. Any active intervention mentioned in the trial was considered part of the intervention, regardless of duration, delivery intensity, setting/modality (i.e., self-guided or in-clinic).

For studies using education as a comparison, we categorized this as an attention control when 1) the study authors noted it was designed to play this role, 2) the time and interaction with study staff allotted to the educational intervention was roughly equivalent to time to the intervention arm, and 3) the study description of education did not suggest other behavioral interventions (such as provide education on relaxation training or contain elements addressing behavioral change suggestive of CBT). If these criteria were not met, yet it was still clearly a control group

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with minimal intervention, we classified it as a minimal control group. Otherwise, we classified it as a standalone behavioral intervention. At least two analysts and our SMEs reviewed all intervention categorizations.

2.9.2 Data Synthesis

We considered three types of data synthesis: qualitative synthesis, quantitative synthesis using standard meta-analysis, and quantitative synthesis using network meta-analysis:

- We planned *qualitative syntheses* for the KQs yielding less evidence, such as KQs 1a and 2a on digital/telehealth, KQ4 on non-headache-focused interventions, and KQ5 on biopsychosocial factors. Generally, we identified only one or two studies per treatment for these KQs.
- We planned *standard meta-analyses* for KQ1 on the effectiveness of treatments (i.e., active versus inactive). We performed random-effects meta-analyses using the restricted maximum-likelihood approach with the meta package (v6.2-1) in R (v4.1.3).¹⁷ Wherever possible, we computed effect sizes and 95% confidence intervals using standard methods. Where necessary, we estimated means and standard deviations from medians and interquartile ranges (IQRs) or ranges using the methods described by Wan et al. (2014).¹⁸ We computed standardized mean differences (SMDs) (often because different studies used different metrics for the same construct). We quantified heterogeneity using τ^2 . For migraine/headache attack frequency, as stated above, we extracted only a single metric per study, so we did not have to prioritize metrics per study. If a study reported multiple metrics of migraine disability or migraine quality of life (QOL), we prioritized the metric that was more commonly reported among our included studies. For timepoints since the start of treatment, we planned to conduct four analyses: ≥ 8 weeks but < 12 weeks, 12 weeks to < 6 months, ≥ 6 months, and any timepoint. For the any-timepoint meta-analyses, when a study reported multiple timepoints, we chose the 1 closest to 12 weeks after the start of treatment, prioritizing the earlier timepoint in case of a tie (e.g., 8 weeks if both 8 weeks and 16 weeks were reported). Due to data sparseness for any specific timeframe, we generally focused our discussion on the “any timepoint” analyses.
- We planned *network meta-analyses* for a combined analysis of KQs 1, 2, and 3. See the results section for details.

We kept separate studies of adults from studies of children/adolescents and the data on our outcome categories. These restrictions, along with our inclusion criteria, ensured a general similarity of patients (at least 80 percent migraine) and outcomes. We describe additional details about our approaches to synthesis in each KQ.

To facilitate interpretation of data on primary outcomes, we converted meta-analytic results from SMDs to the most commonly used metric for a given outcome category (using typical standard differences based on the literature we reviewed). To assess clinical importance of findings, we consulted our TEP and the published literature to determine a minimal important difference (MID) for each key effectiveness metric. For our three primary outcomes:

- For migraine/headache attack frequency, we used *migraine days per month* as the most interpretable metric, based on the advice from our SMEs. For the between-groups MID, we used 1 day per month, based on the advice of our TEP. For conversions from SMD, we used a standard deviation (SD) of 3.25, based on 20 arms from 8 studies reporting the necessary information. Thus, the MID on the SMD scale was 0.31 (MID of 1 migraine day/month divided by the SD of 3.25).

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- For migraine disability, we used *Migraine Disability Assessment (MIDAS)*, because it was the most commonly used metric in this category. This patient-self-report questionnaire addresses migraine's impact on day-to-day life in the past 3 months and takes values ranging from 0–90, where higher scores indicate greater disability. For the between-groups MID, our searches did not locate any published value. We noted that for migraine days per month we used a value corresponding to about 3 percent of the scale range (1/30). Thus, for inter-outcome consistency, we used a value of 3 points on the 0 to 90 MIDAS, because that is also about 3 percent of the scale range. For conversions from SMD, we used an SD of 26.6, based on 21 arms from 10 studies reporting the necessary information. Thus, the MID on the SMD scale was 0.11 (MID of 3 divided by the SD of 26.6).
- For migraine-specific QOL, we used *the Migraine-Specific Quality of Life (MSQoL) v2.1*, because it was the most commonly used metric in this category. This patient-self-report questionnaire takes values ranging from 0 to 100, where higher scores indicate greater impact on QOL (some authors use a range from 14 to 84). For the between-groups MID, we used 19 points on the 0 to 100 scale (representing 19 percent of the scale range), based on adding the MIDs reported by Cole et al. 2009¹⁹ for the three subscales of the MSQOL and translating to the 0 to 100 scale. For conversions from SMD, we used an SD of 14, based on 2 included studies reporting the necessary information. Thus, the MID on the SMD scale was 1.35 (MID of 19 divided by the SD of 14).

The preceding bullet points refer only to our *interpretation* of the data. We included numerous other instruments of all three outcome categories, and we needed ways to interpret the data consistently and convert meta-analytic SMDs to more easily understood numbers.

For migraine disability, we conducted meta-analyses of only the following 11 scales: MIDAS, Pediatric MIDAS (PedMIDAS), Impact of Migraine on Partners and Adolescent Children (IMPAC), Migraine Interictal Burden Scale (MIBS-4), Headache Needs Assessment (HANA), Functional Status Questionnaire (FSQ), Functional Disability Inventory (FDI) (Parent form), FDI (child and adolescent), Henry Ford Hospital Headache Disability Inventory (HDI), Pain Disability Index (PDI), and Functional Impairment Scale (FIS). Other measures of migraine-related disability (such as the HDS [number of headache days per month] used by Fritzsche et al. 2010) were summarized narratively).²⁰ For MSQOL, we conducted meta-analysis of studies reporting data using the MSQoL v2.1 or other MSQOL questionnaires.

2.10 Grading the Strength of the Body of Evidence

Using the 2013 AHRQ Methods Guide recommendations,²¹ we rated SOE for our three primary effectiveness outcomes: migraine/headache attack frequency, migraine-related disability, and MSQOL. The SOE was based on nine considerations: study design, study limitations, consistency of results across trials, directness of the evidence, effect estimate precision, reporting bias, dose-response association, magnitude of effect, and all plausible confounders would reduce the effect. As we included only randomized trials, the initial rating was High in all cases. Five domains (the first five listed above) could then potentially lower the rating, and three other domains (the last three listed above) could potentially raise the rating.

The output is a rating of the SOE: high, moderate, low, or insufficient (defined in Table 2 below). This rating is made separately for each outcome of each comparison of each KQ. If the evidence is sufficient to permit a conclusion, then the rating is deemed high, moderate, or low. A

2. Methods

rating of insufficient is given if the evidence does not permit a conclusion for that KQ's outcome of interest. Two analysts made each rating, with discrepancies resolved by consensus.

Table 2. Definitions of strength of evidence ratings

Rating	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable (i.e., another study would not change the conclusions).
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. No evidence is available, or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

2.11 Peer Review and Public Commentary

Five independent Peer Reviewers (including one statistical reviewer) with a range of expertise, including psychologists, neurologists, and other care providers, provided written comments on the draft report. The AHRQ Task Order Officer, an EPC Associate Editor, and representatives from PCORI provided comments and editorial review. The draft report was posted for public comment on the AHRQ website. A disposition of comments report with authors' responses to the public comments was posted after publication of the final report on the AHRQ website.

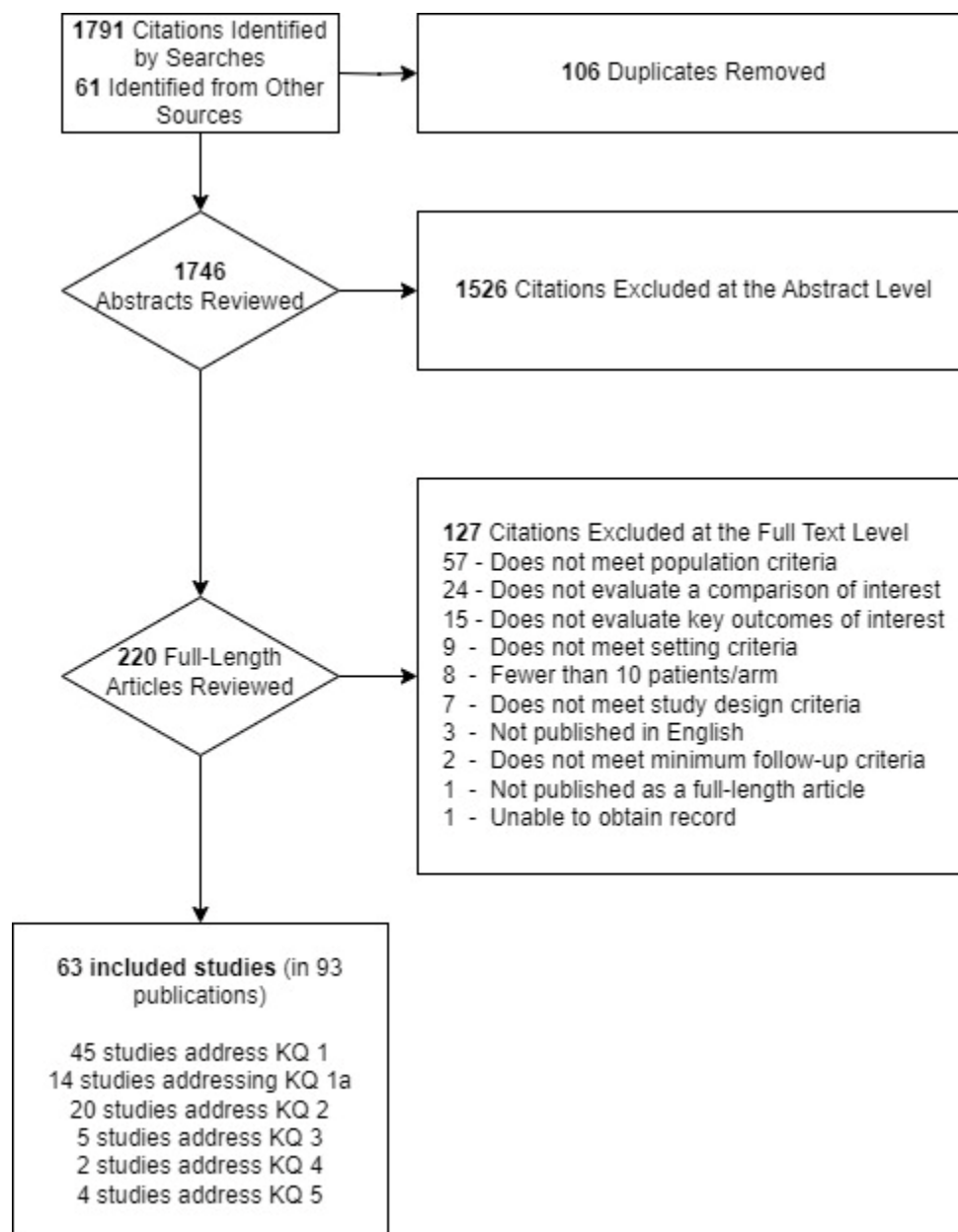
3. Results

3.1 Search Results

Searches identified 1791 potentially relevant references (Figure 2), of which 106 were duplicates. An additional 61 potentially relevant references were identified from the reference lists of relevant systematic reviews. We excluded 1526 citations at the abstract level and ordered the remaining 220 for full-text consideration. Of these, we excluded 127 publications, with the most common reasons for exclusion being: “Does not meet population criteria,” “Does not evaluate a comparison of interest,” and “Does not evaluate a key outcome of interest.” A list of all articles excluded at full text appears in Appendix B.

3.1 Results, Search Results

Figure 2. Study flow diagram



Abbreviation: KQ=Key Question

We included data from 63 studies, consisting of 7766 participants in 93 publications (refer to Appendix C for details).^{20,22-113} The studies reviewed were conducted in the United States, Europe, Japan, and Canada. Thirty-two trials were based in the United States.^{22-27,29,30,32-34,36,45,48,53-59,61-64,69,71-73,76,112,113} The trials evaluated a wide range of behavioral interventions, delivered either in-person (individually or in groups), via digital/telehealth platforms, or as self-guided home-based programs using various digital tools, such as audio records.

The included trials evaluated behavioral interventions in both adolescents and adults. In total, 13 randomized controlled trials (RCTs) included 1414 children/adolescents,^{22,24,29,31,33,42,51,69-73,77}

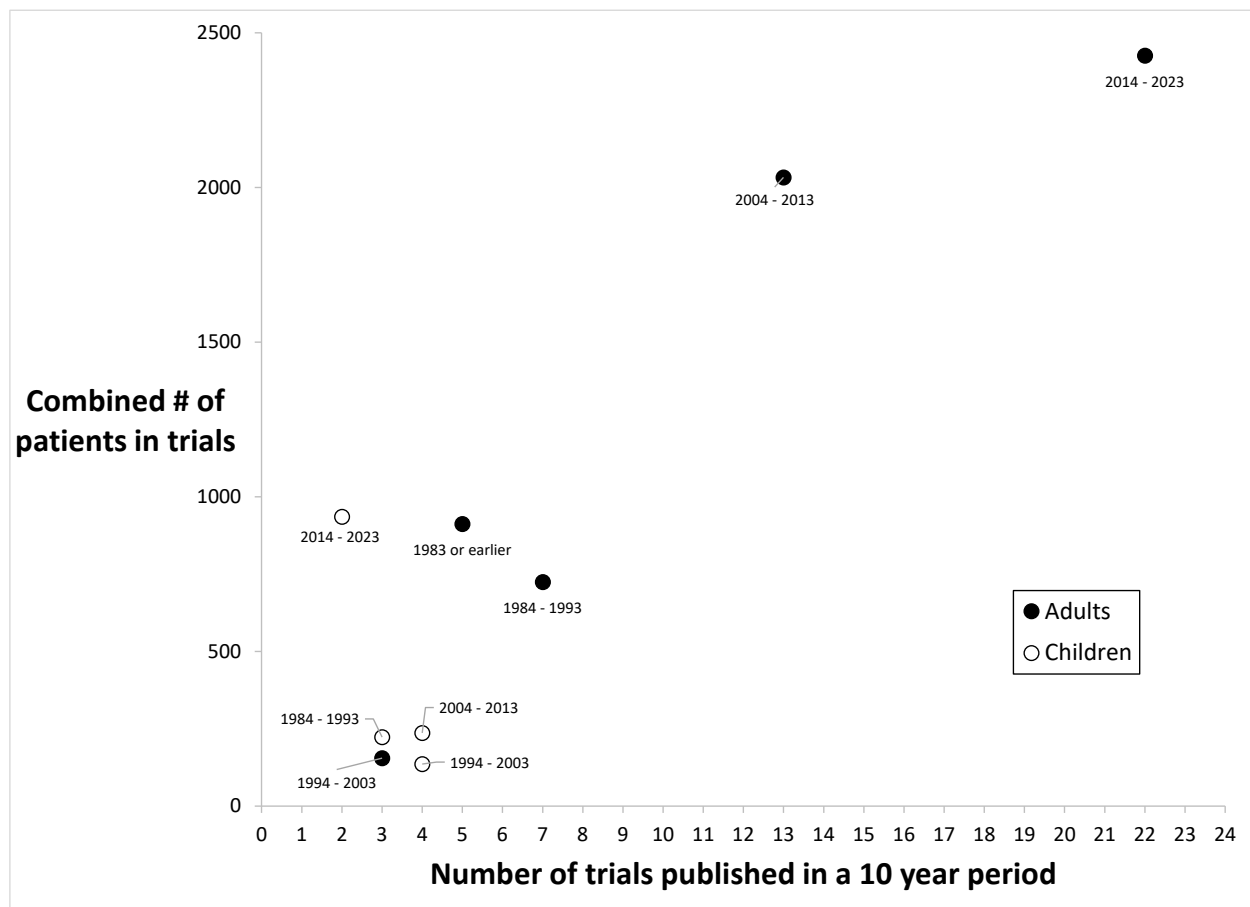
3.1 Results, Search Results

and 50 included 6333 adults.^{20,23,25-28,30,32,34-41,43-50,52-68,74-76,108-113} The weighted average ages were 14.5 years and 42.0 years, respectively.

The adolescent participants included 60.5 percent of girls, while women made up 84 percent of the adult group. Only one adolescent trial⁷³ and nine adult trials reported comorbid conditions.^{34,46,53,54,56,58,64,66} Anxiety was present in 25 percent of adolescents (1 RCT) and 47.3 percent of adults (4 RCTs), while depression rates were 13 percent in adolescents (1 RCT) and 46.2 percent in adults (7 RCTs). One trial with adult-documented epilepsy and a history of stroke (each with a prevalence of 1 to 2 percent), hypertension (23 percent), and coronary artery disease (5.8 percent).⁶⁴

Figure 3 below shows the numbers of trials published in five separate 10-year periods, along with the total numbers of patients in those trials. For adults, the number of trials has risen over the years, to a high of 22 trials published from 2014–2023 (including about 2400 patients and does not even include 10 full years). For children, however, the earliest included trial was published in 1984, and there have been no more than four trials a decade.

Figure 3. Numbers of trials and patients in 10-year periods



Information regarding race or ethnicity was available in 3^{33,69,71} of 8 U.S. adolescent trials and 14 out of 25 U.S. adult trials.^{32,34,36,45,53-59,61,62} The majority of trial participants were White, with the adolescent group comprising 89.5 percent White and the adult group 73.4 percent

3.1 Results, Search Results

White. Black individuals made up an estimated 9.6 percent in one adolescent trial³³ and 13.6 percent in the adult trials.^{32,36,45,53,55,56,58,59,61,62,113} Representation of Asian or Pacific Islander individuals was 0.7 percent in among adolescents and 4.4 percent among adults. Native American or Alaska Native individuals accounted for 0.8 percent in two adult trials. Hispanic ethnicity was reported in 10 U.S. adult trials, comprising 8.3 percent of participants. Ethnicity was not reported in adolescent RCTs.

In terms of migraine types, 10 adolescent trials^{22,24,29,31,42,51,70,71,73,77} and 14 adult trials^{20,25,30,35,37,40,44,46,47,54,59,66,67,75} focused primarily on patients with episodic migraine. Chronic migraine was mainly studied in one adolescent trial³³ and nine adult trials.^{23,26,34,39,45,49,63,64,113} Two adolescent trials^{69,72} and nine adult trials^{28,41,43,48,52,55,65,68,74} included patients with both types of migraine. The average duration of disease history at enrollment was 3.3 years for adolescents and 18.7 years for adults. The average headache frequency at baseline was approximately 14 days per month (10 RCTs) for adolescents and 11.5 days per month (34 RCTs) for adults.

The 63 included studies are listed in Table 3. The largest evidence base was for Key Question (KQ) 1, and there were no studies for KQ2a (comparative-effectiveness studies using digital technologies or telehealth).

Table 3. Included studies

Study	Age Group	KQ1	KQ1a	KQ2	KQ2a	KQ3	KQ4	KQ5
Aguirrezabal et al. (2019) ⁵⁰	Adults	✓	-	-	-	-	-	-
Blanchard et al. (1978) ⁷⁶	Adults	✓	-	✓	-	-	-	-
Bromberg et al. (2012) ⁴⁵	Adults	✓	✓	-	-	-	-	-
Brown et al. (1984) ¹¹⁰	Adults	✓	-	✓	-	-	-	-
Calhoun et al. (2007) ⁶³	Adults	-	-	-	-	-	✓	-
Cousins et al. (2015) ⁴¹	Adults	✓	-	-	-	-	-	-
Cuneo et al. (2023) ¹¹³	Adults	✓	✓	-	-	-	-	-
D'Souza et al. (2008) ⁶²	Adults	✓	✓	-	-	-	-	-
Day et al. (2014) ³²	Adults	✓	-	-	-	-	-	-
de Tommaso et al. (2017) ³⁵	Adults	-	-	✓	-	-	-	-
Dindo et al. (2020) ⁵⁴	Adults	-	-	✓	-	-	-	-
Dittrich et al. (2008) ³⁸	Adults	✓	-	-	-	-	-	-
Flynn et al. (2019) ⁶⁰	Adults	✓	✓	-	-	-	-	-
Fritzsche et al. (2010) ²⁰	Adults	-	-	-	-	✓	-	-
Grazzi et al. (2021) ⁶⁶	Adults	✓	-	-	-	-	-	-
Hedborg et al. (2011) ⁴⁶	Adults	✓	✓	-	-	-	-	✓
Holroyd et al. (1988) ²³	Adults	✓	✓	-	-	-	-	-
Holroyd et al. (2010) ³⁶	Adults	✓	-	✓	-	-	-	-
Janssen et al. (1986) ¹⁰⁸	Adults	-	-	✓	-	-	-	-
Kewman et al. (1980) ²⁵	Adults	✓	-	-	-	-	-	-
Klan et al. (2022) ⁶⁵	Adults	✓	-	✓	-	-	-	-
Kleiboer et al. (2014) ⁴³	Adults	✓	✓	-	-	-	-	-
Kohlenberg et al. (1981) ³⁰	Adults	✓	-	-	-	-	-	-
Kropp et al. (1997) ²⁸	Adults	-	-	✓	-	-	-	-
Lemstra et al. (2002) ⁴⁹	Adults	✓	-	-	-	-	-	-

3.1 Results, Search Results

Study	Age Group	KQ1	KQ1a	KQ2	KQ2a	KQ3	KQ4	KQ5
Matchar et al. (2008) ⁶⁴	Adults	✓	-	-	-	-	-	-
Mathew et al. (1981) ²⁷	Adults	✓	-	✓	-	-	-	-
Mérelle et al. (2008) ⁴⁷	Adults	✓	-	-	-	-	-	-
Minen et al. (2020) ⁵⁶	Adults	✓	✓	-	-	-	-	-
Minen et al. (2020) ⁵⁸	Adults	✓	✓	-	-	-	-	-
Minen et al. (2021) ⁵⁷	Adults	✓	✓	-	-	-	-	-
Odawara et al. (2015) ⁴⁰	Adults	✓	-	-	-	-	-	-
Pickering et al. (2012) ⁴⁴	Adults	✓	-	-	-	-	-	-
Rausa et al. (2016) ³⁹	Adults	✓	-	-	-	-	-	-
Reich et al. (1989) ²⁶	Adults	-	-	✓	-	-	-	-
Richardson et al. (1989) ⁷⁴	Adults	✓	-	-	-	-	-	✓
Rothrock et al. (2006) ⁴⁸	Adults	✓	-	-	-	-	-	-
Sargent et al. (1986) ^{107,112}	Adults	✓	-	✓	-	✓	-	-
Seminowicz et al. (2020) ⁵⁹	Adults	-	-	✓	-	-	-	-
Seng et al. (2019) ⁵⁵	Adults	✓	-	-	-	-	-	✓
Simshäuser et al. (2022) ⁶⁷	Adults	✓	-	-	-	-	-	-
Smitherman et al. (2016) ³⁴	Adults	-	-	-	-	-	✓	-
Sorbi et al. (1984) ⁷⁵	Adults	-	-	-	-	✓	-	-
Sorbi et al. (1986) ^{79,109}	Adults	-	-	✓	-	-	-	-
Underwood et al. (2022) ⁶⁸	Adults	✓	✓	-	-	-	-	✓
Varkey et al. (2011) ³⁷	Adults	-	-	✓	-	-	-	-
Vasiliou et al. (2021) ⁵²	Adults	✓	-	-	-	-	-	-
Wachholtz et al. (2008) ^{61,100}	Adults	-	-	✓	-	-	-	-
Wells et al. (2021) ⁵³	Adults	-	-	✓	-	-	-	-
Wittchen et al. (1983) ¹¹¹	Adults	✓	-	-	-	-	-	-
Albers et al. (2015) ⁴²	Children/adolescents	✓	-	-	-	-	-	-
Allen et al. (1998) ²⁹	Children/adolescents	-	-	-	-	✓	-	-
Connelly et al. (2006) ⁷²	Children/adolescents	✓	✓	-	-	-	-	-
Cottrell et al. (2007) ⁷¹	Children/adolescents	✓	✓	-	-	-	-	-
Fichtel et al. (2001) ⁷⁷	Children/adolescents	✓	-	-	-	-	-	-
Gerber et al. (2010) ⁷⁰	Children/adolescents	-	-	✓	-	-	-	-
Labbe et al. (1984) ²⁴	Children/adolescents	✓	-	-	-	-	-	-
Labbe et al. (1995) ²²	Children/adolescents	✓	-	-	-	✓	-	-
Powers et al. (2013) ³³	Children/adolescents	-	-	✓	-	-	-	-
Rapoff et al. (2014) ⁶⁹	Children/adolescents	✓	✓	-	-	-	-	-
Richter et al. (1986) ³¹	Children/adolescents	✓	-	✓	-	-	-	-
Sartory et al. (1998) ⁵¹	Children/adolescents	-	-	✓	-	-	-	-
Scharff et al. (2002) ⁷³	Children/adolescents	✓	-	-	-	-	-	-

A checkmark indicates that the study was included for that Key Question (KQ).

3.2 Key Question 1: What are the benefits and harms of behavioral interventions, either alone or in combination with other preventive

3.2.1 Results, Key Question 1, Key Points

strategies (including pharmacologic therapy), for migraine prevention compared to inactive control for children and adults?

3.2.1 Key Points

- We included 45 randomized trials (36 in adults, 9 in children/adolescents) published since 1978.
- Most trials used behavioral treatments in combination; the most common components were cognitive behavioral therapy (CBT), biofeedback, relaxation training, and education.
- Adults: Interventions including CBT (alone or in combination with other components) may lower migraine/headache attack frequency (strength of evidence [SOE]: low).
- Adults: Interventions including relaxation training (alone or in combination with other components) may lower migraine/headache attack frequency (SOE: low).
- Adults: Interventions including mindfulness-based therapy may lower migraine/headache attack frequency (SOE: low).
- Adults: Education alone that targets behavior may improve migraine-related disability (SOE: low).
- Other components and treatments for adults, as well as all evidence on children/adolescents, had inconclusive effects, mostly due to wide confidence intervals around potential effects.
- About three-fourths of the studies were at high risk of bias, typically due to concerns with either missing data or potential measurement bias (greater expectations of benefit in inactive control groups). Only five studies used an attention control group.
- Many studies were small or did not report sufficient information for effect size calculation, resulting in underpowered meta-analyses for detecting potential benefits of treatments.

3.2.2 Description of Included Evidence

We included 45 studies for KQ1 (Table 4 for adults and Table 5 for children/adolescents). Thirty-six studies enrolled adults, and the other nine enrolled children/adolescents. Each table is sorted by the types of components included, with the first set of studies employing CBT, followed by studies using biofeedback, relaxation training, mindfulness-based treatments, education, acceptance and commitment therapy, and finally, hypnotherapy. Combination treatments were common, with most studies employing some combination of five primary components: CBT, biofeedback, relaxation training, mindfulness-based treatments, and education. Because education was so common, and may have been an assumed and unmentioned component of one of the other major components, we did not analyze whenever education was used; instead, we analyzed education when it was the only behavioral intervention administered. Two other treatments (acceptance and commitment therapy and hypnotherapy) were only investigated by two studies at most. Thus, our summary of findings below contains 10 sections:

- Adults: CBT
- Adults: Biofeedback
- Adults: Relaxation training

3.2.2 Results, Key Question 1, Description of Included Evidence

- Adults: Mindfulness-based treatments
- Adults: Education only
- Adults: Acceptance and commitment therapy
- Adults: Hypnotherapy
- Children/adolescents: CBT
- Children/adolescents: Biofeedback
- Children/adolescents: Relaxation

For analysis, many trials employed multicomponent treatment packages, with different trials often using different combinations. This complicated our efforts to analyze “treatment” effectiveness. Ultimately, we combined all trials employing a given component, regardless of additional components in that treatment regimen, or the “dosage” (i.e., time or intensity) of each component. For example, the CBT section discusses data on the three-component intervention by Klan et al. (2022)⁶⁵ (CBT + progressive muscle relaxation [PMR] + education) as well as the six-component intervention by Lemstra et al. (2002)⁴⁹ (CBT + relaxation training + education + exercise + massage therapy + physical therapy). This is because both interventions had a CBT component. These same two studies were also discussed in the relaxation training section, because both included relaxation training. We considered mindfulness-based cognitive therapy (MBCT) a form of CBT but also a form of mindfulness-based treatment, so the two MBCT studies (Simshäuser et al. 2022⁶⁷ and Seng et al. 2019)⁵⁵ appear in both of those sections.

We note the wide variety of control groups in the included studies. The most rigorous control groups involve placebo or sham or attention control, which attempt to control for patient expectations and/or the amount of time patients spend with study personnel. This is valuable, because it helps rule out the possibility that some of the observed advantages of active over inactive treatment may be due to higher patient expectations or enhanced interpersonal relationships with study personnel (either of which could bolster patients’ post-treatment subjective reports of reduced migraine attack frequency or enhanced abilities). At the other extreme is the “no intervention/treatment as usual” control group, which is more vulnerable to these alternative interpretations of results. We also encountered a few cases of a “minimal” control group, which provided a middle ground in research rigor with respect to the control groups. Note that we considered many additional aspects of research rigor (see Methods section on Risk of Bias Assessment).

Regarding the details of treatment implementation, such as number of sessions, duration, intensity, therapist expertise, setting, and therapist fidelity, inconsistent reporting and heterogenous data prevented a sensible and generalizable summary of these characteristics. Examples of such heterogeneity include the diverse range of individuals who delivered the interventions (e.g., graduate students, medical trainees, psychologists, neurologists, physical therapists, nurses, lay migraineurs) and the variable number of sessions (e.g., habituation biofeedback 3 times a week for 90 days,³⁵ daily meditation for 30 days,⁶¹ and 1 headache prevention lecture consisting of CBT, relaxation training, and education.)⁴²

As noted in the Methods section, when a trial reported multiple followup timepoints, for meta-analyses we chose the timepoint closest to 12 weeks after the start of treatment.

3.2.2 Results, Key Question 1, Description of Included Evidence

Table 4. Studies included for Key Question 1 for adults

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment	Control Group(s)
Aguirrezabal et al. (2019) ⁵⁰	NR	Education	None	TAU or no intervention
Blanchard et al. (1978) ⁷⁶	NR	<ul style="list-style-type: none"> • Relaxation training (PMR) • Thermal Biofeedback + Relaxation training (Autogenic training) 	None	TAU or no intervention
Bromberg et al. (2012) ⁴⁵	100% Chronic	CBT + Biofeedback + Relaxation training + Education	None	TAU or no intervention
Brown et al. (1984) ¹¹⁰	NR	<ul style="list-style-type: none"> • MBSR via guided imagery, relaxing statements • MBSR via guided imagery, scene details 	None	Attention control
Cousins et al. (2015) ⁴¹	Mixed (%s NR)	CBT + Relaxation training (PMR + Deep breathing)	None	TAU or no intervention
Cuneo et al. (2023) ¹¹³	100% Chronic	Biofeedback	None	TAU or no intervention
D'Souza et al. (2008) ⁶²	NR	Relaxation training (Autogenic training + Deep breathing)	Written emotional disclosure (not an included treatment)	Attention control
Day et al. (2014) ³²	NR	MBCT	None	TAU or no intervention
Dittrich et al. (2008) ³⁸	NR	Relaxation training (PMR) + Exercise	None	TAU or no intervention
Flynn et al. (2019) ⁶⁰	NR	Hypnotherapy	None	TAU or no intervention
Grazzi et al. (2021) ⁶⁶	100% Episodic	Acceptance and Commitment Therapy	None	TAU or no intervention
Hedborg et al. (2011) ⁴⁶	100% Episodic	<ul style="list-style-type: none"> • Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management • Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management + Massage therapy 	None	Minimal control
Holroyd et al. (1988) ²³	100% Chronic	Thermal Biofeedback + Relaxation training	None	Attention control
Holroyd et al. (2010) ³⁶	NR	<ul style="list-style-type: none"> • CBT + Relaxation training (PMR) + propranolol • CBT + Relaxation training (PMR) 	Propranolol	Placebo
Kewman et al. (1980) ²⁵	100% Episodic	Thermal Biofeedback	None	Attention control
Klan et al. (2022) ⁶⁵	96% Episodic, 4% Chronic	<ul style="list-style-type: none"> • CBT + Relaxation training (PMR) + Education • Relaxation training 	None	TAU or no intervention
Kleiboer et al. (2014) ⁴³	Mixed (% NR)	CBT + Relaxation training + Education	None	TAU or no intervention
Kohlenberg et al. (1981) ³⁰	100% Episodic	CBT + Thermal Biofeedback + Education + Relaxation training + MBSR (Meditation)	None	Attention control

3.2.2 Results, Key Question 1, Description of Included Evidence

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment	Control Group(s)
Lemstra et al. (2002) ⁴⁹	100% Chronic	CBT + Relaxation training + Education + Exercise + Massage therapy + Physical therapy	None	TAU or no intervention
Matchar et al. (2008) ⁶⁴	100% Chronic	Relaxation training + Education	None	TAU or no intervention
Mathew et al. (1981) ²⁷	NR	<ul style="list-style-type: none"> • Thermal and EMG Biofeedback • Thermal and EMG Biofeedback + Propranolol • Thermal and EMG Biofeedback + Amitriptyline • Biofeedback + Amitriptyline + Propranolol 	Propranolol Amitriptyline Propranolol + Amitriptyline	TAU or no intervention
Mérelle et al. (2008) ⁴⁷	100% Episodic	Relaxation training (autogenic training) + Education	None	TAU or no intervention
Minen et al. (2020) ⁵⁶	NR	Relaxation training (PMR)	None	TAU or no intervention
Minen et al. (2020) ⁵⁸	NR	Relaxation training (PMR)	None	TAU or no intervention
Minen et al. (2021) ⁵⁷	NR	Heart rate variability Biofeedback	None	TAU or no intervention
Odawara et al. (2015) ⁴⁰	100% Episodic	Thermal Biofeedback + EMG biofeedback + PMR	None	TAU or no intervention
Pickering et al. (2012) ⁴⁴	100% Episodic	Relaxation training	None	TAU or no intervention
Rausa et al. (2016) ³⁹	100% Chronic	EMG Biofeedback	None	Attention control
Richardson et al. (1989) ⁷⁴	Mixed (%s NR)	<ul style="list-style-type: none"> • CBT + Relaxation training (PMR) (in clinic) • CBT + Relaxation training (PMR) (self-administered) 	None	TAU or no intervention
Rothrock et al. (2006) ⁴⁸	19% Episodic, 81% Chronic	Education (general migraine information)	None	Minimal control
Sargent et al. (1986) ^{107,112}	NR	<ul style="list-style-type: none"> • Thermal Biofeedback + Relaxation training • EMG Biofeedback + Relaxation training • Relaxation 	None	TAU or no intervention
Seng et al. (2019) ⁵⁵	48% Episodic, 52% Chronic	MBCT + education	None	TAU or no intervention
Simshäuser et al. (2022) ⁶⁷	100% Episodic	MBCT	None	TAU or no intervention
Underwood et al. (2022) ⁶⁸	45.5% Episodic, 54.5% Chronic	Education (healthy living, general migraine information)	None	Minimal control
Vasiliou et al. (2021) ⁵²	Mixed (%s NR)	Acceptance and Commitment Therapy	None	TAU or no intervention
Wittchen et al. (1983) ¹¹¹	NR	CBT + Relaxation training + Education	None	TAU or no intervention

3.2.2 Results, Key Question 1, Description of Included Evidence

Abbreviations: ACT=acceptance and commitment therapy; CBT=cognitive behavioral therapy; EMG=electromyography MBCT=mindfulness-based cognitive therapy; MBSR=mindfulness-based stress reduction; NR=Not reported; PMR=progressive muscle relaxation; TAU=treatment as usual.

Table 5. Studies included for Key Question 1 for children/adolescents

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment	Control Group(s)
Albers et al. (2015) ⁴²	100% Episodic	CBT + Relaxation training + Education	None	TAU or no intervention
Connelly et al. (2006) ⁷²	76% Episodic, 24% Chronic	CBT + Relaxation training + Education	None	TAU or no intervention
Cottrell et al. (2007) ⁷¹	100% Episodic	CBT + Thermal Biofeedback + Relaxation training (PMR) + Education + Activity pacing	None	Attention control
Fichtel et al. (2001) ⁷⁷	100% Episodic	Relaxation training (PMR)	None	TAU or no intervention
Labbe et al. (1984) ²⁴	100% Episodic	Thermal Biofeedback + Relaxation training (Autogenic training)	None	TAU or no intervention
Labbe et al. (1995) ²²	100% Episodic	<ul style="list-style-type: none"> Thermal Biofeedback + Relaxation training (Autogenic training) Relaxation training (Autogenic training) 	None	TAU or no intervention
Rapoff et al. (2014) ⁶⁹	Mixed (% NR)	CBT + Relaxation training + Pain management education	None	Minimal control
Richter et al. (1986) ³¹	100% Episodic	<ul style="list-style-type: none"> CBT Relaxation training (PMR + Deep breathing) 	None	Attention control
Scharff et al. (2002) ⁷³	100% Episodic	CBT + Thermal Biofeedback + Relaxation training	None	Attention control TAU or no intervention

Abbreviation: CBT=cognitive behavioral therapy; PMR=progressive muscle relaxation; TAU=treatment as usual.

3.2.3 Risk of Bias

All risk-of-bias judgments (including each of the 4 component domains) appear in Appendix C. For KQ1, we judged the overall risk of bias to be Some Concerns for 7 studies (16%) and High for 38 studies (84%). Our concerns mostly surrounded domains 3 (incomplete data) and domain 4 (measurement bias). Specifically, incomplete data often occurred due to the number of patients not providing data at followup sufficient to affect results with either evidence that missingness was differential between groups or insufficient information to demonstrate that missingness was not related to the true value of the outcome. Missing outcome data was judged to present a high risk of bias in 13 studies and some concerns in another 10 studies. Measurement bias was mostly due to differences in attention time from study staff and differential expectations of benefit in control groups (e.g., waitlist) versus treatment groups. The purpose of an attention control group, which eight studies used, is to try to account for these concerns. Specifically, if the control group is seen for approximately the same amount of time by study staff as the actively treated group, and the control group's treatment could reasonably be believed to

3.2.4 Results, Key Question 1, Summary of Findings

improve migraine-related outcomes, then differential expectations are an unlikely reason for why outcomes may have differed. However, few studies did this, and this domain was judged to present a high risk of bias in 29 studies. Domain 1 (concerns about randomization) was often judged as Some Concerns due to authors not reporting how they performed the randomization or stating whether they concealed allocation. Domain 2 (concerns about deviations from intended interventions) was rarely a source of bias, as 38/45 studies (84 percent) were judged at Low risk of bias for this domain.

3.2.4 Summary of Findings

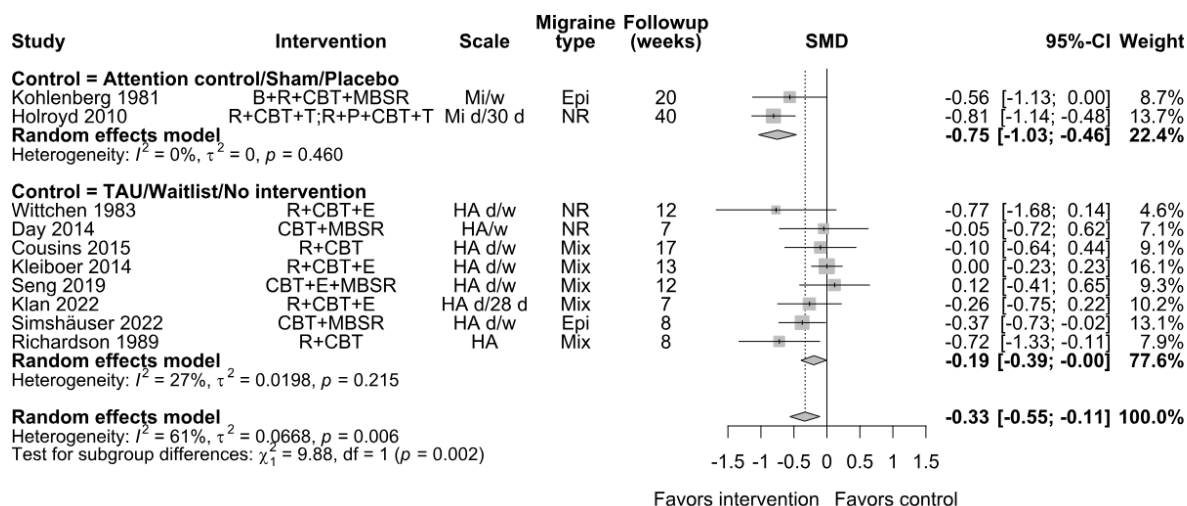
3.2.4.1 Adults: CBT

We included 11 studies for KQ1 that administered CBT to adults. Our meta-analyses of appear in Figure 4, Figure 5, and Figure 6. Only one study (Klan et al. 2022⁶⁵) used CBT as the only treatment component.

3.2.4.1.1 Migraine/Headache Attack Frequency

Our meta-analysis of 10 studies that reported sufficient information for effect size calculation (Figure 4) found a summary standardized mean difference (SMD) of -0.33, with a 95 percent confidence interval (CI) from -0.55 to -0.11 ($\tau^2 = 0.07$, indicating little between-study heterogeneity). On the scale of migraine days per month, this translates to 1.1 fewer migraine days per month with CBT than no treatment, with a 95% CI from 1.8 to 0.4 fewer days. Neither Bromberg et al. (2012)⁴⁵ nor Lemstra et al. (2002)⁴⁹ reported data on this outcome.

Figure 4. Meta-analysis of CBT, adults, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

3.2.4 Results, Key Question 1, Summary of Findings

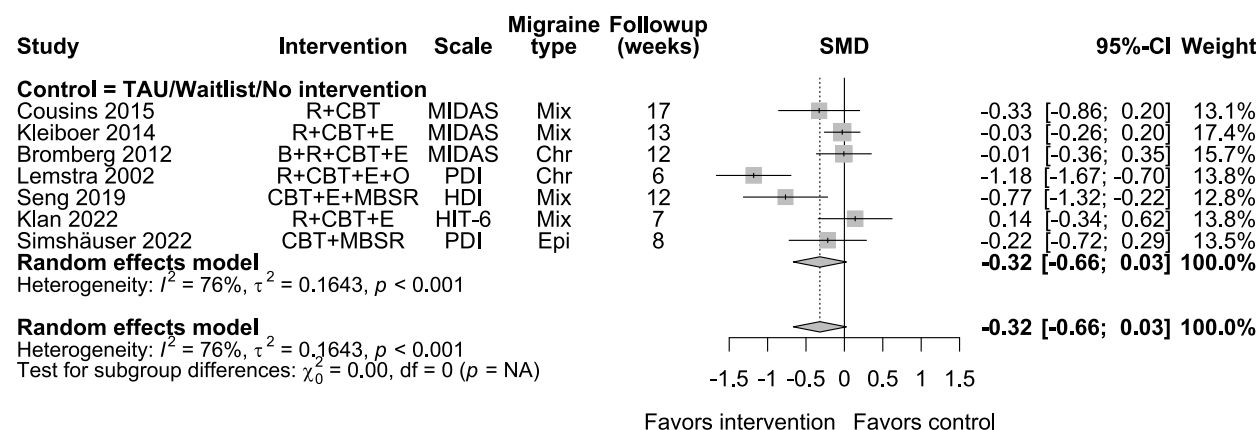
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.1.2 Migraine Disability

Seven studies used one of the key instruments for measuring this outcome and reported enough information for us to calculate effect sizes, and we conducted a meta-analysis (Figure 5). The summary SMD was -0.32 with a 95 percent CI from -0.66 to 0.03, which was not statistically significant. This result corresponds to 9 points on the Migraine Disability Assessment (MIDAS) (95 percent CI -18 to 1). Given that our minimally important difference (MID) for MIDAS of 3 points, this result is inconclusive, as the 95% CI included both no effect (difference of 0) and an important effect (difference of 3). The likely reason for the wide CI is between-study heterogeneity ($\tau^2=0.16$).

Of the other four studies, only one reported disability results. Wittchen et al. (1983)¹¹¹ found that at baseline, the group receiving CBT had an average of 2.4 days per week weekly days with severe performance impairments, which decreased to 1.7 at followup. However, the control group decreased from 3.5 to 3.0 on this same measure, and the between-group statistical test was not reported. We conducted the test using the information provided, and we found that it was not statistically significant. Thus, these results are still inconclusive after considering the non-meta-analyzed study.

Figure 5. Meta-analysis of CBT, adults, disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS – Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

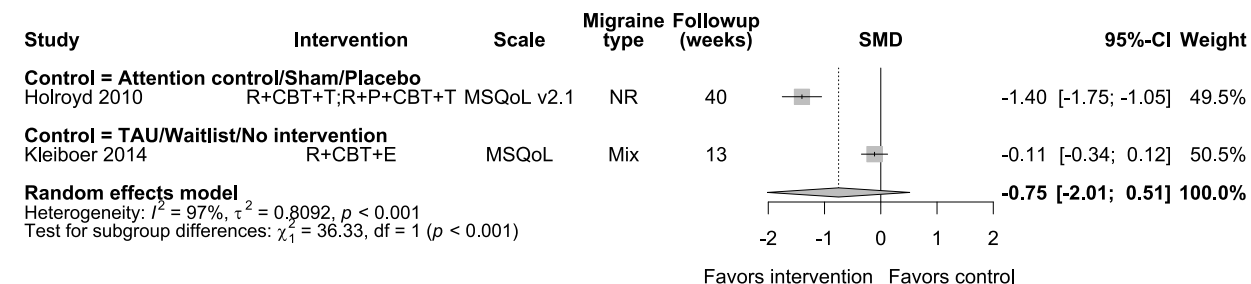
3.2.4.1.3 Migraine-Specific Quality of Life

Only 2 of 11 studies reported data in this category, and both reported calculable effect sizes of key measurement instruments (meta-analysis in Figure 6). While Holroyd et al (2010)³⁶ found a statistically significant advantage for the groups receiving CBT, Kleiboer et al. (2014)⁴³ reported the Dutch version of the Migraine-specific quality of life (MSQOL) instrument and

3.2.4 Results, Key Question 1, Summary of Findings

found no statistically significant difference between groups. The inconsistency produced a wide confidence in the meta-analysis, precluding conclusions.

Figure 6. Meta-analysis of CBT, adults, migraine-specific quality of life



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: MSQoL – Migraine-Specific Quality of Life

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.1.4 Adverse Events

Bromberg et al. (2012)⁴⁵ reported that no adverse events occurred in either the CBT + biofeedback + relaxation training group or the usual care group.

3.2.4.1.5 Other Outcomes

We extracted additional outcomes from nine CBT studies (see Appendix C for all pertinent data). These included other aspects of migraine such as pain intensity (7 studies),^{23,30,34,49,74,75,111} migraine duration (2 studies),^{30,49} and use of rescue medications (7 studies).^{20,23,30,41,43,65,111} Instruments to measure anxiety, depression, or sleep problems were the Beck Depression Inventory,^{23,49} the Generalized Anxiety Disorder-7,³⁴ the Hamilton Anxiety and Depression Scale,^{20,41} the Depression/Anxiety/Stress Scale,^{45,65} the State-Trait Personality Inventory,²³ and the Patient Health Questionnaire.³⁴ One study for KQ1 reported general quality of life (QOL) using visual analog scale for self-rated health.⁴⁹

3.2.4.2 Adults: Biofeedback

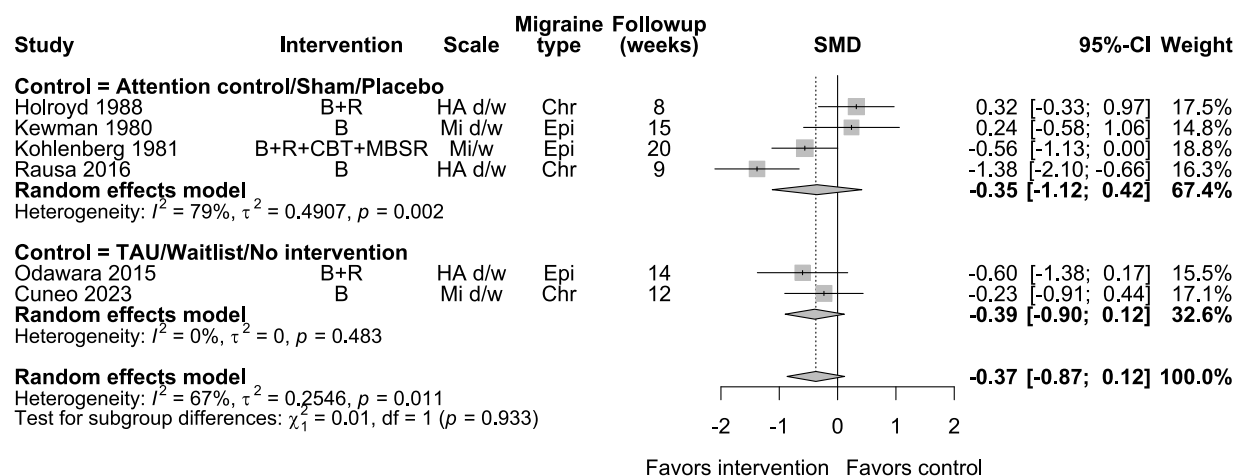
We included 13 studies for KQ1 that administered biofeedback to adults. Five used biofeedback as the only treatment component (Minen et al. 2021,⁵⁷ Rausa et al. 2016,³⁹ Mathew et al. 1981,²⁷ Kewman et al. 1980,²⁵ and Cuneo et al. 2023).¹¹³

3.2.4.2.1 Migraine/Headache Attack Frequency

Six of the 13 reported effect-size-calculable information, allowing meta-analysis (Figure 7). The summary SMD was inconclusive (-0.37, 95% CI -0.87 to 0.12, which corresponds to -3 to 0.4 migraine days per month). The wide confidence was likely due to between-study heterogeneity ($\tau^2 = 0.25$). Of the other seven studies, three reported this outcome. Sorbi et al. (1984)⁷⁵ found no statistically significant difference between groups in the percentage reduction in frequency. Sargent et al. (1986)^{107,112} and Blanchard et al. (1978)⁷⁶ both reported migraine frequency data, but neither reported group-specific standard deviations (SDs) or a statistical comparison between biofeedback and no treatment.

3.2.4 Results, Key Question 1, Summary of Findings

Figure 7. Meta-analysis of biofeedback, adults, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

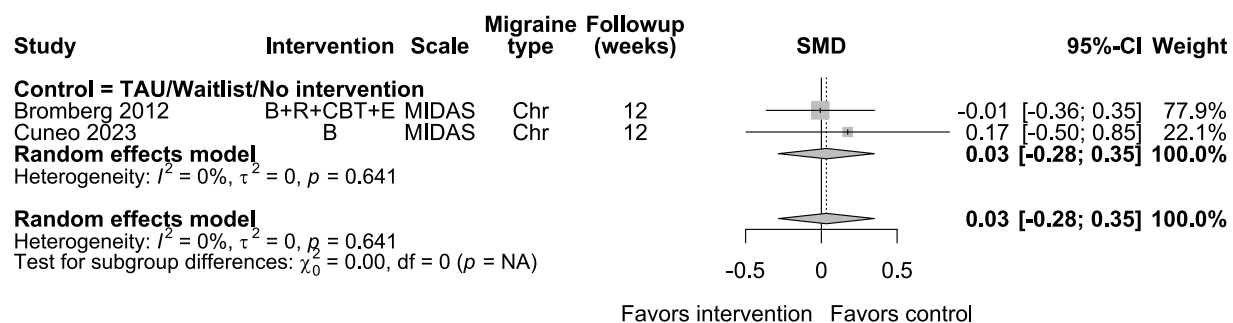
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.2.2 Migraine Disability

Only 2 of the 13 studies (Bromberg et al. 2012)⁴⁵ reported effect-size-calculable information on included instruments for measuring this outcome, and our meta-analysis was inconclusive (Figure 8, summary SMD 0.03, 95 percent CI -0.28 to 0.35, which corresponds to -1 to 1.1 migraine days per month). Of the other studies, three reported this outcome. De Tommaso et al. (2017)³⁵ reported there was no statistically significant between-group difference in the rate of severe MIDAS scores after treatment. Odawara et al. (2015)⁴⁰ did not report the disability scale they used but did report that the biofeedback group improved statistically significantly more than the control group. Minen et al. (2021)⁵⁷ reported this outcome (dichotomized as severe or not severe), and there was no statistically significant difference between groups.

3.2.4 Results, Key Question 1, Summary of Findings

Figure 8. Meta-analysis of biofeedback, adults, disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS - Migraine Disability Assessment; PedMIDAS - Pediatric Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.2.3 Migraine-Specific Quality of Life

Minen et al. (2021)⁵⁷ reported data on the MSQoL v2.1. There was no statistically significant difference between groups.

3.2.4.2.4 Adverse Events

Two adult biofeedback studies reported data on adverse events:

- Mathew et al. (1981)²⁷ reported that withdrawal due to adverse events occurred in 4/45 patients with migraine who received usual care, 0/48 who received biofeedback + relaxation training, 2/39 who received biofeedback + relaxation training + propranolol, 2/43 who received biofeedback + relaxation + amitriptyline, and 3/38 who received biofeedback + relaxation training + propranolol + amitriptyline.
- Bromberg et al. (2012)⁴⁵ reported that no adverse events occurred in either the CBT + biofeedback + relaxation training group or the usual care group.

3.2.4.2.5 Other Outcomes

We extracted additional efficacy outcomes from nine biofeedback studies (see Appendix C for all pertinent data). These included other aspects of migraine such as pain intensity (4 studies),^{23,30,75,112} migraine duration, (1 study),³⁰ and use of rescue medications (6 studies).^{23,30,39,75,76,113}

Instruments to measure anxiety, depression, or sleep problems were the State-Trait Personality Inventory,²³ the Beck Depression Inventory,²³ the Generalized Anxiety Disorder-7,⁵⁷ the Depression/Anxiety/Stress Scale,⁴⁵ the Zung Self-Rating Depression Scale,²⁷ and the Patient Health Questionnaire.^{57,113} None of the biofeedback studies reported general QOL.

3.2.4.3 Adults: Relaxation Training

We included 23 studies for KQ1 that administered relaxation training to adults. Five of them had used relaxation training as the only treatment component (Blanchard et al. 1978,⁷⁶ Minen et al. 2020,⁵⁶ Minen et al. 2020,⁵⁸ Pickering et al. 2012),⁴⁴ and D'Souza et al. (2008).⁶²

3.2.4 Results, Key Question 1, Summary of Findings

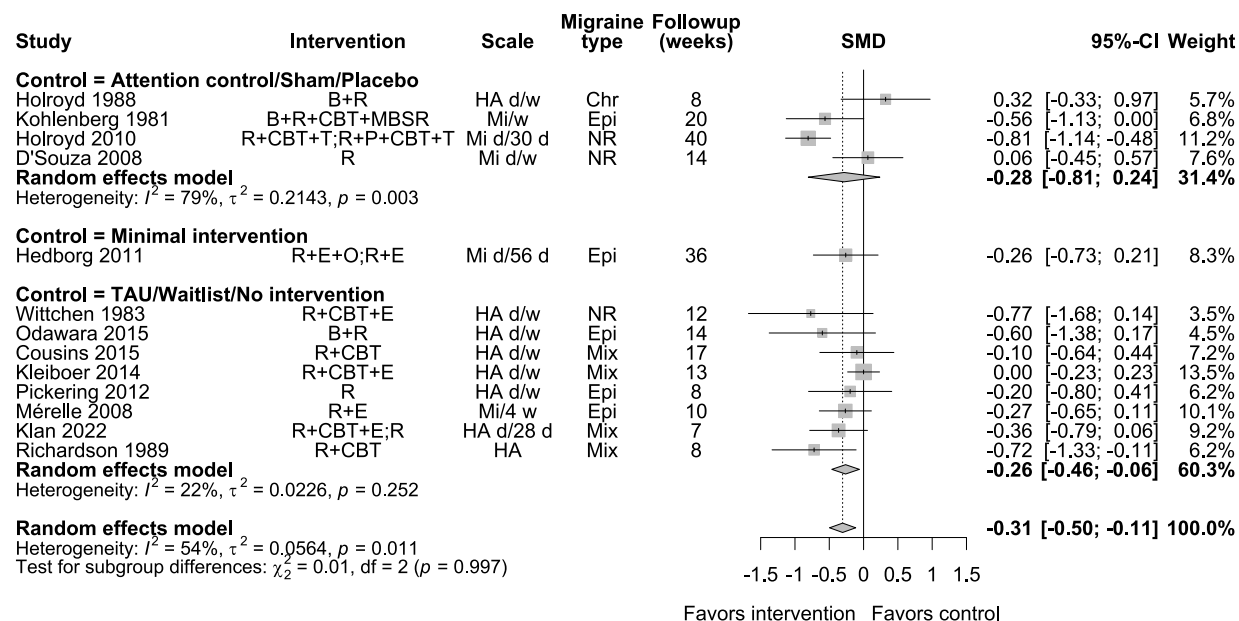
3.2.4.3.1 Migraine/Headache Attack Frequency

Thirteen of 23 studies reported effect-size-calculable information, and we meta-analyzed the data (Figure 9). The summary CI ranged from an SMD of -0.50 to -0.11, indicating statistical significance in favor of relaxation training. Our meta-analysis estimated that compared with a range of controls (ranging from treatment as usual to attention control) relaxation training resulted in one fewer migraine day/month (95 percent CI 0.4 to 1.6 days). Notably, only two trials assessed relaxation training alone; instead, most trials assessed relaxation training in combination with other components (e.g., biofeedback, CBT). The meta-analysis also found statistically significant between-study heterogeneity ($\tau^2 = 0.06$, $p = 0.011$).

Four additional studies reported pertinent data but insufficient data for effect size calculation:

- Dittrich et al. (2008)³⁸ reported self-rated approximate frequency of migraine attacks (rough categories of more than once per year, once per month, more than once per month, or once per week or more) and did not statistically compare the group's percentages at followup. Authors did not test statistical significance, but the data were in the direction of favoring relaxation training.
- Minen et al. (2020)⁵⁸ reported the number of headache and headache-free days in both the relaxation training group and control group, with no statistical comparison reported, but the data were in the direction of favoring the control group.
- Sargent et al. (1986)^{107,112} and Blanchard et al. (1978)⁷⁶ did not report statistical tests, but data were in the direction of favoring relaxation training.

Figure 9. Meta-analysis of relaxation training, adults, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

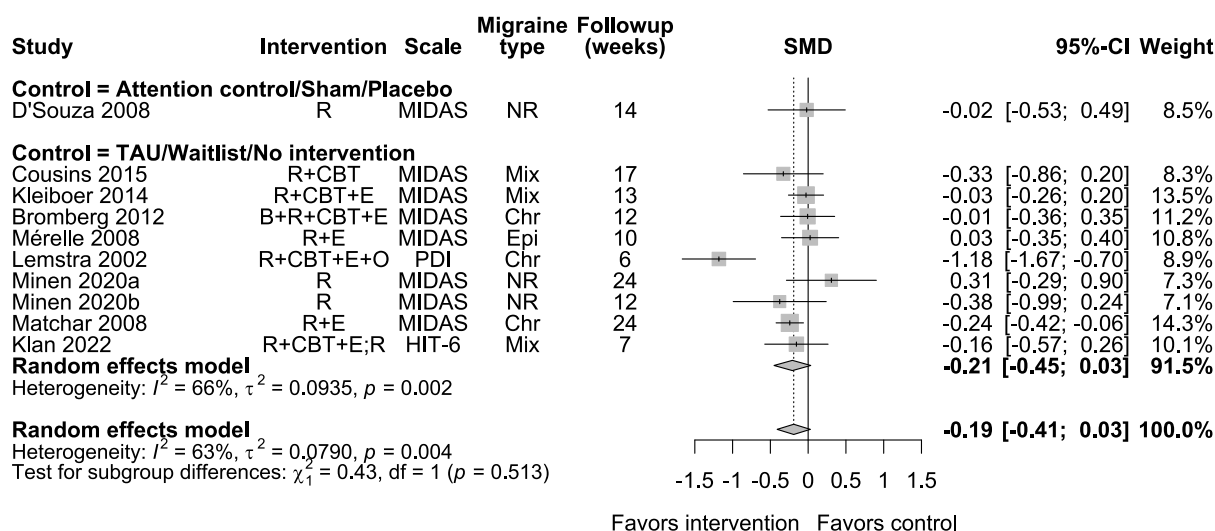
3.2.4 Results, Key Question 1, Summary of Findings

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.3.2 Migraine Disability

Our meta-analysis included 10 of 23 studies (Figure 10). The summary result on the MIDAS scale (range 0 to 90) was -5 points (95 percent CI -11 to 1), which is inconclusive, given our MID of 3 points. The wide confidence was likely due to between-study heterogeneity ($\tau^2=0.079$, $p<0.01$). Three additional studies reported this outcome domain but were not included in meta-analyses: Odawara et al. (2015)⁴⁰ did not report the disability scale they used but reported that the relaxation training group had a statistically significant improvement compared with control, and Holroyd et al. (1988)²³ used the Wahler Physical Symptom Checklist, which was not on our list of meta-analyzed disability scales, and reported no statistically significant between-group difference. Wittchen et al. (1983)¹¹¹ found that at baseline, the group receiving relaxation training had an average of 2.4 days per week with severe performance impairments, which reduced to 1.7 at followup. The control group decreased from 3.5 to 3.0 on this same measure, and the authors did not report the between-group statistical test. We conducted the test using the information provided, and it was not statistically significant.

Figure 10. Meta-analysis of relaxation training, adults, disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS - Migraine Disability Assessment; PedMIDAS - Pediatric Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

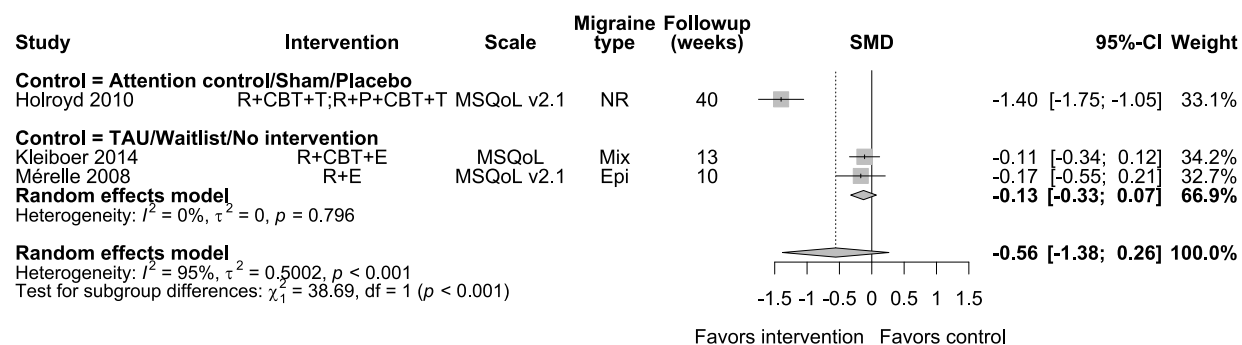
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.3.3 Migraine-Specific Quality of Life

Three of the 23 studies reported effect-size-calculable information, and we meta-analyzed the data (Figure 11). The effect was inconclusive (summary SMD -0.56, 95% CI -1.38 to 0.26, corresponding to an MSQOL difference of -8, 95% CI -19 to 4).

3.2.4 Results, Key Question 1, Summary of Findings

Figure 11. Meta-analysis of relaxation training, adults, migraine-specific quality of life



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: MSQoL – Migraine-Specific Quality of Life

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.3.4 Adverse Events

One adult relaxation training study reported data on adverse events. Bromberg et al. (2012)⁴⁵ reported that no adverse events occurred in either the CBT + biofeedback + relaxation training group or the usual care group.

3.2.4.3.5 Other Outcomes

We extracted additional effectiveness outcomes from 15 relaxation training studies (see Appendix C for all pertinent data). These included other aspects of migraine, such as pain intensity (7 studies),^{23,30,49,62,74,111,112} migraine duration (2 studies),^{23,30} and use of rescue medications (9 studies).^{20,23,30,41,43,46,65,76,111} Instruments to measure anxiety, depression, or sleep problems were the Beck Depression Inventory,^{23,38,49} the Depression/Anxiety/Stress Scale,^{45,65} the HADS,⁴¹ the Montgomery-Asberg Depression Rating Scale,⁴⁶ the Patient Health Questionnaire-9 (PHQ-9),⁶⁴ or the State-Trait Personality Inventory.²³ Four studies reported general QOL using the Symptom Checklist-90-R,⁶² the PQ23 (abbreviation not defined by authors),⁴⁶ self-rated health using a visual analog scale,⁴⁹ or the Short Form 36 (SF-36).⁶⁴

3.2.4.4 Adults: Mindfulness-Based Treatments

We included five studies for KQ1 that administered mindfulness-based treatments to adults. Brown et al. (1984)¹¹⁰ employed single-component treatment. Seng et al. (2019)⁶⁷ reported combination treatment with CBT, mindfulness-based stress reduction (MBSR), and education; Simshäuser et al. (2022)⁶⁷ and Day et al. (2014)³² used both CBT and MBSR (i.e., MBCT); and Kohlenberg et al. (1981)³⁰ reported a multicomponent treatment that included CBT, relaxation training, biofeedback, and meditation.

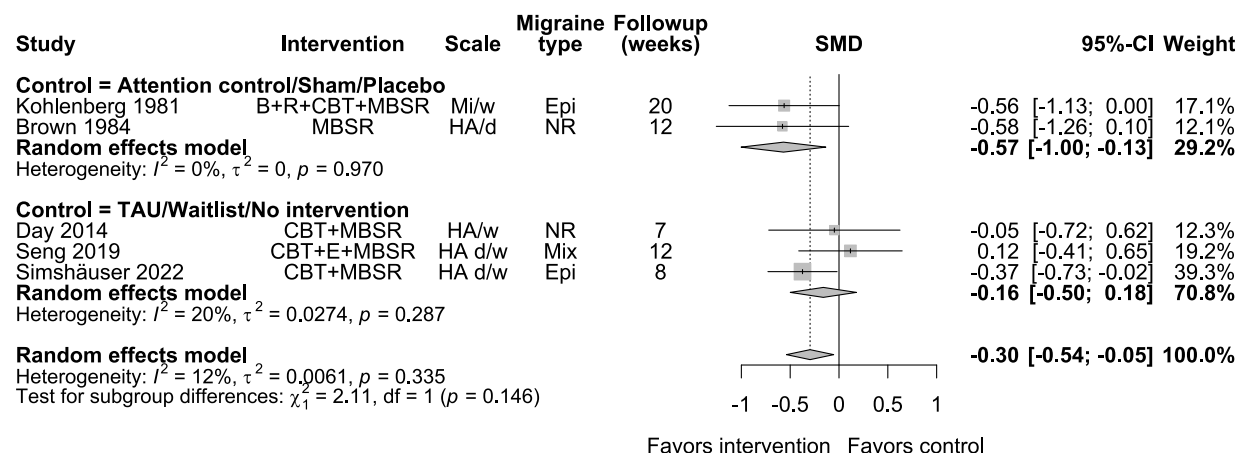
3.2.4.4.1 Migraine/Headache Attack Frequency

All five studies reported this outcome and enough information for effect size calculation (Figure 12). The meta-analytic result statistically favored MBSR-based treatments (SMD -0.30,

3.2.4 Results, Key Question 1, Summary of Findings

95% CI -0.54 to -0.05, which corresponds to one fewer migraine day/month, 95% CI 0.2 to 1.8). There was little between-study heterogeneity ($\tau^2=0.006$).

Figure 12. Meta-analysis of MBSR-based treatment, adults, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

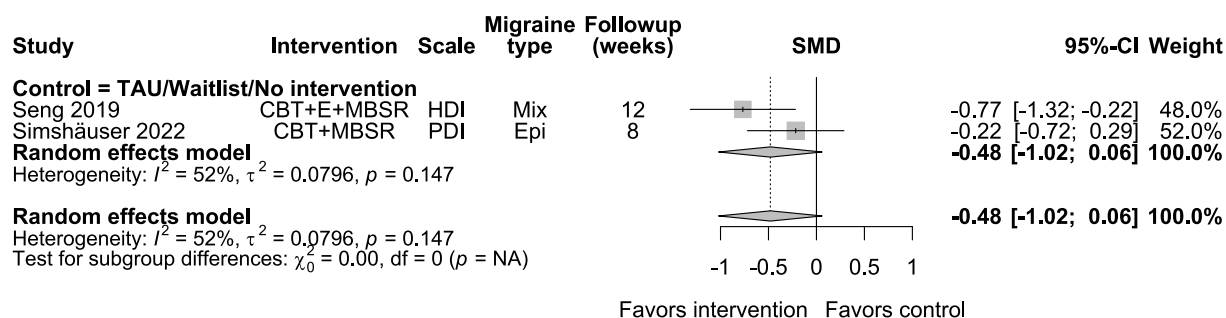
For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.4.2 Migraine Disability

We meta-analyzed the two studies that reported data in this category (Figure 13). A random-effects meta-analysis was inconclusive (SMD= -0.48, 95% CI -1.02 to 0.06).

Figure 13. Meta-analysis of MBSR-based treatment, adults, disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS - Migraine Disability Assessment; PedMIDAS - Pediatric Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4 Results, Key Question 1, Summary of Findings

3.2.4.4.3 Migraine-Specific Quality of Life

None of the five MBSR studies reported this outcome category.

3.2.4.4.4 Other Outcomes

Simshäuser et al. (2022)⁶⁷ reported 7/27 subjects dropped out of the MBCT group because of dissatisfaction with treatment in 3, other diseases in 2, time constraints in 1, and unspecified in 1. Seven of 27 dropouts occurred in the usual care group because of time constraints in four, alleviation of migraine in two, and length of waiting period in one. They also reported that there was no statistically significant difference in medication days between groups. They also reported a statistically significant advantage of MBCT over the control group with respect to anxiety scores but not depression scores.

Seng et al. (2019)⁵⁵ reported that there was no statistically significant difference in pain intensity between groups. Day et al. (2014)³² measured the amount of acetaminophen and morphine taken and found no statistically significant difference between groups. Kohlenberg et al. (1981)³⁰ reported data on pain intensity, use of acute pain medications, and migraine duration, and data for all three of these outcomes favored the combined-treatment group.

3.2.4.5 Adults: Education Alone

Three studies specifically examined education's impact in adults.^{48,50,63,68,74} This section differs from those above on CBT, biofeedback, and relaxation training, because those sections considered any use of a single component regardless of other additional components, whereas this section examines only education when used in isolation (see the beginning of KQ1 for our explanation). Table 4 above lists the specific topics of educational focus in each of the three studies.

3.2.4.5.1 Migraine/Headache Attack Frequency

Underwood et al. (2022)⁶⁸ found a statistically significant effect against education (the comparator was a minimal control group; the effect corresponded to a difference of 0.8 migraine days/month, 95% CI 0.2 to 1.4). In contrast, Rothrock et al. (2006)⁴⁸ reported only mean reductions and no dispersion, but at followup, the education group had improved by six headaches a month and zero change in the control group. Aguirrezabal et al. (2019)⁵⁰ did not report data on this outcome.

3.2.4.5.2 Migraine Disability

All three studies found a statistically significant advantage of education. Rothrock et al. (2006)⁴⁸ reported that MIDAS scores improved statistically significantly more in the education group than in the control group (effect size not calculable). Aguirrezabal et al. (2019)⁵⁰ found that the percentage of patients who experienced at least a 50 percent improvement in MIDAS score was statistically significantly higher in the education group (70 percent versus 35 percent). Underwood et al. (2022)⁶⁸ reported a statistically significant advantage of education (corresponding to Headache Impact Test (HIT-6) difference of 1.2 points, 95% CI 0.1 to 2.3).

3.2.4.5.3 Migraine-Specific Quality of Life

None of the studies reported data in this category.

3.2.4 Results, Key Question 1, Summary of Findings

3.2.4.5.4 Adverse Events

Underwood et al. (2022)⁶⁸ reported six events (none serious) in the education group but only one event (a death) in the control group (statistical comparison not reported). None of the other studies reported adverse events.

3.2.4.5.5 Other Outcomes

Underwood et al. (2022)⁶⁸ reported data on general QOL, anxiety, headache duration, pain severity, and use of painkillers or triptans for acute headache. Rothrock et al. (2006)⁴⁸ reported data on acute medication use, analgesic use, and unscheduled outpatient visits. Aguirrezabal et al. (2019)⁵⁰ reported data on medication intake, headache duration, and pain intensity. Richardson et al. (1989)⁷⁴ reported data on medication intake and pain intensity.

3.2.4.6 Adults: Acceptance and Commitment Therapy

We included two studies for KQ1 that administered acceptance and commitment therapy (ACT) to adults; both compared it with usual care.^{52,66} In both studies, ACT was the only treatment component. Only Grazzi et al. (2021)⁶⁶ reported outcome data on migraine/headache attack frequency, and results statistically significantly favored ACT (SMD corresponding to 2.3 fewer migraine days per month, 95% CI 0.03 to 4.5).

For migraine-related disability, Grazzi et al. (2021)⁶⁶ found no statistically significant difference for either MIDAS or HIT-6 (MIDAS difference of +13 in the direction of the control group 95% CI -5 to 31, and HIT-6 difference of +3 in the direction of the control group 95% CI - to 8, whereas Vasiliou et al. (2021)⁵² reported a statistically significant advantage of ACT (SMD corresponding to a MIDAS difference of -18 in the direction of the ACT group 95% CI 4 to 31). Our random-effects meta-analysis of this outcome was inconclusive due to a wide CI (SMD corresponding to a MIDAS difference of -3; 95% CI -33 to 27).

Neither study reported data on migraine-related QOL.

Grazzi et al. (2021)⁶⁶ reported that no adverse events occurred in patients receiving either ACT or usual care. Vasiliou et al. (2021)⁵² did not report adverse event data.

Both studies^{52,66} reported subscales of the Hospital Anxiety and Depression Scale (HADS). Grazzi et al. (2021)⁶⁶ also reported the number of acute headache medications used. The results all appear in Appendix C.

3.2.4.7 Adults: Hypnotherapy

Flynn et al. (2019)⁶⁰ compared hypnotherapy (the only treatment component) with usual care. For migraine/headache attack frequency, there was no statistically significant difference (SMD corresponding to a difference of 0 with a 95% CI from -2 to 2). For migraine-related disability, the study reported a statistically significant advantage of hypnotherapy (SMD corresponding to a MIDAS difference of 42 with a 95% CI 23 to 61). The study did not report migraine-specific QOL or adverse events. They did report four other outcomes: Pain Catastrophizing Scale, migraine duration, pain severity, and the Medication Index Score. These results all appear in Appendix C.

3.2.4.8 Children/Adolescents: CBT

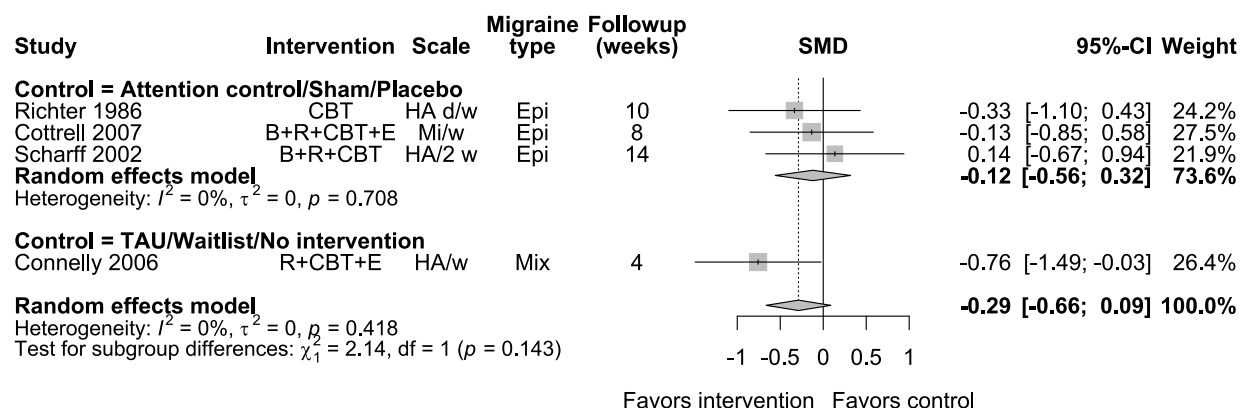
We included six studies for KQ1 that administered CBT to children/adolescents. In one, CBT was the only treatment component (Richter et al. 1986).³¹

3.2.4 Results, Key Question 1, Summary of Findings

3.2.4.8.1 Migraine/Headache Attack Frequency

Our meta-analysis of four studies of this outcome (Figure 14) was inconclusive (SMD -0.29 with a 95% CI from -0.66 to 0.09, corresponding to -2 migraine days/month to +0.3 migraine days a month), as the meta-analytic CI encompassed both a benefit of CBT and of not doing CBT. Heterogeneity was negligible ($\tau^2=0$). A fifth study, Rapoff et al. (2014),⁶⁹ reported data in a different way (the percentage of days that the child reported having had a headache), with both groups reporting a reduction after treatment and no statistically significant difference between groups. Albers et al. (2015).⁴² reported no statistically significant difference between groups for this outcome.

Figure 14. Meta-analysis of CBT, children/adolescents, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

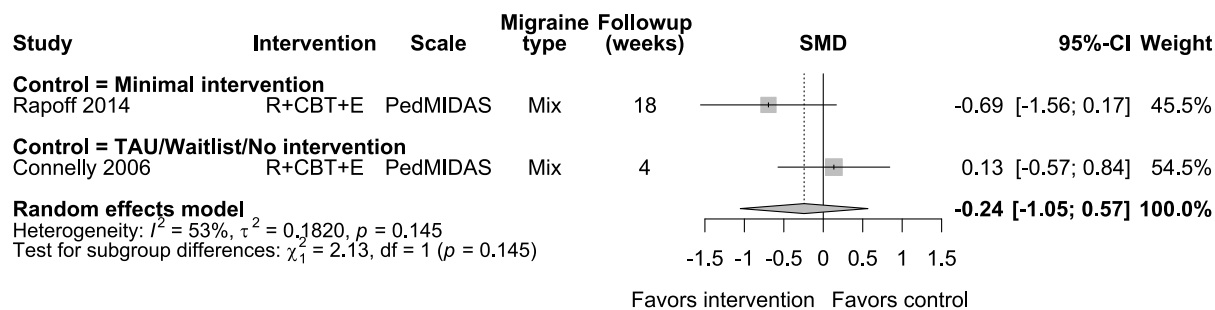
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.8.2 Migraine Disability

Our meta-analysis of two studies of this outcome (Figure 15) was inconclusive (SMD -0.24 with a 95% CI from -1.05 to 0.57, $\tau^2=0.18$). The summary effect corresponds to a MIDAS difference of -6 with a 95% CI from -28 to 15). Cottrell et al. (2007)⁷¹ reported the average number of hours children were disabled instead of using an instrument to measure disability and did not report a statistical comparison of groups, but the pre-post CIs largely overlapped, suggesting no statistically significant difference. The other studies did not report this outcome.

3.2.4 Results, Key Question 1, Summary of Findings

Figure 15. Meta-analysis of CBT, children/adolescents, migraine disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS - Migraine Disability Assessment; PedMIDAS - Pediatric Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.8.3 Migraine-Specific Quality of Life

Only Cottrell et al. (2007)⁷¹ reported this outcome (MSQOL for adolescents), and both groups had improved, with no statistical comparison reported between groups.

3.2.4.8.4 Adverse Events

Not reported.

3.2.4.8.5 Other Outcomes

Five of six studies reported migraine pain intensity.^{31,69,71-73} One study reported general QOL as measured by the Pediatric Quality of Life Inventory (PedsQL).⁶⁹ These results all appear in Appendix C.

3.2.4.9 Children/Adolescents: Biofeedback

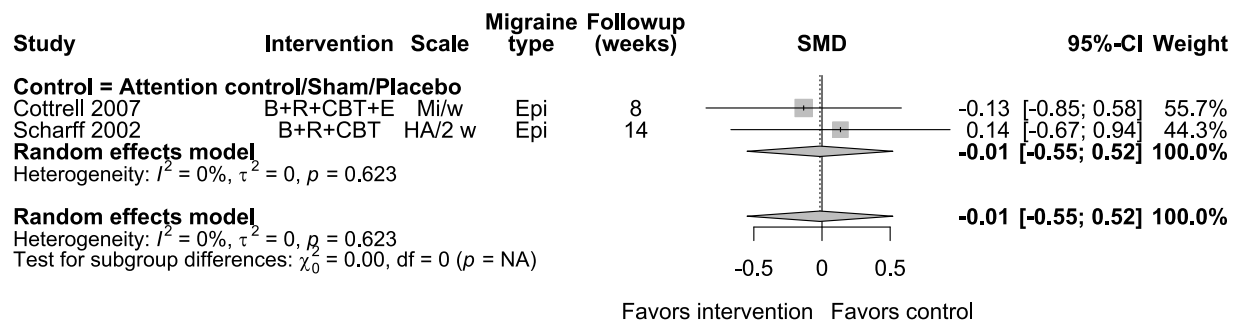
We included four studies for KQ1 that administered biofeedback to children/adolescents. None of the four employed biofeedback as the only treatment component.

3.2.4.9.1 Migraine/Headache Attack Frequency

All four reported this outcome, but only two had calculable effect sizes, which were meta-analyzed (Figure 16). The resulting SMD (-0.01, 95% CI -0.55 to 0.52, $\tau^2 = 0$) corresponds to a difference in migraine/headache days/month of -0.03 (95% CI -1.8 to 1.7), which is inconclusive. Neither of the other two studies, Labbe et al. (1995)²² and Labbe et al. (1984),²⁴ reported dispersion. Both found statistically significantly lower frequencies after treatment in the biofeedback group.

3.2.4 Results, Key Question 1, Summary of Findings

Figure 16. Meta-analysis of biofeedback, children/adolescents, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period.

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference

3.2.4.9.2 Migraine Disability

Cottrell et al. (2007)⁷¹ reported the average number of hours children were disabled instead of using an instrument to measure disability Pediatric Migraine-Specific Disability Assessment (PedMIDAS) and did not report a statistical comparison of groups, but the pre-post CIs largely overlapped, suggesting no statistically significant difference. The other studies did not report this outcome.

3.2.4.9.3 Migraine-Specific Quality of Life

Cottrell et al. (2007)⁷¹ reported this outcome (the MSQOL for adolescents), and both groups had improved, with no statistical comparison reported between groups. The other studies did not report this outcome.

3.2.4.9.4 Adverse Events

None of the KQ1 children/adolescent biofeedback studies reported information about adverse events.

3.2.4.9.5 Other Outcomes

Two of four studies reported pain intensity data,^{24,73} and Labbe et al.²⁴ and Scharff et al. (2002)⁷³ reported medication use. See Appendix C.

3.2.4.10 Children/Adolescents: Relaxation Training

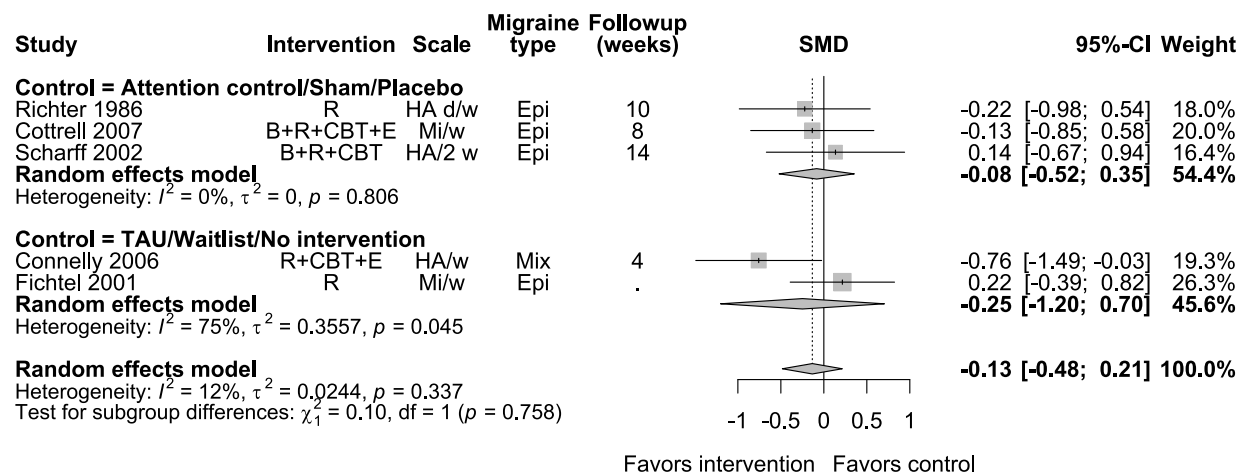
We included nine studies for KQ1 that administered relaxation training to children/adolescents. In two studies, relaxation training was the only treatment component (Labbe et al. 1995²² and Fichtel et al. 2001).⁷⁷

3.2.4 Results, Key Question 1, Summary of Findings

3.2.4.10.1 Migraine/Headache Attack Frequency

We meta-analyzed the five studies of relaxation training in children/adolescents that reported calculable effect sizes (Figure 17). The result was inconclusive (SMD -0.13, 95% CI -0.48 to 0.21, $\tau^2=0.02$, corresponding to a difference of -0.4 migraine/headache days/month, 95% CI -1.6 to 0.7). Three other studies reported data on this outcome. Albers et al. (2015)⁴² reported there was no statistically significant difference between groups in rates of headache cessation (odds ratio [OR] 0.98, 95% CI 0.25 to 3.81). Labbe et al. (1995)²² did not report sufficient information for the calculation of effect sizes but did report that a three-group test (relaxation training only, biofeedback + relaxation training, waitlist control) was statistically significant. The relaxation-only group had reduced the average migraine frequency from 3.67 at baseline to 0.38 at 1 month after the end of treatment, whereas the waitlist control group had a baseline mean of 3.18 with a 1-month followup mean of 2.17. Labbe et al. (1984)²⁴ reported that compared with waitlist control, biofeedback + relaxation training further reduced the number of headache days per week by an average of 1.66 from baseline to 11 weeks.

Figure 17. Meta-analysis of relaxation training, children/adolescents, migraine/headache attack frequency



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA –Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

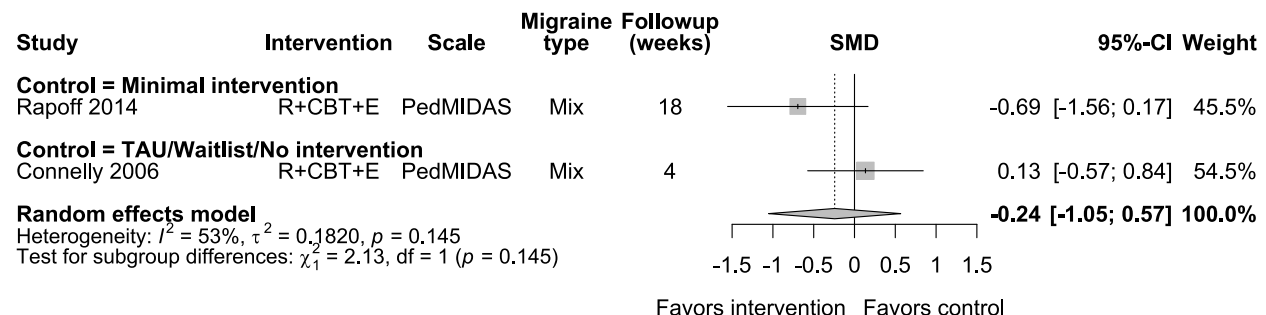
3.2.4.10.2 Migraine Disability

Two studies reported enough information for calculable effect sizes, which we meta-analyzed (Figure 18). The result was inconclusive (SMD -0.24, 95% CI -1.05 to 0.57, $\tau^2=0.18$ corresponding to a MIDAS difference of -6 with a 95% CI from -28 to 15. Of the other studies, only Cottrell et al. (2007)⁷¹ reported this outcome. They reported the average number of hours children were disabled instead of using an instrument to measure disability and did not report a

3.2.4 Results, Key Question 1, Summary of Findings

statistical comparison of groups, but the pre-post CIs largely overlapped, suggesting no statistically significant difference.

Figure 18. Meta-analysis of relaxation training, children/adolescents, disability



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS - Migraine Disability Assessment; PedMIDAS - Pediatric Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

3.2.4.10.3 Migraine-Specific Quality of Life

Cottrell et al. (2007)⁷¹ reported this outcome (the MSQOL for adolescents), and both groups had improved, with no statistical comparison reported between groups. The other studies did not report this outcome.

3.2.4.10.4 Adverse Events

Not reported.

3.2.4.10.5 Other Outcomes

Six studies^{24,31,69,71,73,77} reported pain intensity data, two^{24,77} reported medication data, and one reported general QOL using the PedsQL.⁶⁹

3.2.4.11 Strength of Evidence

Our SOE for KQ1 appears in Table 6 below. We also conducted analyses of *any behavioral treatment* compared with *any inactive treatment*. These analyses were intended to maximize statistical power and determine whether an overall signal can be detected. However, these analyses (see Appendix F) were often inconclusive, possibly because different behavioral interventions were combined generically as “behavioral.”

3.2.4 Results, Key Question 1, Summary of Findings

Table 6. Strength of evidence ratings for Key Question 1 (effectiveness)

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
Adults	CBT	Migraine/headache attack frequency	10 studies, a meta-analysis of all 10 estimated a difference of 1.1 migraine days/month (95% CI 0.4–1.8) favoring CBT.	8 High 2 Mod.	Direct	Consistent	Precise	Not suspected	Low	Favors CBT
Adults	CBT	Migraine-related disability	8 studies, a meta-analysis of 7 of them was inconclusive, estimating a difference of -7 MIDAS points (95% CI -17–3). 1 other study reported the outcome, and the between-group difference was NS.	7 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Adults	CBT	Migraine-specific QOL	2 studies, a meta-analysis was inconclusive, estimating a difference of 11 MSQOL points (95% CI -28–7).	1 High 1 Mod.	Direct	Inconsistent	Imprecise	Not suspected	Insufficient	NA
Adults	Biofeedback	Migraine/headache attack frequency	9 studies, a meta-analysis of 6 of them estimated a difference of 1.2 migraine days/month (95%	6 High 3 Mod.	Direct	Inconsistent	Imprecise	Not suspected	Insufficient	NA

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			CI -3 to 0.4). 3 other studies reported the outcome: 1 was NS, and 2 did not report whether the result was statistically significant.							
Adults	Biofeedback	Migraine-related disability	5 studies, and a meta-analysis of 2 of them estimated a difference of 0.8 MIDAS points (95% CI -1–1.1). 3 other studies reported the outcome: 2 were NS, 1 statistically favored biofeedback.	High	Direct	Inconsistent	Imprecise	Not suspected	Insufficient	NA
Adults	Biofeedback	Migraine-specific QOL	1 study, NS.	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training	Migraine/headache attack frequency	17 studies, a meta-analysis of 13 of them estimated a difference of 1 less migraine day/month with relaxation (95% CI 0.4–1.6). 4 other studies reported the outcome: 3 had no statistical test but in the direction of favoring	12 High 4 Mod.	Direct	Consistent	Precise	Not suspected	Low	Favors relaxation training

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			relaxation, 1 had no statistical test but in the direction of favoring no relaxation training.							
Adults	Relaxation training	Migraine-related disability	12 studies, a meta-analysis of 10 of them estimated a difference of -5 MIDAS points (95% CI -11–1). 3 other studies reported the outcome: 2 were NS, 1 statistically favored relaxation training.	10 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training	Migraine-specific QOL	3 studies, a meta-analysis of all 3 estimated an MSQOL difference of -8, 95% CI -19–4.	2 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Adults	Mindfulness-based therapies	Migraine/headache attack frequency	5 studies, and a meta-analysis of all 5 showed statistically fewer migraine days with MBSR-based therapies (1 fewer migraine day/month, 95% CI 0.2–1.8).	4 High, 1 Mod.	Direct	Consistent	Precise	Not suspected	Low	Favors MBSR-based therapies
Adults	Mindfulness-based therapies	Migraine-related disability	2 studies, and the meta-analysis was inconclusive (SMD	High	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			-0.48, 95% CI -1.02 – 0.06).							
Adults	Education	Migraine/headache attack frequency	2 studies, 1 statistically favored no education and the other was not statistically determinable but was in the direction of favoring education.	1 High 1 Mod.	Direct	Inconsistent	Precise	Not suspected	Insufficient	NA
Adults	Education	Migraine-related disability	3 studies, all statistically significant in favor of education.	2 High 1 Mod.	Direct	Consistent	Precise	Not suspected	Low	Favors education
Adults	ACT	Migraine/headache attack frequency	1 study, favors ACT, 2.3 fewer days/month (95% CI 0.3–4.5).	High	Direct	Unknown	Precise	Not suspected	Insufficient	NA
Adults	ACT	Migraine-related disability	2 studies, 1 favored ACT, the other was NS in the opposite direction. Meta-analysis MIDAS difference of -3 (95% CI -33–27).	High	Direct	Inconsistent	Precise	Not suspected	Insufficient	NA
Adults	Hypnotherapy	Migraine/headache attack frequency	1 study, migraine/headache attack frequency difference of 0 (95% CI -2– 2).	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Hypnotherapy	Migraine-related disability	1 study, favors hypnotherapy, MIDAS difference	High	Direct	Unknown	Precise	Not suspected	Insufficient	NA

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			of -42 (95% CI -61 to -23).							
Adults	Hypnotherapy	Migraine-specific QOL	No studies reported.	NA	NA	NA	NA	NA	NA	NA
Children/adolescents	CBT	Migraine/headache attack frequency	6 studies. A meta-analysis of 4 was inconclusive (95% CI ranging from -2 to 0.3 migraine days/month), and the other 2 studies reported statistically nonsignificant results.	4 High 2 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	CBT	Migraine-related disability	3 studies. A meta-analysis of 2 was inconclusive (95% CI MIDAS difference of -6 with a 95% CI from -28–15). The other study found no statistically significant difference.	2 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	CBT	Migraine-specific QOL	1 study, no statistical comparison between groups.	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Biofeedback	Migraine/headache attack frequency	4 studies, 2 were meta-analyzable, but an inconclusive result (difference in migraine/headache days/month of -0.03 (95% CI -	3 High 1 Mod.	Direct	Inconsistent	Imprecise	Not suspected	Insufficient	NA

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			1.8–1.7). The other 2 studies each had statistically significant results in favor of biofeedback.							
Children/adolescents	Biofeedback	Migraine-related disability	1 study, no statistical comparison between groups, but the 2 pre-post-CIs largely overlapped.	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Biofeedback	Migraine-specific QOL	1 study, no statistical comparison between groups, but the 2 pre-post-CIs largely overlapped.	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Relaxation training	Migraine/headache attack frequency	8 studies, meta-analysis of 5 was inconclusive (difference of -0.4 migraine days/month, 95% CI -1.6– 0.7). 2 studies favored relaxation training. Another study was NS.	7 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Relaxation training	Migraine-related disability	3 studies, 2 meta-analyzed (MIDAS difference -1, 95% CI -3.7–1.8), and in the third study, the 2 pre-post-CIs	2 High 1 Mod.	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA

3.2.4 Results, Key Question 1, Summary of Findings

Age Group	Treatment	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			largely overlapped.							
Children/adolescents	Relaxation	Migraine-specific QOL	1 study, no statistical comparison between groups, but the 2 pre-post-Cis largely overlapped.	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

Abbreviations: ACT=acceptance and commitment therapy; CBT=cognitive behavioral therapy; CI=confidence interval; HIT-6=Headache Impact Test 6; MBCT=mindfulness-based; cognitive therapy; MBSR=mindfulness-based stress reduction; MIDAS=migraine disability assessment; MSQOL=Migraine-specific quality of life; Mod.=moderate risk of bias; NA=not applicable; NS=not statistically significant; QOL=quality of life.

3.3 Results, Key Question 1a

3.3 Key Question 1a: What are the benefits and harms of behavioral interventions delivered via telehealth and digital health (e/mHealth) technology compared to inactive control?

3.3.1 Key Points

For Adults:

- The digital/telehealth technologies employed in 14 studies addressing KQ1a include mobile apps, websites, email, telephone, virtual reality, CD-ROM, digital recordings, manuals, and audiotapes.
- All outcomes and comparisons for adults (and all evidence for children/adolescents) were insufficient to permit conclusions, mostly due to wide CIs from single studies of any given intervention.
- Overall, across studies of both adults and children, adverse events in the intervention arm were reported only in a single study (of education), suggesting they are rare.

3.3.2 Description of Included Evidence

Fourteen included studies (listed in Table 7) used telehealth/digital health/eHealth/mHealth technologies to deliver behavioral treatment(s) and compared them with inactive treatment.^{23,43,45,46,56-58,60,62,68,69,71,72,113} The specific technologies involved apps in three studies, websites in four studies, email support in six studies, telephone support in five studies, CD-ROMs or digital recordings in three studies, manuals/audiotapes in two studies, and a virtual-reality device in one study. Note that studies using these technologies only for patient recruitment or outcome measurement were not included in this KQ. All 14 studies addressed KQ1, and none addressed KQ2a. Of note, these studies represent a subset of studies included in KQ1. Because results from these studies are also presented in that section, here we focus on reporting results on key outcomes (headache frequency, migraine disability/function, and migraine QOL) along with acceptability and feasibility.

Table 8 below provides an overview of interventions, comparators, intervention characteristics, and outcomes reported. All trials performed in children were small (fewer than 35 patients reporting outcomes for each). Trials performed in adults were generally larger; 3 trials were markedly larger than the rest, reporting outcomes for 487 patients (Underwood et al., 2022⁶⁸), 285 patients (Kleiboer et al., 2014⁴³), and 150 patients (Bromberg et al., 2012⁴⁵).

Seven of 11 trials in adults compared interventions with an inactive comparator (e.g., waitlist, treatment as usual). Only two RCTs^{23,62} used an attention control comparator, and two used a minimal intervention.^{46,68} The three RCTs with children used attention control, minimal intervention, and inactive comparator, respectively.

Although migraine/headache attack frequency, migraine-related disability/function, and MSQOL were widely agreed upon as the most critical outcomes, no trials reported all three outcomes. Of 11 RCTs performed in adults, 7 reported on headache frequency, 6 on migraine disability/function, and 3 on MSQOL. Of three RCTs performed in children, three reported on headache frequency, one on migraine disability/function, and one on migraine QOL.

3.3.3 Results, Key Question 1a, Risk of Bias

3.3.3 Risk of Bias

Risk of bias was high for outcomes from 11 trials and some concerns for the other 3.^{23,62,71} Eleven of 14 studies enrolled adults. Below, we present studies focused on adults first, followed by children. More details appear in Appendix C.

Table 7. Studies included for Key Question 1a

Citation	Behavioral Treatment(s) Administered Using Digital/Telehealth	Population	Virtual Reality	App	Website	Email Support	Telephone Support	CD-ROM or Digital Recordings	Manuals/ Audiotapes
Cuneo et al. (2023) ¹¹³	Biofeedback	Adults	✓	-	-	✓	✓	-	-
Minen et al. (2020a) ⁵⁶	Relaxation training	Adults with multiple sclerosis	-	✓	-	-	-	-	-
Minen et al. (2020b) ⁵⁸	Relaxation training	Adults	-	✓	-	-	-	-	-
Minen et al. (2021) ⁵⁷	Biofeedback	Adults	-	✓	-	✓	-	-	-
D'Souza et al. (2008) ⁶²	Relaxation training	Adults	-	-	-	-	-	-	✓
Holroyd et al. (1988) ²³	Relaxation training + biofeedback	Adults	-	-	-	-	✓	-	✓
Kleiboer et al. (2014) ⁴³	CBT + relaxation training + education	Adults	-	-	✓	✓	-	-	-
Bromberg et al. (2012) ⁴⁵	CBT + biofeedback + relaxation training + education	Adults	-	-	✓	✓	-	-	-
Hedborg et al. (2011) ⁴⁶	<ul style="list-style-type: none"> Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management + Massage therapy 	Adults	-	-	✓	-	-	-	-
Flynn et al. (2019) ⁶⁰	Hypnotherapy	Adults	-	-	✓	✓	✓	✓	-
Underwood et al. (2022) ⁶⁸	Education	Adults	-	-	-	✓	✓	✓	-
Rapoff et al. (2014) ⁶⁹	CBT + relaxation training + education	Children /adolescents	-	-	-	✓	-	✓	-
Connelly et al. (2006) ⁷²	CBT + relaxation + education	Children/ adolescents	-	-	-	-	-	✓	-
Cottrell et al. (2007) ⁷¹	Relaxation training + biofeedback + education + activity pacing + stress management training	Children/ adolescents	-	-	-	-	✓	-	-

Abbreviation: CBT=cognitive behavioral therapy.

3.3.3 Results, Key Question 1a, Risk of Bias

Table 8. Intervention characteristics and reported outcomes for Key Question 1a

Citation	Treatment	Comparator	Intervention	N for Outcome	In person Component	Headache Frequency	Disability	Migraine QOL
Cuneo et al. (2023) ¹¹³	Biofeedback	Inactive	Portable biofeedback virtual reality device. Instructed to use for at least 10 minutes per day, at least 3 days per week. Those using it fewer than 3x/week were sent text email or telephone reminders.	36	-	✓	✓	-
Minen et al. (2021) ⁵⁷	Biofeedback	Inactive	HeartMath Sensor attached to earlobe transmits data to app. Instructed to do biofeedback at least 2x per day for 5 minutes or once a day for 10 minutes daily for 60 days. Email: reminders (every 3 days) for adherence	52	-	-	-	✓
Minen et al. (2020a) ⁵⁶	Relaxation training	Inactive	RELAXaHEAD app Instructed to perform PMR at least 20 minutes daily for 90 days	44	-	-	✓	-
Minen et al. (2020b) ⁵⁸	Relaxation training	Inactive	RELAXaHEAD app Instructed to perform PMR at least 15 minutes daily for 90 days	78	-	-	✓	-
D'Souza et al. (2008) ⁶²	Relaxation training	Attention control	Audiotape: for relaxation; were given audiotapes at the end to continue at home. 4 sessions (20 minutes each) over 2 weeks.	59	✓	✓	✓	-
Kleiboer et al. (2014) ⁴³	CBT + relaxation training + education	Inactive	Website: Online portal with videos, interactive exercises, and homework 8 lessons (1 hour each) 2 relaxation training exercises per day (30 minutes each) 1–2 hours of cognitive behavioral homework Telephone: Coaching for behavioral therapy by trained coach (postgraduate psychologist or masters-level psychology student supervised by clinical psychologist). On average 90–120 minutes total, delivered weekly or biweekly.	285	-	✓	✓	-
Holroyd et al. (1988) ²³	Relaxation training + biofeedback	Attention control	In-person visits: Introduced relaxation training, thermal biofeedback with 2 visits early on; 1 final visit performed at end of trial. Audiotapes: provided for home use	37	✓	✓	-	-

3.3.3 Results, Key Question 1a, Risk of Bias

Citation	Treatment	Comparator	Intervention	N for Outcome	In person Component	Headache Frequency	Disability	Migraine QOL
			Telephone: Brief consultations at the end of 2 nd and 6 th week of treatment.					
Bromberg et al. (2012) ⁴⁵	CBT + biofeedback + relaxation training + education	Inactive	Website: Interactive instructions for pain management, graphic and interactive learning for problem solving, self-assessments, text, audio and video advice 8 sessions (20 minutes each) over 4 weeks. At least 5 sessions (20 minutes) over the following month. (Weeks 4 to 8). Weekly checklist reminders.	150	-	-	✓	-
Hedborg et al. (2011) ⁴⁶	Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management + Massage therapy	Minimal intervention	Website: Treatment program and diary 53 pages on stress physiology, physical activity, diet, emotions, attitudes; practice muscle relaxation training program (provided on CD). Patients asked to enter diary data daily or transfer from paper to online within 1 week. No requirements for amount of time spent.	76	-	✓	-	-
Flynn et al. (2019) ⁶⁰	Hypno-therapy	Inactive	Website: patients logged on to listen to an MP track 3 times per week (for 4 weeks). Telephone: 10-minute introduction. Email – reminders.	40	-	✓	-	✓
Underwood et al. (2022) ⁶⁸	Education	Minimal intervention	Telephone: 1-on-1 visit with nurse who provided education on drug management lifestyle change and goal setting. In-person: 2 group sessions (8-10 persons) 1 week apart.	487 ^a 308	✓	✓	✓	-
Cottrell et al. (2007) ⁷¹	Relaxation training + biofeedback + education + activity pacing +	Attention control	Intervention: Telephone calls (30 minutes) for education with counselor to review STOP migraine manual	30	-	✓	-	✓

3.3.3 Results, Key Question 1a, Risk of Bias

Citation	Treatment	Comparator	Intervention	N for Outcome	In person Component	Headache Frequency	Disability	Migraine QOL
	stress management training		Control: initiation with triptan therapy, in-person visits at baseline, 1, 3, 8 months. Both arms received weekly telephone calls.					
Connelly et al. (2006) ⁷²	CBT + relaxation training + education	Inactive	CD-ROM: 1 module per week for 4 weeks; modules took approximately 1 hour to complete and had homework. Telephone: Weekly call to address questions and encourage reporting of headache frequency.	31	-	✓	-	-
Rapoff et al. (2014) ⁶⁹	CBT + relaxation + education	Minimal intervention	CD-ROM: 1 lesson per day for 4 weeks, simple quizzes to assess processing of information; homework assignments required. Telephone: Weekly call to encourage recordkeeping.	22	-	-	✓	-

Note: Several interventions included an initial visit to load and demonstrate a smartphone app or introduce the intervention. In this table, these are not presented as an “in-person” treatment component.

^a For Underwood,⁴ 487 patients contributed to migraine days/month; for disability, only a subset of chronic migraine patients contributed to this outcome (n=308).

Abbreviations: CBT=cognitive behavioral therapy; PMR=progressive muscle relaxation; QOL – Quality of life

3.3.4 Summary of Findings

Overall, 14 RCTs assessed delivery of behavioral interventions using telehealth, eHealth, or mHealth. Specifically, studies used five modalities to deliver behavioral interventions: virtual-reality device, smartphone apps, audiotapes, website/Web-based, and telephone. To provide clarity and consistency in our reporting, we group interventions by their primary delivery mode.

3.3.4.1 Adults: Virtual-Reality Device (Biofeedback)

One RCT addressed use of a virtual-reality device to deliver biofeedback.¹¹³ The intervention group (n=14 at followup) received the Oculus Go Mobile VR Headset, which viewed either a beach or hilltop setting. Each participant's optimal respiratory rate had been determined earlier. Ascending tones cued breathing-in, and descending tones cued breathing-out. The monitor showed them a heart rate variability tracing, and they were encouraged to create a sine-wave-like curve by following the breathing cues. They were encouraged to use the device at least three times a week, with email and text reminders if they used it less often. The control group (n=22 at followup) received standard care.

Migraine/Headache Attack Frequency: Measured at 12 weeks after the start of treatment, both groups improved (by about 8 migraine days per month), with no statistically significant between group difference.

3.3.4 Results, Key Question 1a, Summary of Findings

Migraine Disability: Measured using MIDAS at 12 weeks after the start of treatment, both groups improved (by an average 72 points in the intervention group and 59 points in the control group), with no statistically significant between group difference.

Other Outcomes: Depression scores (measured using PHQ-8 not PHQ-9) at 12 weeks after the start of treatment, the intervention group had statistically significantly better depression scores (mean improvement of 3.6 points) than the control group (no change). The intervention group also had statistically significant greater reduction usage of acute medications at 12 weeks (13 fewer uses a month than baseline) than the control group (4 fewer uses a month than baseline).

3.3.4.2 Adults: Smartphone Apps (Relaxation Training and Biofeedback)

Three RCTs addressed use of smartphone apps to deliver treatment. Two trials⁵⁸ used the RELAXaHEAD smartphone app for relaxation training, incorporating audio files for PMR and features for tracking headache characteristics. The third RCT used the HeartMath app for heart rate variability biofeedback.⁵⁷

Migraine/Headache Attack Frequency: One RCT⁵⁸ assessing RELAXaHEAD reported on headache days. At 90 days, compared with wait list control, participants receiving PMR had increased odds of having a headache day (OR 2.1, (95% 1.002 to 2.6). No other studies reported on migraine/headache attack frequency.

Migraine Disability: The two RCTs assessing RELAXaHEAD for relaxation training described impact on disability/function. Compared with waitlist, participants with migraine and multiple sclerosis found no statistically significant change in disability (MIDAS) at 6 months.⁵⁶ The other RELAXaHEAD trial found the relaxation training group had a larger reduction in MIDAS scores compared to control (-8.7 vs. -22.7) at 3 months; however, when adjusted for baseline MIDAS and anxiety scores, this finding was not statistically significant.

Migraine-Specific Quality of Life: Only one RCT reported on MSQOL. Minen et al., 2021⁵⁷ found that HeartMath for biofeedback did not result in a statistically significant difference between groups at 60 days.

Adverse Events: Of two studies reporting on adverse events, none related to the intervention were reported.^{56,57}

3.3.4.3 Adults: Audiotapes (Relaxation Training and Relaxation Training + Biofeedback)

Two RCTs used audiotapes to deliver relaxation training⁶² and relaxation training + biofeedback.²³ In an RCT by D'Souza et al. 2008,⁶² students (n=59) were assigned to relaxation training or attention control, receiving 4 sessions of audiotapes during 2 weeks. Another RCT (Holroyd 1988, n=37)²³ compared relaxation training + biofeedback with attention control, involving two in-person visits, audiotapes for home use, brief phone consultations at weeks 2 and 6, and a final in-person visit at the end of the intervention.

Migraine/Headache Attack Frequency: Both RCTs^{23,62} reported on migraine/headache attack frequency. Neither study found the intervention resulted in a statistically significant difference in migraine/headache attack frequency at timepoints ranging from 2 months to 14 weeks.

3.3.4 Results, Key Question 1a, Summary of Findings

Migraine Disability: One RCT⁶² reported on disability/function. Compared with attention control, relaxation training did not result in a statistically significant difference in MIDAS at 14 weeks.

Adverse Events: Neither study reported data on adverse events, barriers, acceptability, or feasibility.

Other Outcomes: One RCT⁶² reported that there was a statistically significantly greater reduction in pain intensity in the relaxation training group than in the attention control.

3.3.4.4 Adults: Web-Based (CBT-Based, Relaxation Training, and Hypnotherapy)

Four RCTs used websites (sometimes combined with other modalities) to deliver treatment consisting of multiple behavioral interventions. Interventions assessed included CBT + relaxation training + education (Kleiboer et al. 2014⁴³); CBT + relaxation training + education + biofeedback (Bromberg et al. 2012⁴⁵); relaxation + healthy lifestyle counseling, sleep counseling, and stress management (Hedborg et al., 2011⁴⁶); and hypnotherapy (Flynn et al., 2019⁶⁰).

Migraine/Headache Attack Frequency: Only three of four RCTs reported on migraine/headache attack frequency. Two RCTs (assessing hypnotherapy⁶⁰ and educational packages⁴⁶) found no statistically significant improvement in migraine/headache days (at 10 and 36 weeks).

However, the large 2014 study by Kleiboer (n=285) of CBT + relaxation training + education⁴³ in patients with episodic and chronic migraine found no difference between intervention and control arms at 13 weeks: 0.0 (95% CI -0.8 to 0.8 days). The difference was also not statistically significantly different between groups at 37 weeks from the start of treatment.

Migraine Disability: Both RCTs assessing combination treatments involving CBT also reported on disability/function as captured by the MIDAS. No statistically significant difference (12 weeks, Bromberg⁴⁵ or 13 and 37 weeks, Kleiboer⁴³).⁹⁰ Interestingly, Flynn⁶⁰ reported that compared with treatment as usual (TAU), hypnotherapy resulted in a dramatic improvement in disability at 10 weeks as measured by the Headache disability inventory (HDI) (corresponding to -42.5 [95% CI -61.2 to -23.9] on the MIDAS scale). We note that the study was smaller (n=40) and rated High risk of bias. However, while the size of this effect could have been smaller if the study had used an attention control comparison (instead of TAU), the magnitude far exceeds the MID threshold of 3 points.

Adverse Events: Only two RCTs reported on adverse events. Neither study reported adverse events associated with combination treatment involving CBT⁴⁵ or hypnotherapy.⁶⁰ **Other Outcomes:** Not reported.

3.3.4.5 Adults: Telephone (Education)

One RCT⁶⁸ (n=478) compared an educational intervention—Chronic Headache Education and Self-Management Study (CHESS)—with minimal intervention (relaxation training CD). CHESS included two group sessions a week apart, followed by one-on-one telephone consultations focusing on drug management and lifestyle changes. Both groups received personalized information on diagnosis, use of acute and preventive drugs, and medication overuse.

3.3.4 Results, Key Question 1a, Summary of Findings

Migraine/Headache Attack Frequency: At 4 months, the group receiving the CHES educational intervention had a statistically significant increase in headache frequency compared with the minimal intervention arm, corresponding to 0.78 migraine days/month (95% CI 0.2 to 1.4). However, the magnitude of this effect did not meet our preestablished threshold for clinical significance of one migraine day/month. At 6 and 12 months, this finding was no longer statistically significant, although point estimates at all 3 timepoints favored control.

Migraine-Specific Quality of Life: At 12 months, in a subgroup of patients with chronic migraine (n=308), the treatment group had a statistically significant improvement in MSQOL compared with the minimal intervention arm, corresponding to -1.2 points on the HIT-6 scale (95% CI -2.3 to -0.1). However, this finding did not meet our predetermined threshold for clinical significance of 3 points. At 12 months, there was no benefit for episodic or chronic migraine (total n contributing data=551).

Adverse Events: The intervention arm had six adverse events (description not provided by authors), none of which were deemed serious. One death was reported in the control arm. Authors reported completion of headache diary data on the smartphone was low (44 percent).

3.3.4.6 Children: CD + Telephone

Two small RCTs^{69,72} delivered a treatment (Headstrong) consisting of CBT + relaxation training + education using CD-ROMs. The more recent study by Rapoff et al., 2014⁶⁹ compared this treatment package with a minimal intervention (control arm received a CD-ROM with general information about headaches). Participants were asked to complete one lesson per day for 4 weeks, along with simple quizzes and required homework assignments. They also received a weekly telephone call to encourage recordkeeping. By contrast, the 2006 study by Connelly et al.⁷² compared the treatment package with waitlist. Participants were required to complete only one module (1 hour long) per week with homework. These participants also received weekly telephone calls to encourage reporting.

Migraine/Headache Attack Frequency: Only Connelly et al. (2006)⁷² reported impact on headache frequency; at 1 month (immediately post-treatment), compared with waitlist, Headstrong results in a clinically significant reduction in headache frequency (effect corresponding to -2.8 migraine days/month, 95% CI -4.8 to -0.1).

Migraine Disability: Connelly et al. (2006)⁷² found no statistically significant difference in PedMIDAS at 1 month; however, Rapoff et al. (2014)⁶⁹ found a large, clinically meaningful difference in PedMIDAS at 18 weeks, corresponding to -18.9 (95% CI -37.2 to -0.8) on the MIDAS scale. However, study authors note that data from this timepoint are based on only 22 of 70 randomly selected patients, representing very high attrition (69 percent).

Adverse Events: Neither study reported on adverse events.

3.3.4.7 Adolescents: Telephone + Audiotape (Education + Relaxation Training + Biofeedback)

A small 2007 RCT (n=30)⁷¹ compared a combination treatment (education, relaxation training, biofeedback) with control in adolescents with episodic migraine, delivered via weekly 30-minute telephone calls for 8 weeks. The intervention arm received the STOP migraine treatment manual (the authors did not state whether STOP was an acronym), covering topics such as relaxation training and stress management, and included audiotapes for relaxation therapy. The control arm received instructions on triptan therapy for acute headaches, along with

3.3.4 Results, Key Question 1a, Summary of Findings

weekly calls. The study did not detail the use of triptans or other acute medications in the intervention arm.

Migraine/Headache Attack Frequency: Both study arms⁷¹ reported a 50 percent reduction in headache frequency compared with baseline. However, at 2 months and 7 months, there was no statistically significant difference in headache frequency (corresponding to -0.4 migraine days/month, 95% CI -2.8 to 1.9).

Migraine Disability and Migraine-Specific Quality of Life: Although the study reported disability and MSQOL in measures that could not be included in the meta-analysis, no statistically significant between-group differences were found.

Adverse Events: The study did not report on adverse events. No statistically significant difference in headache severity or headache duration was reported at 2 or 7 months.⁷¹

3.3.4.8 Strength of Evidence

SOE ratings for KQ1a are presented in Table 9 below.

3.3.4 Results, Key Question 1a, Summary of Findings

Table 9. Strength of evidence for Key Question 1a (effectiveness when digital/telehealth was used)

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
Adults	Virtual reality Biofeedback vs. Waitlist	Headache days/ month	Cuneo et al. (2023) ¹¹³ (N=36) At 12 weeks, the intervention group decreased by 8.1 days/month, and the control group decreased by 7.6 days per month (not statistically significant)	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Virtual reality Biofeedback vs. Waitlist	Disability/ function (MIDAS)	Cuneo et al. (2023) ¹¹³ (N=36) At 12 weeks, the intervention group improved by 73 points on the MIDAS scale, and the control group decreased by 59.5 points (not statistically significant)	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Smartphone app Relaxation training vs. Waitlist	Headache days/ month	Minen 2020b ⁵⁸ (n=NR) At 3 months: OR 2.1 (95% 1.002 to 2.6)	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Smartphone app Relaxation training vs. Waitlist	Disability/ function (MIDAS)	Minen 2020b ⁵⁸ (n=78) At 3 months: Larger reduction in relaxation training group than in the control (-8.7 vs. -22.7);	High	Direct	Consistent	Imprecise	Not suspected	None	Insufficient	N/A

3.3.4 Results, Key Question 1a, Summary of Findings

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
			however, not statistically significant when adjusted for baseline MIDAS and anxiety scores. Minen 2020a ⁵⁶ Patients with multiple sclerosis (n=44) at 6 months 8.25 (95% CI - 7.7, 23.9) Not statistically significant								
Adults	Smartphone app Biofeedback vs. waitlist	MSQOL	Minen 2021 ⁵⁷ (n=52) At 60 days Not statistically significant	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Audiotape Relaxation training, biofeedback vs. Attention control (acute headache medications) ²³ Audiotape Relaxation training vs. attention control ⁶²	Migraine days/ month	Holroyd 1988 ²³ (n=37) At 2 months Increase 1 migraine day/month (95% CI -1.1–3.2) Not statistically significant D'Souza 2008 ⁶² (n=59) Increase of 0.2 day/month (95% CI -1.5–1.9) at 14 weeks	Moderate	Direct	Consistent	Imprecise	Not suspected	None	Insufficient	N/A

3.3.4 Results, Key Question 1a, Summary of Findings

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
			Not statistically significant								
Adults	Audiotape Relaxation training vs. Attention control	Disability/ function (MIDAS)	D'Souza 2008 ⁶² (n=59) -0.5 (95% CI -14.1–13) (14 weeks) Not statistically significant	Moderate	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Website, telephone, email Relaxation training + Education Web-based program (with and without massage therapy) vs. Minimal intervention (relaxation training CD)	Migraine days/ month	Hedborg 2011 ⁴⁶ (n=76) (36 weeks) -0.85 days/month (-2.4–0.7) Not statistically significant	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Website CBT + relaxation training + education vs. No intervention	Migraine days/ month	Kleiboer 2014 ⁴³ (n=285) At 13 weeks 0 days (95% CI -0.8 – 0.8)	High	Direct	Unknown	Precise	Not suspected	None	Insufficient	N/A
Adults	Website, telephone, email Hypnotherapy vs. TAU	Migraine days/ month	Flynn 2019 ⁶⁰ (n=40) 0 days/month (95% CI -2 – 2) At 10 weeks	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A

3.3.4 Results, Key Question 1a, Summary of Findings

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
Adults	Website, email CBT+ biofeedback + relaxation training + education vs. TAU	Disability/ function (MIDAS)	Bromberg 2012 ⁴⁵ (n=150) At 12 weeks -0.3 (95% CI -9.6 – 9.3) Not statistically significant	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Website email CBT+ relaxation training + education vs. TAU	Disability/ function (MIDAS)	Kleiboer 2014 ⁴³ (n=285) At 13 weeks -0.8 (95% CI -6.9 – 5.3) Not statistically significant	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Adults	Website, telephone, email Hypnotherapy vs. TAU	MSQL (HDI)	Flynn 2019 ⁶⁰ (n=40) At 10 weeks -42.5 (95% CI - 61.2 to -23.9)	High	Direct	Unknown	Precise	Not suspected	None	Insufficient	N/A
Adults	Telephone Education vs. Minimal intervention (Relaxation training CD)	Migraine days/ month	Underwood 2022 ⁶⁸ (n=487) At 4 months increase 0.78 days (95% CI 0.2 – 1.4) Favors minimal intervention	High	Direct	Unknown	Precise	Not suspected	None	Insufficient	N/A
Adults	Telephone Education vs. Minimal intervention (Relaxation training CD)	Disability/ function (HIT-6)	Underwood 2022 ⁶⁸ (n=308) Subgroup with chronic migraine) at 4 months	High	Direct	Unknown	Precise	Not suspected	None	Insufficient	N/A

3.3.4 Results, Key Question 1a, Summary of Findings

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
			Corresponding to HIT 6: -1.21 (95% CI - 2.3 to -0.1) Favors treatment No benefit at 12 months for episodic or chronic migraine (total n=551)								
Children/adolescents	CD + Telephone reminders CBT+ relaxation training + education vs. No intervention	Migraine days/month	Connelly 2006 ⁷² (n=31) at 1 month -2.8 days/month (95% CI -4.8 to -0.1) Favors intervention	High	Direct	Unknown	Precise	Not suspected	None	Insufficient	N/A
Children/adolescents	CD + Telephone reminders CBT + Relaxation training + vs. Minimal intervention CBT+ relaxation training + education vs. No intervention ⁷²	Disability (PedMIDAS)	Treatment vs. Minimal intervention Rapoff 2014 ⁶⁹ (n=22) At 18 weeks -18.9 (95% CI - 37.2 to -0.8) Favors intervention Treatment vs. Waitlist Connelly 2006 ⁷² (n=31) At 1 month 3.5 (95% CI - 15.2– 22.3) Inconclusive	Moderate	Direct	Inconsistent*	Imprecise	Not suspected	None	Insufficient	N/A

3.3.4 Results, Key Question 1a, Summary of Findings

Age Group	Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
Children/adolescents	Audiotapes (relaxation), Telephone calls (relaxation training, biofeedback, education, activity pacing, stress management training) vs. Attention control	Migraine days/month	Cottrell 2007 ⁷¹ (n=30) At 2 months -0.4 days/month (95% CI -2.8–1.9)	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Children/adolescents Children/adolescents	Audiotapes (relaxation training), Telephone calls (relaxation training, biofeedback, education, activity pacing, stress management training) vs. Attention control	Migraine specific quality of life (MSQL-A)	Cottrell 2007 ⁷¹ (n=30) At 2 months No statistically significant difference at 2 or 7 months)	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A

Abbreviations: CBT=cognitive behavioral therapy; CI – Confidence interval; HIT=Headache Impact Test-6; MIDAS= Migraine Disability Assessment; MSQL=migraine-specific quality of life; N/A – Not applicable, QOL=quality of life; MSQL-A=Migraine-specific quality of life questionnaire- Adolescent; PedMIDAS - Pediatric Migraine-Specific Disability Assessment; TAU=treatment as usual

In most cases, to facilitate comparison we converted results for original scales used by individual studies into a standardized mean difference. To improve interpretability, we then converted these back into corresponding absolute values using one scale per outcome type: migraine days/month (for migraine/headache frequency), MIDAS (for disability/function), and HIT-6 (for migraine-specific quality of life).

*Disability for these two studies was rated together even though the control groups differed (minimal intervention vs. waitlist). We combined these because we felt important concerns regarding consistency of evidence were raised by finding an impact when the treatment was compared with minimal intervention but no effect when compared to waitlist

3.4 Results, Key Question 2

3.4 Key Question 2: What are the comparative effectiveness and harms of a behavioral intervention for migraine prevention compared to either (a) a pharmacologic preventive agent or (b) another behavioral intervention for children and adults?

3.4.1 Key Points

- We included 20 studies that made numerous comparisons among different behavioral components, behavioral versus pharmacologic, and other comparisons.
- In adults, MBSR may result in lower migraine disability (SOE: low) than education. This advantage was clinically important.
- In adults, CBT + relaxation training may result in higher migraine attack frequency than propranolol (SOE: low), but a clinically important advantage over propranolol in MSQOL (SOE: low).
- In adults, MBSR + Education may result in lower migraine attack frequency than stress management training + education (SOE: low).
- In adults, biofeedback may result in lower migraine attack frequency than CBT + relaxation training (SOE: low).
- In children/adolescents, CBT + biofeedback + relaxation training may result in lower migraine attack frequency (SOE: low) and lower disability (SOE: low) than education alone.

3.4.2 Description of Included Evidence

We included 20 studies for KQ2 (Table 10). Sixteen studies enrolled adults, and the other four enrolled children/adolescents (Table 11).

Table 10. Studies included for Key Question 2: Adults

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment
Blanchard et al. (1978) ⁷⁶	NR	<ul style="list-style-type: none">• Relaxation training (PMR)• Thermal biofeedback + Relaxation training (Autogenic training)	None
Brown et al. (1984) ¹¹⁰	NR	<ul style="list-style-type: none">• MBSR via guided imagery, relaxing statements• MBSR via guided imagery, scene details	None
de Tommaso et al. (2017) ³⁵	100% Episodic	<ul style="list-style-type: none">• Nociceptive blink reflex Biofeedback• Nociceptive blink reflex Biofeedback + Topiramate	Topiramate
Dindo et al. (2020) ⁵⁴	100% Episodic	<ul style="list-style-type: none">• ACT Therapy + Education• Relaxation training + Education + Deep breathing	None
Holroyd et al. (2010) ³⁶	NR	<ul style="list-style-type: none">• CBT + Relaxation training (PMR) + Propranolol• CBT + Relaxation training (PMR)	Propranolol
Janssen et al. (1986) ¹⁰⁸	NR	<ul style="list-style-type: none">• Relaxation training (PMR)• Relaxation training (Autogenic training)	None
Klan et al. (2022) ⁶⁵	96% Episodic, 4% Chronic	<ul style="list-style-type: none">• CBT + Relaxation training (PMR) + Education• Relaxation training	None

3.4.2 Results, Key Question 2, Description of Included Evidence

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment
Kropp et al. (1997) ²⁸	Mixed (% NR)	<ul style="list-style-type: none"> • CBT + Relaxation training • Biofeedback 	None
Mathew et al. (1981) ²⁷	NR	<ul style="list-style-type: none"> • Thermal and EMG Biofeedback • Thermal and EMG Biofeedback + Propranolol • Thermal and EMG Biofeedback + Amitriptyline • Thermal and EMG Biofeedback + Amitriptyline + Propranolol 	<ul style="list-style-type: none"> • Propranolol • Amitriptyline • Propranolol+ Amitriptyline
Reich et al. (1989) ²⁶	100% Chronic	<ul style="list-style-type: none"> • Relaxation training • Thermal Biofeedback • Combination of any two interventions from the other groups 	Microelectrical therapy (not an included treatment)
Sargent et al. (1986) ^{107,112}	NR	<ul style="list-style-type: none"> • Thermal Biofeedback + Relaxation training • EMG Biofeedback + Relaxation training • Relaxation training 	None
Seminowicz et al. (2020) ⁵⁹	100% Episodic	<ul style="list-style-type: none"> • MBSR + Education • Stress management training + Education 	None
Sorbi et al. (1986) ^{79,109}	NR	<ul style="list-style-type: none"> • CBT • Relaxation training (Autogenic training) 	None
Varkey et al. (2011) ³⁷	99% Episodic, 1% Chronic	Relaxation training	Topiramate
Wachholtz et al. (2008) ^{61,100}	NR	<ul style="list-style-type: none"> • Spiritual meditation • Internally focused secular meditation • Externally focused secular meditation • Relaxation training (PMR) 	None
Wells et al. (2021) ⁵³	Mixed (% NR)	<ul style="list-style-type: none"> • MBSR • Education (general migraine information, stress) 	None

Abbreviations: ACT- Acceptance and Commitment Therapy; CBT=cognitive behavioral therapy; EMG =electromyography; MBSR=mindfulness-based stress reduction; NR=not reported; PMR=progressive muscle relaxation

Table 11. Studies included for Key Question 2: Children/adolescents

Study	Episodic, Chronic, or Mixed	Behavioral Treatment(s)	Other Active Treatment
Gerber et al. (2010) ⁷⁰	100% Episodic	<ul style="list-style-type: none"> • Thermal Biofeedback + EMG Biofeedback + Relaxation training + Education • CBT+ Relaxation training (PMR) + Education 	None
Powers et al. (2013) ³³	100% Chronic	<ul style="list-style-type: none"> • CBT + Thermal Biofeedback + EMG Biofeedback + Relaxation training + Amytriptyline • Education + Amytriptyline 	None
Richter et al. (1986) ³¹	100% Episodic	<ul style="list-style-type: none"> • CBT • Relaxation training (PMR + Deep breathing) 	None
Sartory et al. (1998) ⁵¹	100% Episodic	<ul style="list-style-type: none"> • CBT+ Relaxation training (PMR) • CBT + Blood volume pulse Biofeedback 	Metoprolol

Abbreviations: CBT=cognitive behavioral therapy; EMG=electromyography; PMR=progressive muscle relaxation

3.4.4 Results, Key Question 2, Summary of Findings

3.4.3 Risk of Bias

All risk-of-bias judgments (including each of the 4 component domains) appear in Appendix C. For KQ2, we judged the overall risk of bias to be Low for 4 studies, Some Concerns for 5 studies, High for 10 studies, and Mixed for 1 study (High for 2 of its treatment comparison and Some Concerns for the other treatment comparison) different ratings for different comparisons, outcomes, or timepoints). Because studies' comparisons for KQ2 often involved two active treatments, and for competing treatments, patients are less likely (than for KQ1) to have differential attention or expectations, so we had fewer concerns (than for KQ1) about domain 4 on measurement bias; only 4/20 were judged as high risk of bias on this domain. We did have concerns about both domain 3 (attrition), with 10/20 (at either high risk of bias or some concerns, and domain 1 (randomization), with 15/20 at either high risk of bias or some concerns. As with KQ1, we had fewer concerns about domain 2 (deviations from intended interventions), with 18/20 studies at low risk of bias on that domain.

3.4.4 Summary of Findings

3.4.4.1 Adults: Comparing Behavioral Components

This section will discuss studies that directly compared one component (e.g., CBT) with another (e.g., relaxation training). The studies did not have to be in isolation, but the study design must have allowed a direct comparison of one component with another (i.e., for CBT versus relaxation training, we included CBT + biofeedback versus relaxation training + biofeedback because both groups received biofeedback, but we excluded CBT + biofeedback versus relaxation training alone because only the CBT group received biofeedback). We also discuss different variants of a component in this section (e.g., two forms of biofeedback).

In adults, eight studies made the following direct comparisons:

- Sorbi et al. (1986)^{79,109} compared CBT with relaxation training.
- Reich et al. (1989)²⁶ compared relaxation training with thermal biofeedback.
- Wachholtz et al. (2008)^{61,100} compared three forms of meditation with relaxation training.
- Wells et al. (2021)⁵³ compared MBSR with education.
- Dindo et al. (2020)⁵⁴ compared ACT with relaxation training.
- Sargent et al. (1986)^{107,112} compared thermal biofeedback with electromyography (EMG) biofeedback.
- Janssen et al. (1986)¹⁰⁸ compared different forms of relaxation training.
- Brown et al. (1984)¹¹⁰ compared different forms of MBSR (guided imagery).

3.4.4.1.1 CBT Versus Relaxation Training

Sorbi et al. (1986)^{79,109} compared CBT with relaxation training (autogenic training) and reported three outcomes (migraine days, usage of analgesic medications, and migraine pain intensity) at 16, 20, and 48 weeks after the start of treatment. None of the between-group comparisons were statistically significant for any outcome at any timepoint (see data in Appendix C).

3.4.4 Results, Key Question 2, Summary of Findings

3.4.4.1.2 Relaxation Training Versus Biofeedback

Reich et al. (1989)²⁶ compared relaxation training with thermal biofeedback.

Migraine/Headache Attack Frequency: The trial assessed migraine attack frequency through the metric of headache hours per week. However, the trial did not conduct a statistical evaluation of the between-group difference in headache frequency. At baseline, both biofeedback and relaxation training groups presented with similar weekly headache durations (26 hours per week, n=100 versus 25 hours per week, n=95 for both). Both groups experienced a decline in headache frequency at 1-month followup, registering frequencies of 1 headache-hours per week in the biofeedback group and 9.5 headache-hours per week in the relaxation training group. However, after 1-month followup, headache durations seem to plateau in the biofeedback group and slightly increase in the relaxation training group until the end of the study (37 weeks). In the biofeedback group, frequencies at the 9-, 25-, and 37-month followup were recorded at 1.3, 1.3, and 1.8 headache-hours per week, respectively. The relaxation training group presented weekly headache hours of 10.5, 12.5, and 13.0 at the same followup times, respectively. Authors did not report a statistical comparison of the two groups' headache frequencies.

Adverse Events: Authors did not report adverse events or study discontinuations.

Other Outcomes: The RCT did not provide a statistical analysis of the difference in headache intensity (measured using the visual analog scale [VAS] 0–5 scale) between the two study groups. At baseline, patients receiving biofeedback reported headache pain similar to those undergoing relaxation training (biofeedback: 3.8, n=100 versus relaxation training: 4.0, n=95). A month into followup, both groups observed a decrease in headache pain scores, registering scores of 1.4 and 2.7 points, respectively. Following the 1-month followup, pain scores appear to plateau or slightly increase in both groups until the end of the followup (37 weeks). In the biofeedback group, scores at the 9-, 25-, and 37-month followup were 1.4, 1.4, and 1.8 points, respectively. The relaxation training group reported pain scores of 2.7, 2.8, and 3.0 at identical followup timepoints, respectively.

3.4.4.1.3 Relaxation Training Versus Meditation

Wachholtz et al. (2008)^{61,100} compared three forms of meditation—spiritual, internally focused-secular, and externally focused secular—with relaxation training.

Migraine/Headache Attack Frequency: There were no statistically significant statistical differences between any of the meditation modalities and relaxation training in terms of headache frequency. The SMD values were -0.25 (95% CI -0.83 to 0.32, n=47) for spiritual meditation, -0.07 (95% CI -0.66 to 0.51, n= 44) for internally focused secular meditation, and 0.05 (95% CI -0.54 to 0.63, n=45) for externally focused secular meditation.

Migraine-Specific Quality of Life: There was no statistically significant difference in MSQOL between meditation interventions and relaxation training at 1-month followup (spiritual meditation SMD 0.45; 95% CI -0.13 to 1.03; internally focused-secular meditation 0.24; 95% CI -0.35 to 0.82; externally focused secular meditation 0.06; 95% CI -0.53 to 0.64).

Adverse Events: No adverse effects were reported.

Other Outcomes: Depression and anxiety were reported among other outcomes. Relaxation training did not outperform any of the meditation interventions regarding depression symptoms on the Center for Epidemiologic Studies Depression Scale (spiritual meditation versus relaxation training SMD 0.22; 95% CI -0.36 to 0.79; internally focused-secular meditation versus relaxation training 0.55; 95% CI -0.05 to 1.14; externally focused secular meditation versus relaxation

3.4.4 Results, Key Question 2, Summary of Findings

training -0.02; 95% CI -0.60 to 0.57). Anxiety was assessed using the Spielberger State-Trait Anxiety Inventory scale. Similarly, there was no statistically significant difference between any meditation intervention and relaxation training at 1-month followup (spiritual meditation versus relaxation training SMD -0.36; 95% CI -0.94 to 0.22; internally focused-secular meditation versus relaxation training 0.34; 95% CI -0.25 to 0.93; externally focused secular meditation versus relaxation training 0.48; 95% CI -0.12 to 1.07).

3.4.4.1.4 MBSR Versus Education

Wells et al. (2021)⁵³ compared MBSR with education (n=82).

Migraine/Headache Attack Frequency: For migraine attack frequency, there was no statistically significant difference in the number of migraine days per month between the two active treatment groups (SMD -0.13; 95% CI -0.55 to 0.28, corresponding to migraine days/month of -0.42, 95% CI -1.8 to 0.9).

Migraine Disability: MBSR was associated with a greater improvement in migraine-related disability, as measured by the MIDAS scale, compared with education (SMD 0.70; 95% CI 0.27 to 1.13). This difference corresponds to an 18-point shift on the 0 to 90 MIDAS scale (95% CI 7.18 to 30.06). MBSR also resulted in a greater improvement in HIT-6 scores at 8-weeks followup (SMD 0.86; 95% CI 0.42 to 1.29). This equates to a HIT-6 difference of 5.8 (95% CI 2.81 to 8.64).

Migraine-Specific Quality of Life: Not reported.

Adverse Events: No adverse events documented.

Other Outcomes: Up to the 36-week followup, depression scores (as measured by the PHQ-9, 0 to 27) in the MBSR group improved more than in the education group (1.6; 95% CI, 0.4 to 2.7, p=0.008). Anxiety, as measured by the Generalized Anxiety Disorder questionnaire (GAD-7) scale (0–21), did not present any statistically significant difference, as both groups exhibited similar improvement rates up to 36 weeks (1.2 [95% CI -0.05 to 2.4] points, p=0.06, no other digits reported).

3.4.4.1.5 Relaxation Training Versus ACT

Dindo et al. (2020)⁵⁴ compared ACT with relaxation training.

Migraine Disability: The study reported neither migraine attack frequency nor migraine-related QOL. At 12-month followup, the evaluation of migraine-related disability, using the HDI scale, demonstrated no statistically significant difference between the groups (SMD -0.30; 95 percent CI -0.64 to 0.04, n=134). This outcome corresponds to -7.98 MIDAS points, within a 95% CI of -17.02 to 1.06.

Adverse Events: There was no statistically significant difference in the number of individuals who discontinued participation at 3- and 6-month followup (OR 1.02; 95% CI 0.49 to 2.13 and OR 1.27; 95% CI 0.64 to 2.54, respectively). The study reported no adverse events.

Other Outcomes: In terms of depression, the study defined improvement as a reduction of ≥ 50 percent in Hamilton Depression Rating Scale scores. At 3-month followup, a statistically significant greater proportion of individuals in the ACT group improved compared with the relaxation training group (OR 3.10; 95% CI: 1.15 to 8.35), however, this distinction was not observed at 6-month followup (OR 2.70; 95% CI 0.97 to 7.49).

The study also analyzed anxiety outcomes, defined by a ≥ 50 percent reduction in Structured Interview Guide for the Hamilton Anxiety Scale scores. At 3 months, no significant statistical difference was observed between the two groups (OR 2.45; 95% CI 0.85 to 7.05). However, at 6-

3.4.4 Results, Key Question 2, Summary of Findings

month followup, the ACT group demonstrated more individuals with improved anxiety than in the relaxation training group (OR 4.25; 95% CI: 1.28 to 14.03).

The World Health Organization Quality of Life measure was used to assess general QOL, with only the social relationship dimension showing a statistically significant improvement in the ACT group versus the relaxation training group at 3 months (1.1 versus -0.3; $p=0.006$). However, this difference was not maintained at 6-month followup (1.5 versus 0.4; $p=0.128$). Other domains of QOL, such as physical health and psychological well-being, showed no significant differences between groups.

3.4.4.1.6 Comparing Different Forms of Biofeedback

Sargent et al. (1986)^{107,112} enrolled one group that received both thermal biofeedback and relaxation training with another group that received both EMG biofeedback and relaxation training. Thus, the study collected data (at baseline and 12 weeks and 32 weeks after the start of treatment) to compare the two forms of biofeedback directly (with relaxation training as a shared component). Outcomes include headaches per week and average pain intensity. The study reported means but no dispersion and no statistical comparison between the two biofeedback groups, so one cannot determine whether EMG biofeedback and thermal biofeedback had statistically significant differences. Comparisons with another group that received relaxation training alone are summarized in KQ 3 (on the impact of adding biofeedback).

3.4.4.1.7 Comparing Different Forms of Relaxation Training

Janssen et al. (1986)¹⁰⁸ administered two forms of relaxation training (progressive muscle relaxation training versus autogenic training) to two separate randomized groups. Authors reported data on both migraine counts and pain intensity at both 13 and 26 weeks after the start of treatment, but reported only means (no dispersion or statistical tests); thus, statistical significance is unknown.

3.4.4.1.8 Comparing Different Forms of MBSR

Brown et al. (1984)¹¹⁰ compared two forms of MBSR (guided imaging using relaxing statements vs. guided imaging focusing on scene details). There was no statistically significant difference in the percentage reduction in migraine counts (37% for focused statements and 46% for scene details; difference in percentages 9%, 95% CI -28% to 46%) or the percentage reduction in migraine intensity (1% for focused statements and 0.5% for scene details; difference in percentages 0.6%, 95% CI -4% to 6%).

Wachholtz et al. (2008)^{61,100} compared three forms of meditation: spiritual, internally focused-secular, and externally focused secular.

Migraine/Headache Attack Frequency: The spiritual meditation group and the internally focused secular meditation groups each had greater pre-post improvement in headache frequency than the externally focused meditation group.

Migraine-Specific Quality of Life: The study reported no statistically significant difference in MSQOL between groups.

Adverse Events: No adverse effects were reported.

Other Outcomes: The study reported no statistically significant difference in pain intensity or depression between groups. The spiritual meditation group had greater pre-post improvement in anxiety than the externally focused meditation group.

3.4.4 Results, Key Question 2, Summary of Findings

3.4.4.2 Adults: Comparing Behavioral With Pharmacologic Treatments

This section discusses results of five studies directly comparing a purely behavioral treatment with a purely pharmacologic treatment:

- de Tommaso et al. (2017)³⁵ compared biofeedback to topiramate.
- Mathew et al. (1981)²⁷ compared biofeedback with propranolol, amitriptyline, and propranolol + amitriptyline.
- Varkey et al. (2011)³⁷ compared relaxation training with topiramate.
- Holroyd et al. (2010)³⁶ compared CBT + relaxation training + education with propranolol.

3.4.4.2.1 Biofeedback Versus Topiramate

De Tommaso et al. (2017)³⁵ compared biofeedback with a daily dose of 30 mg of topiramate over 3 months (n=21). A third group received both biofeedback and topiramate.

Migraine/Headache Attack Frequency: The study found no significant statistical difference in migraine attack frequency or a 50 percent reduction rate in headache frequency between biofeedback and topiramate after 3-month followup. Ten out of 11 participants in the biofeedback group and 8 out of 10 in the topiramate group reported a 50 percent reduction in headache frequency. The study enrolled a third group of patients who had received both biofeedback and topiramate. This group's migraine frequency results were not statistically significantly different from either of the other two groups.

Migraine Disability and Migraine-Specific Quality of Life: The study did not test the difference in migraine disability and QOL between these two groups, but MIDAS and SF-36 scores appear to reduce proportionally across the groups.

Adverse Events: The study reported that there were no adverse events.

3.4.4.2.2 Biofeedback Versus Propranolol, Amitriptyline, and Propranolol/Amitriptyline

Mathew et al. (1981)²⁷ compared biofeedback's effectiveness with that of propranolol (initial dosage of 20 mg/day), amitriptyline (initial dosage of 25 mg/day), and a combination therapy of propranolol and amitriptyline.

Migraine/Headache Attack Frequency, Migraine Disability Migraine-Specific Quality of Life The study did not provide data on migraine attack frequency, migraine-related disability, or QOL.

Adverse Events: The discontinuation rate due to adverse events across all treatment groups was not significantly different at the 6-month followup among those with migraine. The event rate was low, with the biofeedback group having zero events and the amitriptyline group having four events. When considering a subgroup of patients with migraine, biofeedback was associated with a higher risk of discontinuation for any reason compared with both propranolol (OR 3.47; 95% CI: 1.22 to 9.87, n=92) and the combined pharmacologic prevention with propranolol and amitriptyline (OR 6.9; 95% CI: 1.86 to 25.90, n=89). However, in the broader sample that included individuals with both migraine and mixed headaches, biofeedback was associated with a lower risk of study discontinuation due to adverse events than with amitriptyline (OR 0.11; 95% CI: 0.01 to 0.95, n=186). This difference, however, was not statistically significant compared with other treatments.

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Other Outcomes: The study reported depression scores, as measured by the Self Rating Depression Scale (Zung). Participants in all four treatment groups fell within the normal range (indicating no depression; scores between 25 and 49). No statistical test was conducted to ascertain the differences in Zung scores across the groups; however, considerable overlap exists between all groups in terms of their scores' ranges.

3.4.4.2.3 Relaxation Training Versus Topiramate

Varkey et al. (2011)³⁷ compared the effects of relaxation training with topiramate, starting at a dosage of 25 mg/day.

Migraine/Headache Attack Frequency: There was no statistically significant difference in the frequency of migraine attacks, measured by the number of migraine days per month, between the two groups after 12 weeks of followup (SMD -0.27; 95% CI: -0.77 to 0.24, corresponding to -0.9 migraine days/month 95% CI -2.5 to 0.8). Similarly, at the 14-month followup, there was no significant statistical difference in the rate of improvement by 50 percent or more (OR 1.14; 95% CI: 0.36 to 3.67, n=61).

Migraine-Specific Quality of Life: The study assessed the impact of treatments on MSQOL using the MSQoL v.2.1 questionnaire. After 12 weeks of followup, there was no statistically significant difference between the groups (SMD 0.14; 95% CI: -0.36 to 0.64, corresponding to a HIT-6 difference of 0.94 points, 95% CI -2.4 to 4.3).

Adverse Events: The study reported no adverse events in the relaxation training group. However, 20 percent (n=8) of patients in the topiramate group reported various side effects, including paresthesia (n=5), fatigue (n=3), depressed mood (n=3), vertigo (n=2), and infrequent bowel movements (n=2). Additionally, one patient reported the following adverse reactions: headaches, tremors, muscle twitching, mood swings, dysgeusia, nausea, dry eyes, epistaxis, dry mouth, urinary incontinence, amnesia, cognitive disorders, diarrhea, and musculoskeletal chest pain.

Other Outcomes: The authors also evaluated reduction in pain intensity from baseline to mean pain scores, as measured by the VAS (0–100). The topiramate group experienced a greater reduction in pain scores than the relaxation training group at all timepoints. For example, at the 14-month followup, the topiramate group reported an average reduction of 11.3 (SD 3.5) points from baseline, while the relaxation training group reported an average reduction of 4.6 (SD 3.6) points. However, the difference between the groups was not statistically tested. Reduction in acute medication use (counted as doses of tablets, injections, nasal sprays, and suppositories) was similar between the two groups at the 3-month followup (calculated MD -0.01; 95% CI: -0.13 to 0.10). While use of acute medication was slightly lower in the relaxation training group at the 7-month followup (calculated MD -0.73; 95% CI: -0.83 to -0.63), it was slightly higher at the 14-month followup (calculated MD 0.13; 95% CI: 0.04 to 0.22) than in the topiramate group. However, the authors provided no statistical estimates to quantify differences between the two groups at these timepoints.

3.4.4.2.4 CBT + Relaxation Training Versus Propranolol

Holroyd et al. (2010)³⁶ (n=108) compared a combination of CBT and relaxation training with propranolol, which had a starting dosage of 60 mg/day (titrated as tolerated or switched to nadolol).

Migraine/Headache Attack Frequency: After 10 months of followup, the results indicated a statistically significantly greater reduction in migraine attack frequency with the use of

3.4.4 Results, Key Question 2, Summary of Findings

propranolol than with use of the combination of CBT and relaxation training. This was represented by SMD of -0.43 (95% CI: -0.81 to -0.05), equating to an absolute reduction of -1.40 (95% CI: -2.63 to -0.16) migraine days per month. We also note that the study compared a combination of CBT, relaxation training, and propranolol with propranolol alone. The combination of the behavioral and pharmacologic interventions was superior to the pharmacologic intervention alone, with an SMD of -2.63 (95% CI: -3.11 to -2.14) for attack frequency.

Migraine-Related Quality of Life: In terms of MSQOL, the study found that the combined behavioral intervention was associated with a greater improvement than with propranolol. The improvement with the behavioral intervention at the 10-month followup was both clinically important and statistically significant, with an SMD of 0.89 (95% CI: 0.49 to 1.28). This SMD corresponds to a difference of 12 points on the MSQOL scale, with a 95% CI from 7 to 18. The combined behavioral and pharmacologic group had an even greater improvement than pharmacologic alone, with an SMD of 2.78 (95% CI: 2.28 to 3.28).

Adverse Reactions: At the 16-month followup, no statistically significant difference was observed in the number of participants reporting adverse reactions (OR 0.66; 95% CI: 0.19 to 2.22) between the two groups.

3.4.4.3 Adults: CBT + PMR + Education Versus Relaxation Training

Klan et al. (2022)⁶⁵ compared CBT + PMR + education versus relaxation training.

Migraine/Headache Attack Frequency: For migraine attack frequency, authors found no statistically significant difference (SMD 0.19, 95% CI -0.27 to 0.64, corresponding to a difference in migraine days/month of 0.6, 95% CI -0.9 to 2.1).

Migraine Disability: For migraine disability, authors found no statistically significant difference (SMD 0.06, 95% CI -0.32 to 0.45, corresponding to a MIDAS difference of 1.6, 95% CI -8 to 12). However, for the HIT-6, the data favored relaxation training over CBT + PMR + education (SMD 0.58, 95% CI 0.11 to 1.04, corresponding to a HIT-6 difference of 3.9, 95% CI 0.7 to 7.0).

Migraine-Specific Quality of Life: Not reported.

Adverse Events: The study reported no adverse events and specifically stated that no patients had dropped out due to adverse events. Four of 51 patients in the CBT + PMR + education group had discontinued treatment, and 1 of 49 patients dropped out of the relaxation training group.

Other Outcomes: There was no statistically significant difference between groups in emotional distress as measured by the Depression, Anxiety and Stress Scales or in medication use.

3.4.4.4 Adults: MBSR + Education Versus Stress Management Training

Seminowicz et al. (2020)⁵⁹ compared MBSR + education versus stress management training + education.

Migraine/Headache Attack Frequency: For migraine attack frequency, authors found a statistically significant difference favoring MBSR + education (SMD -0.64 95% CI -1.06 to -0.23, corresponding to a difference in migraine days/month of -2.1, 95% CI -3.5 to -0.8).

Migraine Disability: The comparison was not statistically significant (SMD -0.34, 95% CI -0.75 to 0.07, corresponding to a HIT-6 difference of -2.3, 95% CI -5 to 0.5).

Migraine-Specific Quality of Life: Not reported.

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Adverse Events: Not reported.

Other Outcomes: Regarding other outcomes, authors reported there was no between-group difference in pain severity, the Pittsburgh sleep quality index, the GAD-7, or the PHQ-9.

3.4.4.5 Adults: CBT + Relaxation Training Versus Biofeedback

Kropp et al. (1997)²⁸ compared CBT + relaxation training versus biofeedback.

Migraine/Headache Attack Frequency: For migraine attack frequency, authors found a statistically significant difference favoring biofeedback (SMD -0.69, 95% CI -1.34 to -0.03, corresponding to a difference in migraine days/month of -2.2, 95% CI -4.4 to -0.1).

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: Not reported.

Other Outcomes: There was no statistically significant difference in migraine intensity as measured by a 0-9 VAS or in medication use.

3.4.4.6 Children/Adolescents: Comparing Behavioral Interventions

3.4.4.6.1 CBT Versus Biofeedback

Migraine/Headache Attack Frequency: Gerber et al. (2010)⁷⁰ used a subjective rating scale for migraine attack frequency (1=daily headache, 2=several times per week, 3=once per week, 4=1–3 times per week, 5=once per month). While both groups had reduced headache frequency, there was no statistically significant difference between groups in the extent of reduction.

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: Not reported.

Other Outcomes: For other outcomes, general QOL (as measured by the KINDL; the authors did not define the acronym), authors reported that there was no statistically significant interaction between treatment and time, suggesting the treatments did not differentially affect general QOL. For pain intensity, only the biofeedback group showed statistically significant improvements over time. For headache duration, only the CBT group showed statistically significant improvements over time.

3.4.4.6.2 CBT Versus Relaxation Training

Richter et al. (1986)³¹ compared CBT with relaxation training.

Migraine/Headache Attack Frequency: For migraine attack frequency, there was no statistically significant difference between groups (corresponding to a difference in migraine days per month of -0.4, 95% CI -2.7 to 1.9).

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: Not reported.

Other Outcomes: The authors measured peak headache intensity, and as with attack frequency, there was no statistically significant difference between CBT and relaxation training.

3.4.4.6.3 Biofeedback Versus Relaxation Training

Sartory et al. (1998)⁵¹ compared biofeedback with relaxation training (both groups also received CBT).

Migraine/Headache Attack Frequency: There was no statistically significant difference for migraine attack frequency (corresponding to a difference in migraine days/month of -0.07, 95% CI -2.8 to 2.7).

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Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: Not reported.

Other Outcomes: For pain intensity and analgesic use, there were no statistically significant between-groups effects.

3.4.4.7 Children/Adolescents: Comparing Behavioral With Pharmacologic Treatments

Sartory et al. (1998)⁵¹ compared biofeedback or relaxation training (both groups also received CBT) with metoprolol.

Migraine/Headache Attack Frequency: For migraine attack frequency, pharmacologic treatment did not statistically differ from either behavioral treatment (comparison with biofeedback, a difference in migraine days/month of -0.8, 95% CI -2.5 to 4.1, and comparison with relaxation training, a difference in migraine days/month of -0.6, 95% CI -2.6 to 3.9).

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: Not reported.

Other Outcomes: For pain intensity, there were no statistically significant between-groups effects. For analgesic use, the behaviorally treated groups used statistically significantly fewer analgesics.

3.4.4.8 Children/Adolescents: Other Behavioral Interventions

Powers et al. (2013)³³ compared a combination of CBT, biofeedback, and relaxation training with education alone (both groups received amitriptyline).

Migraine/Headache Attack Frequency: For migraine attack frequency, there was a statistically significant difference between groups (corresponding to a difference in migraine days per month of -1.6, 95% CI -2.7 to -0.4).

Migraine Disability: The same difference occurred in migraine disability as measured by PedMIDAS (PedMIDAS difference of -14, 95% CI -25 to -3). Use of amitriptyline in both groups may have affected the observed difference between treatment groups.

Migraine-Specific Quality of Life: Not reported.

Adverse Events: As both study groups had amitriptyline, all adverse events could have been due solely to that medication. Authors noted that the headache education + amitriptyline group reported more regular-level adverse events than the group treated behaviorally, but there was no difference in serious events.

3.4.4.9 Strength of Evidence

SOE ratings for KQ2 appear in Table 12 below.

3.4.4 Results, Key Question 2, Summary of Findings

Table 12. Strength of evidence ratings for Key Question 2 (comparative effectiveness)

Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
Adults	CBT vs. Relaxation training	Migraine attack frequency	Sorbi et al. (1986) ^{79,109}	Moderate	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training vs. biofeedback	Migraine attack frequency	Reich et al. (1989) ²⁶ did not statistically compare the groups; results were in the direction favoring biofeedback	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training vs. meditation	Migraine attack frequency	Wachholtz et al. (2008) ^{61,100} found a statistically nonsignificant difference between relaxation training and each meditation group (see main text for details)	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training vs. meditation	Migraine-specific quality of life	Wachholtz et al. (2008) ^{61,100} found a statistically nonsignificant difference between relaxation training and each meditation group (see main text for details)	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	MBSR vs. education	Migraine attack frequency	Wells et al. (2021) ⁵³ found a statistically nonsignificant difference (difference of -0.42 migraine days/month, 95% CI - 1.8— 0.9)	Low	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

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Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
Adults	MBSR vs. education	Migraine disability	Wells et al. (2021) ⁵³ found an advantage of MBSR, estimated 18 points on the MIDAS scale (95% CI 7–30), For the HIT-6, advantage of MBSR, estimated 5.8 points (95% CI 2.8–8.6)	Low	Direct	Unknown	Precise	Not suspected	Low	Favors MBSR, clinically important effect
Adults	Relaxation training vs. ACT	Migraine disability	Dindo et al. (2020) ⁵⁴ found a statistically nonsignificant difference (difference of -8 points on the MIDAS scale, 95% CI -17–1)	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	EMG biofeedback vs. thermal biofeedback	Migraine attack frequency	Sargent et al. (1986) ^{107,112} collected pertinent data but did not report enough information to statistical compare the 2 forms of biofeedback	Moderate	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training using PMR vs. relaxation training using autogenic training	Migraine attack frequency	Janssen et al. (1986) ¹⁰⁸ collected pertinent data but did not report enough information to statistical compare the 2 forms of biofeedback	Moderate	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	MBSR using guided imagery of scene details vs. relaxation training using	Migraine attack frequency	Brown et al. (1984) ¹¹⁰ found no statistically significant difference between groups	Moderate	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

3.4.4 Results, Key Question 2, Summary of Findings

Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
	guided imagery and relaxing statements									
Adults	MBSR meditation spiritual vs. internally focused secular vs. externally focused secular	Migraine attack frequency	Wachholtz et al. (2008) ^{61,100} found a greater improvement in attack frequency with spiritual and internally focused meditation than with externally focused meditation	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	MBSR meditation spiritual vs. internally focused secular vs. externally focused secular	Migraine-specific quality of life	Wachholtz et al. (2008) ^{61,100} found no statistically significant difference	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Biofeedback vs. topiramate	Migraine attack frequency	de Tommaso et al. (2017) ³⁵ found no statistically significant difference in rates of 50% headache reduction (91% biofeedback vs. 80% topiramate)	Moderate	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training vs. topiramate	Migraine attack frequency	Varkey et al. (2011) ³⁷ found no statistically significant difference, migraine days/month -0.9, 95% CI -2.5—0.8	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Relaxation training vs. topiramate	Migraine-specific quality of life	Varkey et al. (2011) ³⁷ found no statistically significant difference, HIT-6 difference of	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

3.4.4 Results, Key Question 2, Summary of Findings

Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			0.94 points, 95% CI -2.4–4.3							
Adults	CBT + Relaxation training vs. propranolol	Migraine attack frequency	Holroyd et al. (2010) ³⁶ found a difference favoring propranolol, -1.40 migraine days/month (95% CI: -2.63 to -0.16)	Moderate	Direct	Unknown	Precise	Not suspected	Low	Favors propranolol
Adults	CBT + Relaxation training vs. propranolol	Migraine-specific quality of life	Holroyd et al. (2010) ³⁶ found a difference favoring CBT + relaxation + education, MSQOL difference of 12 points, 95% CI 7–18	Moderate	Direct	Unknown	Precise	Not suspected	Low	Favors CBT + relaxation training, clinically important
Adults	CBT + Relaxation training + Education vs. Relaxation	Migraine attack frequency	Klan et al. (2022) ⁶⁵ found no statistically significant difference (0.6 migraine days/month, 95% CI -0.9– 2.1)	Low	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	CBT + Relaxation training + Education vs. Relaxation	Migraine disability	Klan et al. (2022) ⁶⁵ found no statistically significant difference (MIDAS difference of 1.6, 95% CI -8–12). However, for the HIT-6 scale, authors found a statistically significant difference in favor of relaxation (HIT-6 difference of 3.9, 95% CI 0.7– 7	Low	Direct	Inconsistent	Imprecise	Not suspected	Insufficient	NA
Adults	MBSR + Education vs. Stress	Migraine attack frequency	Seminowicz et al. (2020) ⁵⁹ found a statistically significant	Low	Direct	Unknown	Precise	Not suspected	Low	Favors MBSR + Education

3.4.4 Results, Key Question 2, Summary of Findings

Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
	management training + Education		difference in favor of MBSR + Education (difference in migraine days/month of -2.1, 95% CI -3.5 to -0.8)							
Adults	MBSR + Education vs. Stress management training + Education	Migraine – disability	Seminowicz et al. (2020) ⁵⁹ found no statistically significant difference (HIT-6 difference of -2.3, 95% CI -5 to 0.5)	Low	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	CBT + Relaxation training vs. Biofeedback	Migraine attack frequency	Kropp et al. (1997) ²⁸ found a statistically significant difference favoring biofeedback (difference in migraine days/month of -2.2, 95% CI -4.4 to -0.1)	Mod.	Direct	Unknown	Precise	Not suspected	Low	Favors biofeedback
Children/adolescents	CBT vs. biofeedback	Migraine attack frequency	Gerber et al. (2010) ⁷⁰ found no statistically significant difference between groups	High	Direct	Unknown	Precise	Not suspected	Insufficient	NA
Children/adolescents	CBT vs. relaxation	Migraine attack frequency	Richter et al. (1986) ³¹ found no statistically significant difference (-0.4 migraine days per month, 95% CI -2.7 to 1.9)	Mod.	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Biofeedback vs. relaxation training	Migraine attack frequency	Sartory et al. (1998) ⁵¹ found no statistically significant difference, migraine days/month -0.07, 95% CI -2.8—2.7	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

3.4.4 Results, Key Question 2, Summary of Findings

Age Group	Comparison	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
Children/adolescents	Biofeedback vs. metoprolol	Migraine attack frequency	Sartory et al. (1998) ⁵¹ found no statistically significant difference, migraine days/month -0.8, 95% CI -2.5 – 4.1	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	Relaxation training vs. metoprolol	Migraine attack frequency	Sartory et al. (1998) ⁵¹ found no statistically significant difference, migraine days/month -0.6, 95% CI -2.6 – 3.9	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/adolescents	CBT + biofeedback + relaxation training vs. education	Migraine attack frequency	Powers et al. (2013) ³³ found an advantage of CBT + biofeedback+ relaxation training corresponding to a difference in migraine days/month of -1.6, 95% CI -2.7 to -0.4).	Low	Direct	Unknown	Precise	Not suspected	Low	Favors CBT+ biofeedback + relaxation training
Children/adolescents	CBT + biofeedback + relaxation training vs. education	Migraine disability	Powers et al. (2013) ³³ found an advantage of CBT + biofeedback + relaxation training corresponding to a MIDAS difference of -11, 95% CI -20 to -2)	Low	Direct	Unknown	Precise	Not suspected	Low	Favors CBT+ biofeedback + relaxation training

Abbreviations: ACT=acceptance and commitment therapy; CBT=cognitive behavioral therapy; CI – Confidence interval; EMG – Electromyography; HIT-6=Headache Impact Test-6; MBSR=mindfulness-based stress reduction; MIDAS=Migraine Disability Assessment; NA – Not applicable; .

3.6 Results, Key Question 3

3.5 Key Question 2a: What are the comparative effectiveness and harms of behavioral interventions delivered via telehealth and digital health (e/mHealth) technology compared to (a) pharmacologic prevention or (b) other behavioral interventions?

No studies addressed this KQ.

3.6 Key Question 3. For multicomponent or combined behavioral interventions, what are the effects of individual behavioral intervention components?

3.6.1 Key Points

- We included five studies examining the specific impact of adding a behavioral component to other behavioral components: one of CBT in adults, two of biofeedback in adults, one of biofeedback in children/adolescents, and one of education in children/adolescents.
- The evidence was insufficient to permit conclusions for all rated outcomes, mostly due to imprecision and single studies.

3.6.2 Description of Included Evidence

This section discusses results of five studies directly investigating the contribution of a specific behavioral component (Table 13).

Table 13. Studies Included for Key Question 3

Study	Age Group	Behavioral Treatment(s)	Other Active Treatment
Allen et al. (1998) ²⁹	Children/adolescents	• Thermal biofeedback + Education • Thermal biofeedback	None
Fritsche et al. (2010) ²⁰	Adults	• Cognitive behavioral therapy (CBT) + Relaxation training (progressive muscle relaxation [PMR]) + Education • PMR + Education	None
Labbe et al. (1995) ²²	Children/adolescents	• Thermal biofeedback + Relaxation training (Autogenic training) • Relaxation training (Autogenic training)	None
Sargent et al. (1986) ^{107,112}	Adults	• Thermal biofeedback + Relaxation training • EMG biofeedback + Relaxation training • Relaxation training	None
Sorbi et al. (1984) ⁷⁵	Adults	• CBT + PMR + Thermal biofeedback • CBT+PMR	None

Abbreviations: CBT – Cognitive behavioral therapy; EMG – Electromyography; PMR – Progressive muscle relaxation

3.6 Results, Key Question 3

3.6.3 Risk of Bias

All risk-of-bias judgments (including each of the 4 component domains) appear in Appendix C. For KQ3, we judged the overall risk of bias to be Some Concerns for two studies, High for two studies, and Mixed for the other study (different ratings for different timepoints). Our reasons for concerns about risk of bias were similar as those for KQ2 (attrition and the randomization process).

3.6.4 Summary of Findings

3.6.4.1 Adults: Impact of Adding CBT

Fritsche et al. (2010)²⁰ provided both relaxation training and education to two groups of patients, and one group also received CBT; the study measured the impact of adding CBT to other behavioral treatments.

Migraine/Headache Attack Frequency: Fritsche et al. (2010)²⁰ found no statistically significant effect of adding CBT. The between-group effect size was inconclusive, 0.19 (95% CI -0.17 to 0.56).

Migraine Disability: Fritsche et al. (2010)²⁰ reported headache disability scores (range 0 to 10, no other scale details reported) that were not statistically significantly different between groups (the change scores slightly favored the non-CBT group, which had a 0.09 worsening versus 0.15 worsening in the CBT-added group).

Migraine-Specific Quality of Life and Adverse Events: Not reported.

Other Outcomes: Fritsche et al. (2010)²⁰ also reported results on anxiety and depression using the HADS. Neither outcome showed statistical significance between groups.

3.6.4.2 Adults: Impact of Adding Biofeedback

Two RCTs investigated the impact of adding biofeedback to other behavioral treatment(s). Sorbi et al. 1984⁷⁵ recruited adults with episodic migraine (n=21) to evaluate thermal biofeedback's effects when added to the combined treatment of CBT and PMR. Sargent et al. (1986)^{107,112} added either of two forms of biofeedback (thermal or EMG) with relaxation training.

Migraine/Headache Attack Frequency: In the Sorbi⁷⁵ RCT, after 4.1 months of treatment, the frequency of headaches was reduced by 43 percent for participants in the CBT + PMR group and by 53 percent for those who also received thermal biofeedback. Headache frequency continued to decline in both groups at 7-months followup, reducing by 59 percent in the CBT + PMR group and by 58 percent among those with thermal biofeedback. These reductions did not differ statistically significantly between groups, but the small study size (N=21 total) means the data were inconclusive (Cis not reported). Sargent et al. (1986)^{107,112} reported that when comparing the relaxation training-only group with the EMG biofeedback group, there was no statistically significant difference between groups. The authors did not report whether relaxation training-only group versus thermal biofeedback was statistically significant.

Migraine Disability and Migraine-Specific Quality of Life: Not reported by either study.

Adverse Events: The Sorbi⁷⁵ RCT did not collect adverse events. Three patients across both groups dropped out of the study due to anxiety, concurrent treatment, and lack of motivation to participate.

Other Outcomes:

3.6.4 Results, Key Question 3, Summary of Findings

Headache Intensity. Sorbi⁷⁵ reported that there was no between-group statistical significance in pain intensity at any followup timepoint. Sargent et al. (1986)^{107,112} compared EMG biofeedback plus relaxation training with relaxation training alone and found no statistically significant difference in pain intensity.

Medication Use Index. Sorbi⁷⁵ reported that there was no between-group statistical significance in medication use at any followup timepoint. Sargent et al. (1986)^{107,112} compared EMG biofeedback plus relaxation training with relaxation training alone and found no statistically significant difference in medication use.

3.6.4.3 Children/Adolescents: Impact of Adding Biofeedback

One RCT (Labbe et al., 1995)²² with children and adolescents ages 7 to 18 years (mean 12 years) with episodic migraine (n=30) provided data to isolate the effect of thermal biofeedback added to an autogenic relaxation training (AT) alone.

Migraine/Headache Attack Frequency: The RCT did not provide a statistical evaluation of the difference in headache frequency between the two study groups. At the baseline, patients who were administered biofeedback in conjunction with AT showed a slightly lower monthly headache incidence than those receiving AT only (2.71 versus 3.67, respectively). Both groups saw a reduction in headache frequency during the 1.6-, 2.5-, and 8-month followups. In the biofeedback-plus-AT group, the recorded frequencies were 0.60, 0.05, and 0.12 headaches per month, respectively. In the AT-alone group, the frequencies were 1.00, 0.38, and 0.42 headaches per month at the same intervals, respectively. At the 2.5-month followup, 2 more individuals from the biofeedback-plus-AT group reported being symptom-free, making it 9 out of 10 patients in this group and 7 out of 10 in the AT-alone group. This difference increased by 1 at the 8-month followup, at which 8 out of 10 patients in the biofeedback-plus-AT group reported being symptom-free compared with 5 out of 10 patients in the AT-alone group.

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: No adverse events were reported.

3.6.4.4 Children/Adolescents: Impact of Adding Education

One RCT (Allen 1998,²⁹ United States) with children and adolescents aged 7 to 18 years (mean 12.2 years) with episodic migraine (n=27) provided data to isolate the effect of education added to thermal biofeedback. Education consisted of the pain behavior management guidelines delivered by parents.

Migraine/Headache Attack Frequency: Adding education to the treatment plan resulted in a greater statistically significant reduction in headache frequency at the 4.1-month followup compared with biofeedback alone ($p \leq 0.05$; with a calculated mean difference of 1.4; 95% CI: 0.5 to 2.3). However, this difference did not maintain statistical significance by the 13.5-month followup (calculated MD of 0.7; 95% CI: -0.5 to 1.9). Supplementary education was associated with a statistically significantly more individuals who experienced a reduction of 50 percent or more in headache frequency at the 4.1-month followup. The difference between the groups decreased by the 13.5-month followup and was not statistically significant. For instance, at the postintervention, 11 of 14 (78.6 percent) patients who received additional education and only 3 of 14 (28.1 percent) patients who were given biofeedback alone showed at least a 50 percent reduction in headache frequency. However, the number of patients who were free of headaches was proportionally similar in both groups during both the 4.1-month and 13.5-month followups.

3.6.4 Results, Key Question 3, Summary of Findings

Five out of 14 patients (35.7 percent) in the education group reported being headache-free at the 4.1-month followup, while none in the biofeedback-only group reported being headache-free.

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

Adverse Events: This study did not collect adverse event data. Attrition was observed with three patients from each group dropping out by the 13.5-month followup.

3.6.4.5 Strength of Evidence

SOE ratings for KQ3 appear in Table 14 below.

3.6.4 Results, Key Question 3, Summary of Findings

Table 14. Strength of evidence ratings for Key Question 3 (effect of individual components)

Age Group	Impact of Component	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
Adults	CBT	Migraine attack frequency	Fritzsche et al. (2010) ²⁰ found no statistically significant difference between groups (effect size not calculable)	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	CBT	Migraine-related disability	Fritzsche et al. (2010) ²⁰ found no statistically significant difference between groups (effect size not calculable)	High	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Adults	Thermal biofeedback	Migraine attack frequency	2 studies. Sorbi et al., 1984, ⁷⁵ found no statistically significant difference between groups (effect size not calculable). Sargent et al. (1986) ^{107,112} also had data on the impact of adding thermal biofeedback but did not report a statistical comparison between these 2 groups	1 Mod. 1 High	Direct	Consistent	Imprecise	Not suspected	Insufficient	NA
Adults	EMG biofeedback	Migraine attack frequency	Sargent et al. (1986) ^{107,112} reported that there was no statistically		Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

3.6.4 Results, Key Question 3, Summary of Findings

Age Group	Impact of Component	Outcome	Evidence	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Rating	Conclusion
			significant difference between EMG biofeedback+ relaxation training vs. relaxation training alone							
Children/ adolescents	Thermal biofeedback	Migraine attack frequency	Labbe et al., 1995 ²² , statistical test not reported	Mod.	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA
Children/ adolescents	Education	Migraine attack frequency	Allen et al., 1998, ²⁹ found a statistically significant benefit of adding education to biofeedback at 4 months, but no significant difference at 13 months	Mod.	Direct	Unknown	Imprecise	Not suspected	Insufficient	NA

Abbreviations: CBT – Cognitive Behavioral therapy; EMG – Electromyography; NA – Not applicable

3.7 Comments on Network Meta-Analyses for KQ1, KQ2, and KQ3

Due to sparse evidence and similarities in overlapping components of treatments, we investigated network meta-analysis (NMA) for addressing KQs 1, 2, and 3. Initially developed to answer questions about pharmacologic treatments, NMA methods allow estimation of differences between treatments that have never been directly compared. This estimate is achieved through connections in the network. The simplest example is two medications that each have placebo-controlled studies but have never been compared directly. Under certain key assumptions, the drug-drug comparison is achieved by comparing their effects versus placebo.

NMA makes numerous assumptions, but three are critical. The first is *patient similarity*: to compare A versus B using a common comparator C, the patients in the A versus C trials must have been similar to the patients in the B versus C trials. If they were different, then the estimated A versus B difference may be biased as a result. The second assumption involves *treatment implementation*: the specifics of the intermediary treatment (treatment C) must be similar in the two types of trials. For example, if C is a medication, its dose may have differed in the two types of trials, creating bias in the A versus B comparison. The third assumption is *instrument compatibility*. Some outcomes (e.g., migraine disability) can be measured in a variety of ways (e.g., MIDAS, Functional Impairment Scale [FIS], Pain Disability Inventory [PDI]). If treatments affect these outcomes differentially, then it would be problematic to lump them as the same “outcome.” Before proceeding to NMA, we first examined the reasonableness of these assumptions.

Regarding patient similarity, our inclusion criteria required that at least 80 percent of patients be experiencing migraine, and we did separate analyses for trials of adults versus trials of children/adolescents. One valid concern is that our networks did not account for episodic versus chronic migraine, and we ignored this distinction for our NMAs because it has fallen out of favor in the field of migraine research; we did not want overly disperse networks. Regarding instrument compatibility, we had three outcome categories. For migraine/headache attack frequency, we used a prioritization scheme (see Methods section), but there could be important concerns that a treatment could affect one measure (migraine days per month) differently than another (migraine attacks per month). For the other two categories, our SMEs confirmed that instruments were categorized appropriately as either migraine-related disability or migraine-related QOL.

By far the most problematic assumption for our networks was treatment implementation. When two studies employed a combination of CBT and relaxation training, the details of their implementation may have differed substantially (e.g., one study may have used graduate students providing CBT, whereas another may have used more experienced therapists; one study’s relaxation training may have been giving people a CD, whereas another’s may have been a formal setting one-on-one with an experienced therapist). Violations of this assumption may take the form of non-additivity, which we planned to test for any component networks under consideration. Non-additivity is the assumption that the degree of pre-post change associated with a given component does not vary based on the presence or absence of components being administered.

We investigated two types of NMAs for this project: *standard* NMA and *components* NMA. In standard NMA, each node is a treatment or multicomponent treatment given to at least one group of patients in at least one trial. For example, there would be a node for CBT + education

3.7 Results, Comments on Network Meta-Analyses for KQ1, KQ2, and KQ3

and a separate node for CBT + relaxation training + education. By comparison, a components NMA defines each node as a possible component of any treatment. In this analysis, there would be a CBT node, a relaxation training node, a biofeedback node, etc., and any trial employing a given component would contribute data to that node. For inactive control groups, both sets of networks included an attention control node, a minimal control node, and a no-treatment node.

All networks appear in Appendix G. Unfortunately, neither the standard networks nor the components networks yielded fruit. The two standard networks (one for migraine attack frequency and one for migraine disability) yielded no unique conclusions, and the two components networks (same outcomes) had clear violations of the assumption of additivity. For more details, see Appendix G.

3.8 Key Question 4. What are the benefits and harms of non-headache focused behavioral interventions (e.g., CBT for insomnia, CBT for depression/anxiety, parent training) for migraine prevention in children and adults with migraine?

3.8.1 Key Points

- Only two RCTs assessed behavioral interventions aimed at sleep in adults with chronic migraine. No studies addressed behavioral interventions for individuals with migraine and anxiety or depression.
- For children with migraine, no studies addressed behavioral interventions for sleep, anxiety, or depression.
- In adults with chronic migraine, behavioral sleep modification may reduce headache frequency at 6 weeks (1 RCT, SOE: low).

3.8.2 Description of Included Evidence

Two RCTs conducted in the United States addressed KQ4 (Table 15). Both assessed the impact of behavioral interventions for sleep on adults with comorbid insomnia and migraine. No studies addressed children or interventions for adults with migraine and comorbid depression or anxiety.

Table 15. Studies included for Key Question 4

Study	Patients	Behavioral Treatment(s)	Other Active Treatment	Nature of the Comparison(s)
Smitherman et al. 2016 ³⁴	Chronic migraine and insomnia (Adults)	Cognitive behavioral therapy for insomnia (CBTi)	Usual care (acute and preventive migraine medications prescribed before enrolment)	CBTi vs. Sham control
Calhoun et al. 2007 ⁶³	Chronic migraine (Adults)	Behavioral sleep modification (BSM)	Usual care for migraine management, including advice to discontinue overused medication (is applicable)	BSM vs. Sham control

Of the 2 included studies, the first RCT (Smitherman et al. 2016, n=32³⁴) investigated the effects of cognitive behavioral therapy for insomnia (CBTi) on adults with chronic migraine and insomnia. Participants were randomly assigned to either the CBTi or sham control group for 2

3.8.2 Results, Key Question 4, Description of Included Evidence

weeks. The CBTi strategies included specific sleep behaviors, while the sham control involved maintaining a consistent dinner time and other unrelated instructions. Participants were allowed to continue acute and preventive medicines prescribed before enrollment.

The second study by Calhoun et al. (2007)⁶³ explored behavioral sleep modification (BSM) in adult women with chronic migraine without primary sleep disorders. Participants were randomly assigned to the BSM or sham control group for 6 weeks. The BSM group received instructions to improve sleep hygiene and modify sleep behavior. The control group received sham instructions.

3.8.3 Risk of Bias

The trial by Smitherman et al.,³⁴ which compared CBTi with sham control, was rated as low risk of bias. The other included RCT by Calhoun 2007⁶³ (BSM versus sham control) was rated as moderate (some concerns). The primary issues stemmed from unclear concealment of the allocation sequence and signs of potential inadequate randomization. Furthermore, the method used to ascertain the baseline headache frequency was not robust. Instead of using a standardized diary, the study relied on the patients' recall of their headache frequency.

3.8.4 Summary of Findings

3.8.4.1 Adults: CBTi Versus Sham Control

Migraine/Headache Attack Frequency: For headache frequency, the Smitherman et al. 2016³⁴ RCT reported headache frequency 2-weeks postintervention and at 10 weeks. The authors found no statistically significant difference between CBTi and sham control groups at 2 weeks after the end of the intervention: OR (inverse probability weighting) 1.06; 95% CI: 0.52 to 2.15, $p=0.883$. However, at 10 weeks, the CBTi group had a larger reduction in probability of headache: OR (inverse probability weighting) 0.40; 0.17 to 0.91, $p=0.028$. However, this result was not considered statistically significant after adjusting for multiple comparisons ($p<0.025$ required for significance).

Migraine Disability: For migraine disability, using the MIDAS scale, the Smitherman et al. 2016³⁴ RCT reported clinically meaningful reductions in MIDAS scores for both groups at 6 weeks (2 weeks after intervention completion) and at 10 weeks. However, both groups remained in the severe migraine disability category (MIDAS grade IV), with no statistically significant between-group differences between at any timepoint.

Smitherman et al. 2016 also reported that HIT-6 scores were severely affected for both intervention and sham groups at baseline (HIT-6 66.9 [SD 3.8] in the CBTi group and 64.8 [3.9] in the control group).³⁴ Compared with sham, there was no statistically significant difference between groups at 10 weeks (59.9 SD 5.5, 59.6 [SD 7.2] for CBTi and sham groups, respectively).

Migraine-Specific Quality of Life and Adverse Events: Not reported.

Other Outcomes:

Anxiety. Smitherman et al. 2016³⁴ evaluated anxiety using the GAD-7 scale. The study reported improvement in anxiety scores from moderate to mild post-treatment and at 10-weeks followup, with no significant difference between groups. The calculated MD was 0.4 (95% CI: -3.2 to 4.01) postintervention and 0.6 (95% CI: -3.0 to 4.2) at 8-weeks followup.

Depression. The same RCT evaluated CBTi versus sham intervention and reported depression using the PHQ-9. The between-group difference was not statistically significant after

3.8.4 Results, Key Question 4, Summary of Findings

controlling for baseline scores ($p=0.054$). The calculated mean difference was 1.5 (95% CI: -2.0 to 5.0) postintervention and 2.3 (95% CI: -1.1 to 5.7) at 8-weeks followup.

Using a 10-point VAS scale, the included RCT³⁴ found no statistically significant difference in headache intensity postintervention and at 10-weeks followup (calculated MD 0.1, 95% CI: -1.2 to 1.4 postintervention and 0.6, 95% CI: -0.7 to 1.9 at 8-weeks followup).

One trial³⁴ evaluated CBTi's impact on sleep outcomes, including total sleep time, sleep efficiency, sleep quality, and daytime sleepiness. The CBTi group increased their sleep time at a greater rate than the control group (group-by-time interaction $p=0.049$); however, there was no statistically significant difference between the total sleep time at postintervention and 10-weeks followup. At the followup, the CBTi group slept 52.7 minutes longer and the control slept 5.9 minutes longer than at baseline ($p=0.068$).

The CBTi group increased sleep efficiency more than the control group ($p=0.001$). The MD was 3.3 (95% CI: -2.4 to 9.0) postintervention and -4.0 (95% CI: -7.5 to -0.5) at 10-weeks followup.

Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). The CBTi group demonstrated a greater increase in sleep quality (lower PSQI scores, $p=0.009$) at followup (calculated MD 3.3, 95% CI: 0.9 to 5.7 postintervention and 4.5, 95% CI: 1.9 to 7.1 at 8-weeks followup).

Daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESS). The ESS scores did not differ statistically between the groups at followup. The MD was 0.2 (95% CI: -2.7 to 3.1) postintervention and -0.1 (95% CI: -3.1 to 2.9) at 8-weeks followup.

3.8.4.2 Adults: Behavioral Sleep Modification Versus Sham

For headache frequency, Calhoun et al.⁶³ compared BSM with a sham control in terms of headache frequency.

Migraine/Headache Attack Frequency: At 6 weeks, the Calhoun et al. RCT reported a greater statistically significant reduction of headache frequency in the BSM group than in the control postintervention (from mean 24/month at baseline to 17, compared with the control group mean 23/month at baseline to 24/month); however, the BSM group appeared to be more clinically complex at baseline.

Adverse Events: The study did not report adverse events.

Migraine Disability and Migraine-Specific Quality of Life: Not reported.

3.8.4.3 Strength of Evidence

SOE ratings for KQ4 appear in Table 16 below.

3.8.4 Results, Key Question 4, Summary of Findings

Table 16. Strength of evidence ratings for Key Question 4 (non-headache focused interventions)

Treatment	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
CBTi vs. Sham control	Headache reduction (Odds of having a headache)	Smitherman et al. 2016 ³⁴ (n=31) At 10 weeks OR 0.40 (95% CI 0.17 to 0.91), p=0.028 Not statistically significant after adjusting for multiple comparisons.	Low	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
CBTi vs. Sham control	Disability/Function (MIDAS) and HIT-6	Smitherman et al. 2016 ³⁴ At 10 weeks (n=31) No statistically significant difference for either measure	Low	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
BSM vs. Sham	Headache reduction	Calhoun 2007 ⁶³ (n=36) At 6 weeks Statistically significant reduction of headache frequency Favors BSM	Moderate	Direct	Unknown	Precise	Not suspected	None	Low	In adults with chronic migraine, BSM may reduce headache frequency at 6 weeks.

Abbreviation: BSM=behavioral sleep modification; CBTi=cognitive behavioral therapy for insomnia; CI= confidence interval; HIT-6 – Headache Impact Test; MIDAS = Migraine Disability Assessment Questionnaire; N/A= Not applicable; OR=odds ratio; n=number of patients.

3.9 Results, Key Question 5

3.9 Key Question 5: For KQs 1–4, how do the findings vary by baseline biopsychosocial factors (e.g., sex, socioeconomic status, co-occurring mental health conditions)?

3.9.1 Key Points

- Four included studies addressed the possible association between biopsychosocial factors and the various questions we asked in this report.
- Results were insufficient to permit conclusions due to high study limitations, and the existence of only one study per association.

3.9.2 Description of Included Evidence

Four studies (all at high risk of bias) addressed this KQ.

- Seng et al. (2019)⁵⁵ reported subgroup analyses of episodic/chronic migraine and age for the comparison between mindfulness-based cognitive therapy + education and no intervention.
- Richardson et al. (1989)⁷⁴ reported subgroup analyses of more severe migraine attacks versus less severe migraine attacks for the comparison between three groups (CBT + PMR in clinic CBT + PMR self-administered, and no intervention).
- Hedborg et al. (2011)⁴⁶ reported a gender subgroup analysis for the comparison between a multicomponent intervention (relaxation training + healthy lifestyle counseling + sleep counseling + stress management with and without massage therapy) and minimal intervention
- Underwood et al. (2022)⁶⁸ reported three subgroup analyses for the comparison between education and minimal intervention: high versus low anxiety, high versus low depression, and high versus low HIT-6 scores.

3.9.3 Summary of Findings

3.9.3.1 Overall Evidence

Seng et al.^{55,95} conducted a randomized trial of the effectiveness of a combination of two components: mindfulness-based cognitive therapy and education. The primary publication⁵⁵ reported benefits on various outcomes, and a secondary publication⁹⁵ conducted a preplanned analysis specifically of whether treatment benefits differed for those with episodic migraine versus those with chronic migraine.

Authors examined five outcomes for these subgroup analyses: 1) whether patients had severe migraine disability defined as MIDAS ≥ 21 , 2) the HDI, 3) Migraine Disability Index scores, 4) number of headache days per month, and 5) average headache pain intensity. All outcomes are listed in Appendix C. The results were mixed:

- For severe migraine disability, authors found a statistically significant interaction between whether one received treatment and whether one had episodic or chronic migraine. Essentially, treatment was better than no intervention only for those with episodic migraine. Specifically:
 - For those with episodic migraine, before the start of treatment, 79 percent (23/26) had severe migraine disability. After treatment (month 4 in the publication), this

3.9.3 Results, Key Question 5, Summary of Findings

dropped to about 34 percent in the treated group but had dropped to only about 73 percent in the no-intervention group.

- For those with chronic migraine, before the start of treatment, 87 percent (27/31) had severe migraine disability. After treatment (month 4 in the publication), this stayed about the same (91 percent) in the treated group and had dropped to about 77 percent in the no-intervention group.
- For the HDI, while there was not a statistically significant interaction effect, authors noted that the group by time interaction was statistically significant for the episodic migraine group but not the chronic migraine group. Thus, the findings were in the same direction as outcome 1.
- For the Migraine Disability Index, while there was not a statistically significant interaction effect, authors noted that the group by time interaction was statistically significant for the chronic migraine group but not the episodic migraine group. Thus, the findings were in the opposite direction as outcomes 1 and 2.
- For the other two outcomes, there was no statistically significant interaction with migraine status, and neither patient group had a statistically significant group by time interaction.

Regarding the impact of patient age, the primary publication⁵⁵ also noted that advantages of treatment over no intervention (all outcomes listed above) did not change after adjusting for age, suggesting there is no subgroup effect of age.

Richardson et al. (1989)⁷⁴ conducted a randomized trial comparing three groups: CBT + PMR in clinic, CBT + PMR self-administered, and no intervention. Based on a headache index (specifics not reported), authors categorized each patient's condition as either "more severe" or "less severe" (authors did not report the cutpoint). They measured four outcomes (peak intensity, frequency, total duration, and medication), and none revealed a statistically significant interaction between group and severity.

Hedborg et al. (2011)⁴⁶ compared a multicomponent intervention (relaxation training + healthy lifestyle counseling + sleep counseling + stress management with and without massage therapy) and minimal intervention. Authors reported statistical nonsignificance ($p=0.505$, Table III in the paper) for the interaction between study group and gender for the outcome of the percentage of patients with 50% or more migraine reduction. They did not report the four rates.

Underwood et al. (2022)⁶⁸ compared education and minimal intervention and conducted subgroup analyses for high versus low baseline anxiety, high versus low baseline depression, and high versus low baseline HIT-6 scores. None of these subgroup analyses showed statistically significant interactions between group and subgroup with respect to HIT-6 scores at 12 months (Table 4 of the paper).

3.9.3.2 Strength of Evidence

SOE ratings for KQ5 appear in Table 17 below.

3.9.3 Results, Key Question 5, Summary of Findings

Table 17. Strength of evidence ratings for Key Question 5 (biopsychosocial factors)

Treatment	Factor	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
MBCT + education vs. TAU	Episodic vs. chronic migraine	MIDAS ≥ 21	Seng et al. ^{55,95} : MBCT + education was better than TAU only for those with episodic migraine	High	Direct	Unknown		Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Episodic vs. chronic migraine	HDI	Seng et al. ^{55,95} : the group x time interaction was statistically significant only for the episodic migraine group	High	Direct	Unknown		Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Episodic vs. chronic migraine	MDI	Seng et al. ^{55,95} : the group x time interaction was statistically significant only for the chronic migraine group	High	Direct	Unknown		Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Episodic vs. chronic migraine	Headache days/month	Seng et al. ^{55,95} : no statistically significant interaction, and neither group showed a statistically significant interaction with time	High	Direct	Unknown		Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Age	MIDAS ≥ 21	Seng et al. ^{55,95} only reported that the group difference did not change after adjusting for age	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A

3.9.3 Results, Key Question 5, Summary of Findings

Treatment	Factor	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
MBCT + education vs. TAU	Age	HDI	Seng et al. ^{55,95} reported only that the group difference did not change after adjusting for age	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Age	MDI	Seng et al. ^{55,95} reported only that the group difference did not change after adjusting for age	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
MBCT + education vs. TAU	Age	Headache days/month	Seng et al. ^{55,95} reported only that the group difference did not change after adjusting for age	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
CBT + PMR (in clinic) vs. CBT + PMR (self-administered) vs. no intervention	Headache index more severe vs. less severe	Headache frequency	Richardson et al. (1989) ⁷⁴ reported only that there was no statistically significant interaction between group and severity	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Relaxation training + Healthy lifestyle counseling + Sleep counseling + Stress management vs. Relaxation training + Healthy	Gender	% of patients with 50% or more reduction in migraine attack frequency	Hedborg et al. (2011) ⁴⁶ reported that there was no statistically significant interaction between group and gender	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A

3.9.3 Results, Key Question 5, Summary of Findings

Treatment	Factor	Outcome	Study Findings	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Factors	Strength of Evidence	Conclusion
lifestyle counseling + Sleep counseling + Stress management + Massage therapy vs. minimal intervention											
Education vs. minimal intervention	High vs. low baseline anxiety	HIT-6 at 12 months	Underwood et al. (2022) ⁶⁸ reported that there was no statistically significant interaction between group and anxiety	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Education vs. minimal intervention	High vs. low baseline depression	HIT-6 at 12 months	Underwood et al. (2022) ⁶⁸ reported that there was no statistically significant interaction between group and depression	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A
Education vs. minimal intervention	High vs. low baseline HIT-6 score	HIT-6 at 12 months	Underwood et al. (2022) ⁶⁸ reported that there was no statistically significant interaction between group and baseline HIT-6 score	High	Direct	Unknown	Imprecise	Not suspected	None	Insufficient	N/A

Abbreviations: CBT=cognitive behavioral therapy; HDI – Headache disability inventory; HIT-6=Headache Impact Test; MBCT=mindfulness-based cognitive therapy MDI – Migraine disability index; N/A – Not applicable; MIDAS – Migraine Disability Assessment; PMR=progressive muscle relaxation; TAU=treatment as usual.

4. Discussion

4.1 Summary of Evidence

Behavioral therapies can be used as standalone treatments or combined with other types of therapies (e.g., pharmaceutical, neuromodulation). Some patients with migraine may either have contraindications to medication, or a preference against them (potentially due to a desire to avoid the risk of adverse effects and/or to general beliefs about pharmaceuticals). Thus, behavioral interventions represent a critical alternative.

We included 63 randomized trials published since 1978 that provided data on the effectiveness or comparative effectiveness of various behavioral interventions for migraine prevention. The trials varied greatly in the specific behavioral components employed, the nature of control groups used for comparison, and the types of outcomes assessed. Despite many concerns about the evidence (detailed below in the section Limitations of the Evidence and Future Research Needs), our review permitted a few tentative conclusions (see Table 18).

For Key Question (KQ) 1 (effectiveness), we found potentially promising results for interventions, including cognitive behavioral therapy (CBT), relaxation training, mindfulness-based therapy, and education. Specifically, in adults, low strength of evidence (SOE) suggests that behavioral interventions that include any of three components (CBT, relaxation training, and/or mindfulness) have potential to lower migraine/headache attack frequency. The estimated reduction was similar for these three components (about 1 migraine day/month, but could be as low as 0.2 days/month or as high as 1.9 days/month). We also found that education alone may improve migraine-related disability, based on two trials (SOE: low; effect size not estimable due to insufficient reporting). “Low” SOE ratings mean we have limited confidence in the effectiveness of behavioral therapies, primarily due to concerns about study biases and the reliability of findings from small or inconsistent studies. It should not be interpreted as a reflection of the effect or its size.

A reduction of 1 migraine day/month was the minimum clinically important difference identified *a priori* by our technical experts. Our point estimates for this outcome, therefore, were on the border of clinical importance. When we examined direct evidence comparing behavioral interventions to medications, we found little: two studies^{35,37} reported inconclusive data comparing biofeedback or relaxation to topiramate, another study²⁷ reported inconclusive data comparing biofeedback to propranolol, amitriptyline and their combination, and a fourth study³⁶ had mixed results. As context, we note that a recent systematic review found that CGRP (calcitonin gene-related peptide) antagonists, widely hailed as a key migraine prevention strategy, reduced migraine days/month by only around two migraine days/month (estimated advantage beyond placebo).¹¹⁴

Beyond attack frequency, it is important to determine if behavioral interventions also reduce disability or improve quality of life. Many trials reported disability data, typically using the MIDAS. However, the data were too sparse and/or inconsistent to permit conclusions. Migraine-specific QOL data were less often reported, and were also inconclusive. Thus, future trials are needed to assess the impact of behavioral interventions on these important outcomes. Many behavioral trials have measured additional constructs such as improvements in depressive and anxious symptomology, self-efficacy, catastrophizing, locus of control, stigma and other aspects of functioning and well-being; these were not within scope for this review.

Our findings require a few important qualifications. The first concerns our analyses for effectiveness based on any-presence-of-this-component. This nonspecific but consistent

4. Discussion

approach allowed us to indirectly estimate the effectiveness of a given component, but other components in the packages may also have influenced outcomes. For example, interventions including CBT were primarily composed of CBT combined with other behavioral components; however, a 2010 trial by Holroyd 2010³⁶ included two behavioral interventions arms, both of which received CBT and relaxation training, and one of which also received propranolol. Thus, for CBT, these findings not only reflect synthesis across trials with variable types of behavioral components, but also reflect the impact of relaxation training and propranolol, a pharmacologic intervention estimated to reduce migraine days/month by 0.8 days/month. Second, few trials compared intervention with an attention control, raising the possibility of overestimating the impact of interventions. For example, while we included 11 trials that included a CBT component, only one of them had an attention control group, while the other 10 had compared CBT to waitlist or usual care or no intervention. Third, we recognize that MBCT is primarily a mindfulness-based treatment, with a small CBT component. Thus, one might argue that it should not have been included in the CBT analyses. However, our effectiveness analyses did not incorporate the time or intensity of each component within a treatment package. Thus, for consistency with how we analyzed other treatment packages, we included MBCT in both the mindfulness analyses and the CBT analyses. Fourth, our analysis and intervention classification were further complicated by the varying terminology used by different researchers since 1978. Researchers could have used different terms for the same component, or the same term for different components. Intervention intensity and implementation also varied widely across the included trials (see the full report for details).

4. Discussion

Table 18. Summary of conclusions

Age Group	Comparison	Outcome	Amount of Evidence	Evidence Favors	Estimated Difference	SOE
Adults	Behavioral intervention that includes CBT vs. control	Migraine/headache attack frequency	10 RCTs (all 10 in meta-analysis)	CBT component	1.1 fewer migraine days/month (95% CI 0.4–1.8)	Low
Adults	Behavioral intervention that includes relaxation training vs. control	Migraine/headache attack frequency	16 RCTs (12 in meta-analysis)	Relaxation training component	1 fewer migraine day/month (95% CI 0.4–1.6))	Low
Adults	Behavioral intervention that includes MBSR vs. control	Migraine/headache attack frequency	5 RCTs (all 5 in meta-analysis)	MBSR component	1 fewer migraine day/month (95% CI 0.2–1.8))	Low
Adults	Education alone vs. control	Migraine-related disability	3 RCTs (no meta-analysis)	Education alone	NC	Low
Adults	MBSR vs. education	Migraine-related disability	1 RCT	MBSR	18 points on the MIDAS scale (95% CI 7–30)	Low
Adults	CBT + relaxation training vs. propranolol	Migraine/headache attack frequency	1 RCT	Propranolol	1.4 fewer migraine day/month (95% CI 0.2–2.6)	Low
Adults	CBT + relaxation training vs. propranolol	Migraine-specific QOL	1 RCT	CBT + relaxation training	12 points on the MSQOL scale (95% CI 7–18)	Low
Adults	MBSR + education vs. stress management training + education	Migraine/headache attack frequency	1 RCT	MBSR + education	2 fewer migraine days/month (95% CI 0.8–3.5)	Low
Adults	CBT + relaxation training vs. biofeedback	Migraine/headache attack frequency	1 RCT	Biofeedback	2.2 fewer migraine days/month (95% CI 0.1–4.4)	Low
Children/adolescents	CBT + biofeedback + relaxation training vs. education	Migraine/headache attack frequency	1 RCT	CBT + biofeedback + relaxation training	1.6 fewer migraine days/month (95% CI 0.4–2.7)	Low
Children/adolescents	CBT + biofeedback + relaxation training vs. education	Migraine-related disability	1 RCT	CBT + biofeedback + relaxation training	11 points on the PedMIDAS scale (95% CI 2–20)	Low

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; MBSR=mindfulness-based stress reduction; MIDAS=Migraine Disability Assessment; MSQOL= migraine-specific quality of life; NC=not calculable; PedMIDAS=Pediatric Migraine Disability Assessment; QOL=quality of life; RCTs=randomized controlled trials; SOE=strength of the evidence.

4. Discussion

Thirteen of our included studies used some form of technology to deliver behavioral treatments (KQ1a). For adults, these included smartphone apps, audiotapes, Web-based programs, and telephones; for children, they include CD-ROMs and telephone. When we examined this evidence specifically (KQ1a), the evidence was inconclusive. This was typically due to a high risk of bias (e.g., greater expectations of benefit in control groups), single studies, and/or low precision. Given the increasing use of telehealth and mHealth interventions, understanding the role they play is crucial for future migraine prevention.

KQ2 involved comparative effectiveness. Most comparisons were made by single studies, and we drew a few conclusions. In adults, one study compared mindfulness-based stress reduction (MBSR) with education and found advantages of MBSR for both migraine disability and migraine-specific QOL (SOE Low for both outcomes). A different study compared relaxation training + education with propranolol and found better results for propranolol when the outcome was migraine attack frequency (SOE: low), but clinically importantly better results for relaxation training + education when the outcome was migraine-specific QOL. Yet another study found that adding CBT and education to relaxation training reduces migraine-specific QOL (SOE: low). A fourth study found that MBSR + education may result in lower migraine attack frequency than stress management training + education (SOE: low). A fifth study of adults found that biofeedback may result in lower migraine attack frequency than CBT + relaxation training (SOE: low). For children/adolescents, we drew conclusions from only one study, specifically that CBT + biofeedback + relaxation training may result in lower migraine attack frequency (SOE: low) and lower disability (SOE: low) than education alone.

For KQ3, we specifically sought to determine the impact of individual behavioral intervention components. Only five studies addressed this, on four separate comparisons, and all were inconclusive, due mostly to risk of bias and small sample size.

KQ4 addressed behavioral interventions directed toward co-occurring conditions (anxiety, depression, insomnia) common in individuals with migraine to assess whether addressing these other conditions results in migraine reduction. We identified only two studies both targeting insomnia in adults. One study assessed cognitive behavioral therapy for insomnia (CBTi), and the other assessed a behavioral sleep management intervention. While data on the former were inconclusive, we concluded that behavioral sleep modification can reduce headache frequency (SOE: low).

KQ 5 considered whether biopsychosocial factors affect any of the answers to the above KQs. Only four studies provided pertinent data, and there were some suggestive findings but none conclusive. One trial had found that a combination of mindfulness-based cognitive therapy and education may be more beneficial for episodic migraine than chronic migraine in reducing the risk of severe migraine disability.

A 2019 systematic review by Sharpe¹¹ had included 21 randomized trials of psychological treatments for migraine, all of which we considered for this report. They rated all the studies as “very low” quality and concluded that “we are uncertain whether there is any difference between psychological therapies and controls.” The review had combined all behavioral treatments in their primary analysis, and we conducted a similar set of analyses (see Appendix F). These analyses were also inconclusive, which may be due to creating a generic “behavioral treatment” category; effectiveness may depend on the behavioral intervention’s nature. Thus, we conducted separate analyses of each of five primary components. Even though they were component-focused, most of these analyses were still inconclusive, likely due to a combination of factors,

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including small studies, variability among patients, varying components, varying implementations of a given component, and inconsistent outcome reporting.

In the sections below, we summarize the applicability of the evidence, the Contextual Questions, limitations of our review, limitations of the evidence, and future research needs.

4.2 Applicability

Several factors may limit the applicability of our findings. First, our inclusion criteria were deliberately inclusive; thus, our included studies were published as early as 1978, and we did not require studies to use formal criteria for diagnosis of migraine and allowed studies including mixed headache types as long as study participants had migraine. Given the anticipated sparse evidence base, this inclusive approach allowed us to capture older studies considered important. However, older studies have applicability concerns. Of studies addressing effectiveness, comparative effectiveness, or adverse effects (KQs 1 to 3) 25 percent (n=15) were published before 1990, and over half (54 percent) were published in 2010 or before. Factors limiting applicability of these older studies include differences in diagnostic criteria, delivery methods, available migraine treatments, acceptability of behavioral interventions, and changes in clinical medicine. Particularly in the past decade, treatment options for both acute migraine and migraine prevention have expanded, with new pharmacologic and nonpharmacologic options available. These additional options could affect which patients continue to have refractory migraine (and seek treatments such as behavioral interventions) as well as what background interventions study participants in our included studies received.

As noted, we did not require studies to use formal International Headache Society (IHS)/International Classification of Headache disorders (ICHD) criteria for migraine diagnosis for inclusion. Of 55 studies reporting on KQs 1 to 3, 32 percent (n=20) either failed to report what criteria were used for migraine diagnosis or used an alternative criteria (e.g., Ad Hoc Committee on classification of headache criteria, “verified diagnosis by their personal physician,” or “medical chart diagnosis of migraine”). Furthermore, as we included studies extending back to 1978, even among studies using formal ICHD criteria, studies differed in their criteria using the 1991 ICHD-1 to the most recent IHS criteria, the ICHD-3 published in 2013. These differences, particularly failure to use formal criteria, may result in important differences in study population that could affect applicability of findings.

Another key consideration for applicability involves the use of concomitant treatments during trials. Study reporting had large variability as to whether patients were allowed to use co-interventions; 21 of 61 studies included for KQs 1 to 3 failed to mention whether patients were allowed to use other treatments during the study period. Sixty-six percent of studies described parameters for use of concomitant medications during the trial: however, these parameters differed widely across trials. For example, some trials specified sole use of as-needed acute treatments, some allowed patients to remain on preventive medications, while others specified that physicians prescribed preventive and acute medications at their discretion to patients across study arms. Some studies specified that prevention medications should remain unchanged for the study’s duration, while others did not.

Finally, two important additional considerations pertain to challenges of acceptability and access. First, regarding acceptability, behavioral interventions assessed in this review included a wide range of delivery modalities and time commitments, with some requiring weekly in-person sessions, while others were minimal, consisting of delivery of educational materials or self-guided materials describing therapies, such as relaxation training. Behavioral interventions that

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require significant time commitment and travel may not be feasible for many patients, particularly if they already face baseline challenges resulting from migraine-related disability and function.¹¹⁵ Second, even if patients find the intervention acceptable, pragmatic challenges with accessing interventions such as CBT and biofeedback are well known. These challenges stem from both a shortage of providers, lack of awareness of potential providing physicians, and insurance coverage. A 2020 survey of over 400 migraine patients with 4 or more headache-days per month found that respondents reported being “somewhat likely” (median 4 of 5, Likert scale) to pursue behavioral treatment for migraine if covered by insurance.¹¹⁶ However, if required to pay out of pocket, this response changed to “not very likely” (median 2 of 5, Likert scale). Thus, these factors may ultimately limit the real-world impact of behavioral interventions on migraine prevention.

4.3 Contextual Questions

Contextual Question 1: What evidence is available on the benefits of behavioral preventive treatments for children and adults with migraine that include intervention components targeting caregivers (e.g., parents, spouses, other key support people)?

Behavioral treatments for migraine prevention that include components targeting caregivers are primarily focused on the parents and caregivers of adolescents and/or children with migraine (not caregivers of adults with migraine). Parents and caregivers are often involved in treatment and undoubtedly play a vital role in its management, particularly for elements that are self-guided, such as those that are Web-based.¹¹⁷ Notably, having a child or children with migraine often results in caregiver burden¹¹⁸ and increases parental stress;¹¹⁹ therefore, incorporating caregivers into treatment may also benefit their well-being directly (through targeted intervention components) or indirectly (because of improvements experienced by their child).

Two well-known examples of behavioral interventions for pediatric migraine with caregiver components are the “Headstrong” and “MIPAS-Family” studies (MIPAS is an acronym for Migraine Patient Seminar Program). The Headstrong RCT evaluated the effectiveness of a self-guided CD-ROM program containing cognitive-behavioral self-management strategies for preventing pediatric headaches and additionally evaluated headache-related disability and QOL.⁶⁹ Parents were given a manual containing directions on how to use the Headstrong program, their role in the intervention (e.g., how to assist with homework assignments, how to complete headache diaries), lesson overviews, and technical assistance information in case their child had problems running the program. Participants and their parents completed all measures independently. Compared with an educational control, Headstrong resulted in lower pain severity at post-treatment and less migraine-related disability at 3 months postintervention, by child and parent report, respectively. No significant differences were observed for headache frequency or QOL. The MIPAS-Family RCT compared the impact of a multi-modal behavioral education and training program with a combined biofeedback treatment.⁷⁰ Parents were given four training sessions that spanned three modules: diagnostic, education, and behavioral training. Child and parent components alternated to facilitate parents becoming co-trainers who helped employ the techniques at home. Both intervention groups showed significant improvements concerning headache intensity and duration. The RCT found no significant differences in the main headache parameters between the two groups. After the treatments, children were less disturbed by their headaches in the domains of school, homework, and leisure time.

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An additional example is an older controlled study that explored the use of parent-mediated pain behavior management strategies as an adjunct to the biofeedback treatment of children with migraine.²⁹ Children receiving parent-mediated pain management guidelines evidenced significantly greater reductions in headache frequency, were more likely to experience clinically significant improvements, were more likely to be headache-free, and demonstrated better adaptive functioning during treatment and at 3-month follow-up. Generally, studies like these suggest that behavioral treatments for pediatric/adolescent migraine benefited from using a holistic, caregiver-centered approach.

CQ 2: What are patient and provider perceptions of the benefits, harms, and barriers to engaging with behavioral treatments for migraine prevention in children and adults?

Behavioral treatments for migraine prevention are prone to underutilization, high attrition, and suboptimal adherence.¹²⁰⁻¹²² Various barriers have been identified that contribute to these issues, such as limited availability of primary headache providers offering appropriate interventions or referrals; insufficient knowledge and training of behavioral treatments among providers; financial burden; limited access to behavioral providers in underserved communities; and stigma associated with headache/mental health diagnoses and treatment. Other psychological factors may also play a role, such as attitudes or beliefs, lack of motivation, poor awareness of triggers, low levels of pain acceptance, and engagement in maladaptive coping styles.¹²⁰⁻¹²² In fact, even after referral for behavioral therapy, many patients with migraine still do not inquire about making an appointment.¹¹⁵

A narrative review highlighted both provider-, system-level, and patient-related barriers to CBT for pediatric migraine.¹²³ Provider- and system-level barriers included providers' lack of specific knowledge about CBT, confidence explaining CBT, time to discuss, and referral options. Patient-related barriers included stigma, family uninterest, and perception of both treatment and financial burden. For caregivers of children participating in behavioral treatment, communication and balancing treatment with school and activity schedules are further challenges.¹¹⁷

A recent meta-synthesis aimed to collate research on patients with migraine treatment perspectives to identify common patterns across various types of migraine treatment studies, including behavioral treatments.¹²⁴ Five main themes were identified: difficulties with healthcare utilization and cost of treatment; perceived relationships with providers; thoughts about the various migraine treatments; understanding diagnosis/triggers; and societal implications. Regarding behavioral treatment delivery, patients with migraine have reported to prefer in-person and smartphone-based behavioral therapy to telephone-based behavioral therapy.¹¹⁶ Similarly, digital CBT for insomnia in women with chronic migraine has been found to be acceptable.¹²⁵

A recent qualitative study conducted focus groups in people who had participated in mobile health (mHealth) studies of behavioral interventions for migraine to better understand participant experience in the recruitment/enrollment process, participant experience during the studies themselves, and ideas for improving participant experience for future studies.¹²⁶ Regarding recruitment and enrollment, participants joined studies out of an interest in research and/or a desire to try new modalities of behavioral therapy. When asked about their experiences during the studies, participants thought it was difficult to participate in study followup and compliance phone calls, preferred choosing among various options for contact with the study team. Barriers that limited mHealth use related to migraine itself including challenges to complete diaries on a daily basis and technical difficulties and uncertainties about mHealth. However, they also felt

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that being part of a research study promoted daily behavioral therapy use, that progressive muscle relaxation was enjoyable and has a positive impact on life, and that behavioral therapy was a preferred treatment to reduce migraine pain.

In exploring barriers to receiving behavioral interventions for migraine prevention, virtual care and apps present unique challenges beyond mere access to the internet and smart devices. For example, in the study conducted on the HeartMath app,⁵⁷ 9 out of 16 participants encountered technical difficulties. Several factors contributed to non-utilization of the app/sensor, including forgetfulness, inconvenience, the inability to use it during a migraine/headache, and feelings of self-consciousness when using the sensor in public spaces. Almost one-fifth of the participants were either unwilling or hesitant to recommend this app to other patients.

4.4 Limitations of Our Review

A major challenge for this review was the complexity of combination interventions and their intersecting components. This challenge was compounded by the semantic problem that different researchers since 1978 could have used different terms for the same component or the same term for different components. Further, a given component (e.g., CBT) could vary widely in its intensity (number of sessions, hours per session, time between sessions) or implementation (level of experience of the person[s] providing treatment, the setting of treatment, the degree of fidelity to planned interventions).

These differences introduced subjectivity in our decisions about *categorizing treatments*. A behavioral psychologist and a neurologist with expertise in migraine reviewed our decisions. We encountered the most difficulty with education as a treatment component. Education about migraine in general (e.g., know your triggers) is technically a behavioral intervention, but many researchers explicitly described it as a control intervention. We ultimately chose to call education an active intervention only if 1) the authors appeared to treat it that way, 2) study staff time/interaction was similar to an obvious intervention arm, and 3) the education intervention did not clearly involve other behavioral components. We recognize the fallibility of some of these decisions.

The semantic vagaries of various combinations also introduced subjectivity about *separating or combining different studies*. For our analysis for KQ1, we first considered analyses ignoring the specific behavioral treatment, as was done by a Cochrane review by Sharpe,¹¹ comparing any behavioral treatment with any control. This strategy seemed naïve because different behavioral approaches may have different effects. At the other extreme, we considered a pure combination approach, in which each analysis is specific to a particular combination and a particular control group, but that approach seemed tedious and statistically underpowered. Thus, we struck a middle ground in our decision to combine any studies that used a given component (e.g., CBT) regardless of whether additional components were used, in an attempt to measure (albeit indirectly) that component's impact.

One strength of behavioral interventions is the ability to tailor components to individuals. For example, during a treatment a psychologist can decide, based on patient preferences or likelihood of effectiveness, which of several components should be encouraged or discouraged for a specific patient. By contrast, tailoring a given medication can only be dose-based. While the flexibility of treatment implementation for behavioral interventions may benefit patients, it introduces critical problems for evidence synthesis, as discussed above.

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Regarding outcome timepoints, for KQs 1-3, we had initially planned to analyze data separately in each of three timepoint categories (at least 8 weeks but <12 weeks, 12 weeks to <6 months, and 6 months or more). The sparseness of corresponding data, however, led us to perform “any-timepoints” analyses, whereby we chose from each study the timepoint that was closest to 12 weeks since the start of treatment. We chose 12 weeks because that (or “3 months,” which is 13 weeks) was the most commonly reported timepoint. This analytic choice’s potential flaw is that studies may have found different results at other timepoints. For some questions (e.g., KQ1a, KQ3), we discussed data per timepoint.

KQ4 involved non-headache-focused treatments and whether they generally reduce migraine attacks and/or migraine-related disability. We chose to focus only on treatments targeting three comorbidities (insomnia, depression, anxiety) because these seem to be the most common comorbidities in individuals with migraine.¹²⁷ Other comorbidities include hypertension, irritable bowel syndrome, epilepsy, and stroke, and future reviews should consider evidence on treatments targeting these conditions.

For interpreting data, we chose an MID for each of our three primary outcomes (migraine/headache attack frequency, migraine disability, and migraine-specific QOL). This number served two key purposes: 1) it allowed us to determine whether a statistically significant difference could also be deemed clinically important, and 2) it allowed us to determine whether a statistically nonsignificant difference could support a conclusion of approximate equivalence. Had we used different numbers, we may have had different interpretations of the data. For migraine/headache attack frequency, we relied on a number (1 migraine day/month) provided by our Technical Expert Panel. For the other outcomes, we relied on prior published articles or used a similar scale range of 3 percent. In our review, due to large confidence intervals, none of the observed differences clearly indicated clinical importance, and only one of the observed non-differences clearly indicated equivalence. Thus, our numerical choices regarding MIDs likely had little impact on our overall conclusions.

4.5 Limitations of the Evidence and Future Research Needs

Research on behavioral interventions for migraine prevention is limited by variable components, small studies, unreported effect sizes, and inconsistently measured outcomes. For components, most studies employed a multicomponent approach, whereby patients each received two or more behavioral interventions (such as both CBT and biofeedback). When compared with an inactive control group, this design can permit inferences about the combination, but not about either component individually. Decisions about which behavioral components to use would be better informed by more specific study designs. Our KQ3 specifically asked about components, but the evidence was insufficient to permit conclusions for all primary outcomes, mostly due to imprecision and single studies.

Many studies were small (30 of 63 included studies enrolled fewer than 50 patients), resulting in wide confidence intervals around effect sizes. These intervals were often wide enough to be consistent with both a conclusion of an important difference but also a conclusion of a difference in the opposite direction. We performed numerous meta-analyses to maximize statistical power, but these were still greatly limited by imprecision; also, many studies could not be included in meta-analyses due to insufficient reporting (e.g., no standard deviations reported). Some authors seemed convinced that if one group improved statistically significantly, but the other group’s pre-post difference was not statistically significant, then one can conclude that the first group did better. However, what is needed for that conclusion is a statistically significant

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between-groups comparison. This could take the form of a comparison at a specific followup timepoint, a comparison of change scores at a specific followup timepoint, or a statistically significant group \times time interaction followed by contrast tests.

Another major limitation concerned outcome measurement. For frequency, while all studies reported data on patients at least 80 percent of those having migraine attacks, some studies reported data on headache frequency, not migraine attack frequency. Some authors may have meant migraine when they indicated headache, but their intentions were unclear. Furthermore, some studies reported migraine attack frequency, whereas others reported the number of migraine-days in a month. While these measures are correlated, they are not the same, and we felt that the true burden of migraine attack frequency is best measured by migraine-days/month. This is why we created a metric prioritization to place greater emphasis on the more important metrics. Ideally, however, all studies would have reported the same metric. For migraine disability, the most common instrument was the Migraine Disability Assessment (MIDAS), but the use of other instruments raised the possibility of measurement inconsistency. Migraine-related QOL was less often reported, and only three instruments were used; thus, the measurement problem was less concerning.

Several studies used attention control groups, and we encourage this practice to attribute outcome differences to the treatment itself, rather than to the amount of time spent with investigators and/or differential expectations of benefit. Such control groups may be particularly important with children due to the relatively high placebo response rates in that population (one article in 2014¹²⁸ even stated that “placebo response rates are known to be high in pediatric migraine trials”).

Some have raised concerns that effectiveness of treatments may vary depending on gender, race/ethnicity, or other factors. Our findings (KQ5) suggest that evidence addressing these potential differences is sparse. One key challenge to addressing these variables is under-reporting of key factors, such as migraine type, comorbidities, and race/ethnicity, and we encourage future studies to comprehensively report key patient factors and to conduct subgroup analyses to investigate whether observed effects vary by patient factors.

Future RCTs of behavioral interventions for preventing migraine attacks will ideally 1) use the same core outcomes measured across studies including attack frequency, but specifically how reduced attacks relate to improvements in patient-centered outcomes such as disability and migraine-specific QOL, 2) employ homogeneous and standardized behavioral intervention components to improve reproducibility by other providers as well as categorizations by evidence reviewers, 3) use attention control comparison groups, and 4) use standardized diagnostic criteria for migraine for inclusion. Given the complexity and heterogeneity of the studies identified in this review with numerous small, single-center trials, future designs might use large, multi-center, multi-arm, multi-stage adaptive design to quickly evaluate the effectiveness of multiple behavioral components simultaneously.

4.6 Conclusions

The literature on behavioral treatments for migraine prevention is primarily characterized by small trials of combination interventions of variable components compared with several types of controls. Changing terminology and treatment implementations over the past 45 years further complicate efforts at evidence synthesis. The literature on children and adolescents is particularly inconclusive. Despite these challenges, we deemed the evidence sufficient to conclude that CBT,

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relaxation training, mindfulness-based therapy, and education may have benefits for adults with migraine.

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6. Abbreviations and Acronyms

AAFP	American Academy of Family Physician
ACT	Acceptance and commitment therapy
AHS	American Headache Society
BSM	Behavioral self-management
CBT	Cognitive behavioral therapy
CBTi	Cognitive behavioral therapy for insomnia
CD-ROM	Compact disc read-only memory
CDI	Children's Depression Inventory
CI	Confidence interval
EMG	Electromyography
EQ-5D	EuroQol-5D
FDI-Child Form	Functional Disability Inventory - Child and Adolescent Form
FDI-Parent Form	Functional Disability Inventory - Parent Form
FIS	Fatigue Impact Scale
FSQ	Functional status questionnaire
GAD-7	General Anxiety Disorder-7
HADS	Hospital Anxiety and Depression Scale
HANA	Headache Needs Assessment
HDI	Headache disability inventory
HIT-6	Headache Impact Test
IMPAC	Impact of Migraine on Partners and Adolescent Children
MBCT	Mindfulness-based cognitive therapy
MBSR	Mindfulness-based stress reduction
MIBS	Migraine Interictal Burden Scale
MIBS-4	Migraine Interictal Burden Scale (Special version)
MIDAS	Migraine Disability Assessment
MSQ	Migraine-Specific Quality of Life Questionnaire v. 2.1
MsQOL	Migraine-specific quality of life
NA	Not applicable
NRS	Numeric rating scale
NS	Not statistically significant
PDI	Pain Disability Inventory
PedMIDAS	Pediatric Migraine-Specific Disability Assessment
PedsQL	Pediatric Quality of Life Inventory
PHQ-9	Patient Health Questionnaire
PICOTS	Patients, Interventions, Comparators, Outcomes, Timepoints, Settings
PQ-LES-Q	Pediatric quality of life enjoyment and satisfaction
PCORI	Patient-Centered Outcomes Research Institute
PMR	Progressive muscle relaxation
PROMIS	Patient-Reported Outcomes Measurement Information System
QOL	Quality of life
RCT	Randomized controlled trial
RoB 2	Revised Cochrane risk-of-bias tool for randomized trials
SD	Standard deviation
SF-12	12-Item Short Form Survey

SF-36	36-Item Short Form Survey
SOE	Strength of evidence
TAU	Treatment as usual
VAS	Visual Analogue Scale

Appendix A. Search Strategies

Search Details and Data Sources

The search strategy was designed and conducted by an experienced systematic review/medical reference Librarian with input from the investigators. Another librarian peer reviewed the search strategies using the Peer Review of Electronic Search Strategies (PRESS) Checklist. We consulted with SMEs, Key Informants, and Technical Experts, to identify additional relevant keywords and concepts. We tested the final search against references pertaining to behavioral treatments for migraine that were cited in 2021 PCORI Topic Brief *Nonpharmacologic Interventions for Migraine Prevention*. We applied the following limits or filters to the database searches:

- *Date*. Our SME's recommended a search parameter covering the years 1975-2023 to ensure that key studies published in the 1970's would be captured. *Note: some databases did not go back that far.*
- *Language*. Publications were excluded if they were written in a language other than English. This was due to resource constraints.
- *Publication status*. We searched for published studies.
- *Human or organism*. The search was limited to limited to human studies.
- *Study design*. The search was limited to randomized controlled trials, systematic reviews, and meta-analyses.
- *Study location*. Retrieval was not limited to any geographic location.
- We conducted a comprehensive literature search in January 2023 (updated scheduled for May 2023). We searched the following databases:
- EMBASE and MEDLINE (searched simultaneously in Embase.com) (1975 to January 11, 2023) Date searched January 11, 2023
- PubMed (publisher supplied/in process citations/PubMed not Medline)(1975 to January 11, 2023) Date searched: January 11, 2023
- PsycINFO (1987 to January 11, 2023) Date searched January 11, 2023
- Cochrane Database of Systematic Reviews (1975 to January 11, 2023) Date searched: January 11, 2023

We conducted a gray literature search in January 2023 to address the key questions in the Systematic Review and the Contextual Questions. Searches were executed using the search function of the website, browsing the menu items, and searching the website via Google. The following search terms were used: migraine, headache, behavioral, cognitive, nonpharmacologic, psychotherapy, psychology, CBT, biofeedback, neurobiofeedback. Retrieval was at the discretion of the searcher and focused on white papers, monographs, reports, recommendations, policies, guidelines, regulatory information, ongoing clinical trials, and original research. The following resources were included in the grey literature search:

Strategies: browse menu items, use websites search engine, search via Google

- *Trials/research registries*.
 - ClinicalTrials.gov www.clinicaltrials.gov Date searched: January 25, 2022.
Methods: see strategy below

- *Web search engines/specific web sites.* We searched the following associations for relevant materials posted/published through March 2023. Methods: Searches were conducted using the website search and browsing capabilities and the Google site search tool.
 - Agency for Healthcare Research and Quality (AHRQ). www.ahrq.gov/ Date searched Mar 2, 2023
 - American Academy of Neurology. <https://www.aan.com/> Date searched Mar 3, 2023
 - Association for Applied Psychophysiology and Biofeedback. <https://aapb.org/> Date searched 2023 Mar 6.
 - Association for Behavioral and Cognitive Therapies (ABCT). <https://www.abct.org/> Date searched 2023 Mar 3.
 - American Headache Society. <https://americanheadachesociety.org/>. Date searched 2023 Mar 2.
 - American Psychiatric Association. <https://www.psychiatry.org/>. Date searched 2023 Mar 6.
 - American Psychological Association. <https://www.apa.org/>. Date searched 2023 Mar 3.
 - National Institutes of Health. <https://www.nih.gov/> Date searched 2023 Mar 6.
 - Patient-centered Outcomes Research Institute (PCORI). <https://www.pcori.org/> Date searched 2023 Mar 2.
 - Society of Behavioral Medicine. <https://www.sbm.org/> Date searched 2023 Mar 6.

Database Search Strategies

Embase.com Strategy: (Combines Medline and EMBASE) January 1, 1975 through January 11, 2023

- 1 'migraine'/exp OR migrain*:ti,ab,kw OR headache*:ti
- 2 ('drug free' OR non-drug OR nondrug OR non-pharmacologic* OR nonpharmacologic* OR collaborative OR 'inter disciplinary' OR interdisciplinary OR 'multi disciplinary' OR multidisciplinary OR psych* OR behav* OR cognitive):ti
- 3 Psychotherapy/exp OR 'psychological care'/mj/exp OR 'behavior therapy'/exp OR 'cognitive therapy'/exp OR 'cognitive behavioral therapy'/exp OR 'stress management'/de OR 'coping behavior'/exp OR 'caregiver support'/de OR 'parent counseling'/de OR 'problem solving'/de OR 'problem-focused coping'/exp OR ((behav* OR cognitive) NEAR/2 (intervention* OR modif* OR therap* OR treatment* OR manag*)):ti,ab,kw OR (manag* NEAR/2 stress):ti,ab,kw OR coping:ti,ab,kw OR (cope NEAR/3 trigger*):ti,ab,kw OR ((caregiver* OR mother* OR father* OR parent*) NEAR/4 (behav* OR counsel* OR educat* OR intervention* OR mediated OR support* OR train* OR operant* OR therapy)):ti,ab,kw OR ('parent child interaction therapy' OR PCIT OR 'supportive care'):ti,ab,kw OR (problem NEXT/3 (solving OR coping)):ti,ab,kw OR psychotherap*:ti,ab,kw
- 4 'biofeedback'/exp OR 'neurofeedback'/de OR 'biofeedback system (device)'/de OR 'biofeedback software (device)'/de OR (biofeedback OR 'bio feedback' OR neurofeedback OR 'neuro feedback' OR neurobiofeedback* OR neurotherapy*):ti,ab,kw OR (Handwarming OR 'hand warming'):ti,ab,kw OR (feedback NEAR/5 (thermal OR

- temperature OR EMG OR electromyograph* OR 'heart rate' OR electrocardiogra* OR pulse OR "blood volume" OR respiratory OR respiration OR breathing OR electroencephalogra* OR EEG OR ECG OR BVP)):ti,ab,kw OR (finger* NEAR/3 temp*):ti,ab,kw OR (skin NEAR/3 conduct*):ti,ab,kw
- 5 'relaxation training'/de OR 'muscle relaxation'/de OR 'autogenic training'/exp OR 'breathing exercise'/exp OR 'guided imagery'/exp OR (Autogenic NEAR/3 (feedback OR training OR exercise)):ti,ab,kw OR ('AFTE' OR 'progressive muscle relaxation'):ti,ab,kw OR (relaxation NEXT/2 (techniques OR therapy OR training)):ti,ab,kw OR breathing:ti OR relaxation:ti,ab,kw OR (Breathing NEAR/4 (exercise* OR deep OR guided OR diaphragm* OR paced OR belly)):ti,ab,kw OR ((guided OR visual) NEXT/3 imagery):ti,ab,kw
- 6 meditation/exp OR 'mindfulness-based stress reduction'/exp OR 'mindfulness based cognitive therapy'/exp OR (mindfulness* OR 'mind body' OR MBSR OR MBCT OR meditat*):ti,ab,kw
- 7 'acceptance and commitment therapy'/de OR (acceptance NEXT/2 commitment):ti,ab,kw
- 8 'dialectical behavior therapy'/de OR 'dialectical behav* therapy'
- 9 'motivational interviewing'/de OR 'transtheoretical model'/de OR (motivational NEXT/2 (enhancement OR interview*)) OR 'stages of change' OR (transtheoretical NEXT/2 model*)
- 10 'education program'/de OR 'patient education'/de OR 'patient guidance'/de OR 'patient counseling'/exp OR 'nutritional counseling'/de OR 'counseling'/de OR 'lifestyle modification'/de OR 'self care'/de OR coaching:ti,ab,kw OR counseling:ti,ab,kw OR counselling:ti,ab,kw OR (((education* OR management* OR training) NEXT/3 (intervention* OR program*)):ti,ab,kw) OR (((weight OR nutrition* OR lifestyle OR neuroscience OR sleep* OR diet* OR exercis* OR hydrat*) NEAR/3 (education* OR training* OR coaching OR counseling OR counselling)):ti,ab,kw) OR 'self care':ti,ab,kw OR 'self management':ti,ab,kw OR ((trigger* NEAR/3 avoid*):ti,ab,kw) OR motivation*:ti,ab,kw OR ((goal* NEAR/3 set*):ti,ab,kw) OR diary:ti,ab,kw OR diaries:ti,ab,kw OR journaling:ti,ab,kw OR (((keep* OR record*) NEXT/2 journal*):ti,ab,kw)
- 11 'hypnosis'/de OR (hypnosis OR hypnotherap*):ti,ab,kw
- 12 'eye movement desensitization and reprocessing'/de OR EDMR OR 'eye movement desensiti*' OR (trauma NEXT/3 (informed OR focused)):ti,ab,kw
- 13 'group therapy'/exp OR 'support group'/exp OR ((group OR peer* OR 'self help') NEAR/2 (counseling OR meeting* OR therap* OR support*)):ti,ab,kw OR ((mutual OR community OR peer) NEAR/2 (help OR group* OR meeting* OR 'self help' OR support* OR aided OR led OR assist*)):ti,ab,kw
- 14 'sleep hygiene'/de OR chronotherapy/de OR ((sleep OR insomnia*) NEAR/2 (behav* OR educat* OR habit* OR health OR hygiene OR quality OR specialist* OR therap* OR intervention*)):ti,ab,kw OR (CBTi OR chronotherap*):ti,ab,kw
- 15 bluetooth/mj OR 'e therapy'/mj OR 'internet'/mj OR 'mobile application'/exp OR 'mobile phone'/exp OR 'short message service'/mj OR 'social media'/mj OR 'tablet computer'/mj OR 'teleconsultation'/exp OR 'telehealth'/mj OR 'telemedicine'/mj OR 'telemonitoring'/mj OR 'telephone'/mj OR 'telepsychiatry'/mj OR 'telepsychology'/mj OR 'telepsychotherapy'/mj OR 'teletherapy'/mj OR 'text messaging'/mj OR 'web-based intervention'/mj OR 'wireless communication'/mj OR 'video consultation'/mj OR

- 'videoconferencing'/mj OR bluetooth:ti OR 'blue tooth':ti OR (((distance OR mobile OR remote OR tele* OR virtual) NEAR/3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psychiatr* OR psycholog* OR psychotherap* OR therapy OR visit*)):ti) OR android*:ti OR app:ti OR apps:ti OR asynchronous*:ti OR cellphone*:ti OR 'computer based':ti OR cyber*:ti OR digital:ti OR 'e health*':ti OR ehealth*:ti OR 'e therapy':ti OR etherapy:ti OR facebook:ti OR facetime:ti OR internet:ti OR ipad:ti OR iphone:ti OR 'lap top*':ti OR laptop*:ti OR 'm health*':ti OR mhealth*:ti OR (((mobil* OR portab*) NEXT/1 (computer* OR device* OR health OR tablet*)):ti) OR 'on line':ti OR online:ti OR phone:ti OR phones:ti OR samsung:ti OR 'short messag* service*':ti OR smartphone*:ti OR (((sms OR text) NEXT/2 messag*)):ti OR ((social NEXT/1 (media OR network* OR platform*)):ti) OR software:ti OR synchronous*:ti OR teleconsult*:ti OR telecounsel*:ti OR telehealth*:ti OR telemed*:ti OR telemonitor*:ti OR telephone*:ti OR telepsych*:ti OR teletherapy:ti OR televisit*:ti OR texting*:ti OR video*:ti OR web:ti OR website*:ti OR zoom:ti
- 16 1 AND (2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15)
- 17 16 NOT (([animals]/lim NOT [humans]/lim) OR ((animal OR animals OR canine* OR dog OR dogs OR feline OR hamster* OR lamb OR lambs OR mice OR monkey OR monkeys OR mouse OR murine OR pig OR piglet* OR pigs OR porcine OR primate* OR rabbit* OR rat OR rats OR rodent* OR sheep* OR swine OR veterinar* OR (vitro NOT vivo)) NOT (human* OR patient*)):ti)
- 18 17 NOT ('book'/de OR 'case report'/de OR 'conference paper'/exp OR 'editorial'/de OR 'letter'/de OR (book OR chapter OR conference OR editorial OR letter):it OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [editorial]/lim OR [letter]/lim OR (abstract OR annual OR conference OR congress OR meeting OR proceedings OR sessions OR symposium):nc OR ((book NOT series) OR 'conference proceeding'):pt OR ('case report' OR comment* OR editorial OR letter OR news):ti OR ((protocol AND (study OR trial)) NOT ('therapy protocol*' OR 'treatment protocol*')):ti)
- 19 18 AND [english]/lim
- 20 19 AND (('meta analysis'/exp OR 'systematic review'/de OR cochrane:jt OR [cochrane review]/lim OR systematic*:ti OR (cochrane* OR metaanaly* OR 'meta analy*' OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR 'science direct*' OR sciencedirect* OR scopus* OR systematic* OR 'web of knowledge*' OR 'web of science'))) OR (systematic* NEAR/3 review*)):ti,ab) NOT ((protocol NEXT/3 review) OR 'review protocol'):ti)
- 21 19 AND ('random sample'/de OR 'randomization'/de OR 'randomized controlled trial'/exp OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'major clinical study'/de OR 'phase 3':ti,ab OR 'phase iii':ti,ab OR random*:ti,ab OR rct:ti,ab OR (control* NEAR/3 (trial* OR study OR studies)):ti,ab
- 22 20 OR 21
- 23 22 AND [1975-2023]/py

Embase.com Syntax

**** = truncation***

/exp = explode to include all terms in the tree

/mj = limit to terms indexed as major concepts

/de = search term without exploding

:ti = search in the title field

:kw = search in the author keywords field

:ab = search in the abstract field

NEAR/# - search the terms within # of each other in any order

NEXT/# - search terms within # of each other in the specified order.

PubMed (In Process Citations): January 1, 2011 through January 6, 2022

- 1 Migrain*[tiab] OR headache*[ti]
- 2 'drug free'[ti] OR non-drug[ti] OR nondrug[ti] OR non-pharmacologic*[ti] OR nonpharmacologic*[ti] OR collaborative[ti] OR 'inter disciplinary'[ti] OR interdisciplinary[ti] OR 'multi disciplinary'[ti] OR multidisciplinary[ti] OR psych*[ti] OR behav*[ti] OR cognitive[ti]
- 3 Psychotherap*[tiab] OR psychologist*[ti] OR "behavior therap*" OR "behaviour therap*" OR "cognitive behavior*" OR "cognitive behaviour*" OR "cognitive therap*" OR "stress manage*" OR "managing stress"[tiab:~3] OR "problem solving"[tiab:~3] OR "problem focused"[tiab] OR cope[ti] OR coping[ti] OR stress[ti] OR trigger*[ti] OR ((behav*[ti] OR cognitive[ti]) AND (intervention*[ti] OR modif*[ti] OR therap*[ti] OR treatment*[ti] OR manage[ti])) OR ((caregiver*[ti] OR mother*[ti] OR father*[ti] OR parent*[ti]) AND (behav*[ti] OR counsel*[ti] OR educat*[ti] OR intervention*[ti] OR mediated[ti] OR support*[ti] OR train*[ti] OR operant*[ti] OR therapy[ti])) OR "parent child interaction therapy" OR PCIT[tiab] OR "supportive care"[tiab]
- 4 biofeedback[tiab] OR "bio feedback"[tiab] OR neurofeedback[tiab] OR "neuro feedback"[tiab] OR neurobiofeedback*[tiab] OR neurotherap*[tiab] OR Handwarming[tiab] OR "hand warming"[tiab] OR (feedback[tiab] AND (thermal[tiab] OR temperature[tiab] OR EMG[tiab] OR electromyograph*[tiab] OR "heart rate"[tiab] OR electrocardiogra*[tiab] OR pulse[tiab] OR "blood volume"[tiab] OR respiratory[tiab] OR respiration[tiab] OR breathing[tiab] OR electroencephalogra*[tiab] OR EEG[tiab] OR ECG[tiab] OR BVP[tiab])) OR "finger* temperature*" [tiab] OR "skin conduct*" [tiab] OR "finger temperature"[tiab:~3] OR "skin conductance"[tiab:~3]
- 5 "autogenic feedback"[tiab:~3] OR "autogenic training"[tiab:~3] OR "autogenic exercise*" [tiab] OR relaxation[tiab] OR breathing[ti] OR "breathing exercise*" [tiab] OR "deep breathing"[tiab] OR "guided breath*" [tiab] OR "muscle relaxation"[tiab:~3] OR "diaphragm* breath*" [tiab] OR "pace* breath*" [tiab] OR "belly breath*" [tiab] OR "guided imagery"[tiab:~3]
- 6 mindfulness*[tiab] OR "mind body"[tiab] OR MBSR[tiab] OR MBCT[tiab] OR meditat*[tiab]
- 7 "acceptance commitment"[tiab:~3]
- 8 "dialectical behavior therapy"[tiab] OR "dialectical behaviour therapy"[tiab] OR "dialectical behavioral therapy"[tiab] OR "dialectical behavioural therapy"[tiab]
- 9 "motivational interview*" [tiab] OR "motivational enhance*" [tiab] OR "stages of change"[tiab] OR "transtheoretical model*" [tiab]
- 10 Coaching[tiab] OR (counseling[tiab] NOT "genetic counseling"[tiab]) OR (counselling[tiab] NOT "genetic counselling"[tiab]) OR education[ti] OR training[ti] OR ((weight[tiab] OR nutrition*[tiab] OR lifestyle[tiab] OR neuroscience[tiab] OR sleep*[tiab] OR diet*[tiab] OR exercise*[tiab] OR hydrat*[tiab]) AND (education*[tiab]

- OR training[tiab] OR coaching[tiab] OR counseling[tiab] OR counselling[tiab])) OR "self care"[tiab] OR "self manag*"[tiab] OR (trigger*[tiab] AND avoid*[tiab]) OR motivation[tiab] OR "goal setting" OR diary[tiab] OR diaries[tiab] OR journaling[tiab] OR "keep journal"[tiab:~3] OR "record journal"[tiab:~3]
- 11 Hypnosis[tiab] OR hypnotherap*[tiab]
- 12 EDMR[tiab] OR "eye movement desensiti*"[tiab] OR "trauma informed"[tiab:~3] OR "trauma focused"[tiab:~3] OR trauma*[ti]
- 13 "group therap*"[tiab] OR "group counsel*"[tiab] OR "support group*"[tiab] OR "group support*"[tiab] OR ((peer*[tiab] OR community[tiab] OR mutual[tiab]) AND (counsel*[tiab] OR therapy[tiab] OR support[tiab]))
- 14 chronotherapy[tiab] OR "sleep hygiene"[tiab] OR "sleep habit*"[tiab] OR ((sleep[ti] OR insomnia*[ti]) AND (behav*[ti] OR education[ti] OR habit*[ti] OR health[ti] OR hygiene[ti] OR quality[ti] OR specialist*[ti] OR therapy[ti] OR intervention*[ti])) OR "CBTi"[tiab] OR "CBT I"[tiab]
- 15 "e therapy"[tiab] OR "internet"[tiab] OR "mobile application"/exp OR "mobile phone"/exp OR "short message service"[tiab] OR "social media"[tiab] OR "tablet computer"[tiab] OR "teleconsultation"/exp OR "telehealth"[tiab] OR "telemedicine"[tiab] OR "telemonitoring"[tiab] OR "telephone"[tiab] OR "telepsychiatry"[tiab] OR "telepsychology"[tiab] OR "telepsychotherapy"[tiab] OR "teletherapy"[tiab] OR "text messaging"[tiab] OR "web-based intervention"[tiab] OR "wireless communication"[tiab] OR "video consultation"[tiab] OR "videoconferencing"[tiab] OR ((distance[ti] OR mobile[ti] OR remote[ti] OR tele[ti] OR virtual[ti]) AND (care[ti] OR counseling[ti] OR counselor*[ti] OR consult*[ti] OR health[ti] OR medical[ti] OR medicine[ti] OR monitor*[ti] OR psychiatr*[ti] OR psychologist*[ti] OR psychotherap*[ti] OR therapy[ti] OR visit*[ti])) OR android*[ti] OR app[ti] OR apps[ti] OR asynchronous*[ti] OR bluetooth[ti] OR "blue tooth"[ti] OR cellphone*[ti] OR "computer based"[ti] OR cyber*[ti] OR digital[ti] OR "e health*"[ti] OR ehealth*[ti] OR "e therapy"[ti] OR etherapy[ti] OR facebook[ti] OR facetime[ti] OR internet[ti] OR ipad[ti] OR iphone[ti] OR "lap top*"[ti] OR laptop*[ti] OR "m health*"[ti] OR mhealth*[ti] OR ((mobil*[ti] OR portab*[ti]) AND (computer*[ti] OR device*[ti] OR health[ti] OR tablet*[ti])) OR "on line"[ti] OR online[ti] OR phone[ti] OR phones[ti] OR samsung[ti] OR "short messag*"[ti] OR smartphone*[ti] OR ((sms[ti] OR text[ti]) AND messag*[ti]) OR "social media"[tiab] OR software[ti] OR synchronous*[ti] OR teleconsult*[ti] OR telecounsel*[ti] OR telehealth*[ti] OR telemed*[ti] OR telemonitor*[ti] OR telephone*[ti] OR telepsych*[ti] OR teletherapy[ti] OR televisit*[ti] OR texting*[ti] OR video*[ti] OR web[ti] OR website*[ti] OR zoom[ti]
- 16 1 AND (2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15)
- 17 16 NOT ((animal[ti] OR animals[ti] OR canine*[ti] OR dog[ti] OR dogs[ti] OR feline[ti] OR hamster*[ti] OR lamb[ti] OR lambs[ti] OR mice[ti] OR monkey[ti] OR monkeys[ti] OR mouse[ti] OR murine[ti] OR pig[ti] OR piglet*[ti] OR pigs[ti] OR porcine[ti] OR primate*[ti] OR rabbit*[ti] OR rat[ti] OR rats[ti] OR rodent*[ti] OR sheep*[ti] OR swine[ti] OR veterinar*[ti]) NOT (human*[ti] OR patient*[ti]))
- 18 17 NOT (booksdocs[Filter] OR "case reports"[pt] OR comment[pt] OR congress[pt] OR editorial[pt] OR letter[pt] OR "case report"[ti] OR comment*[ti] OR editorial[ti] OR

- letter[ti] OR news[ti] OR ((protocol[ti] AND (study[ti] OR trial[ti])) NOT ("therapy protocol"[ti] OR "treatment protocol"[ti]))
- 19 18 AND ((meta-analysis[pt] OR "systematic review"[pt] OR "cochrane database syst rev"[ta] OR systematic*[ti] OR cochrane*[tiab] OR "meta analy*[tiab] OR metaanaly*[tiab] OR (search*[tiab] AND (cinahl*[tiab] OR databases[tiab] OR ebSCO*[tiab] OR embase*[tiab] OR psychinfo*[tiab] OR psycinfo*[tiab] OR "science direct*[tiab] OR sciencedirect*[tiab] OR scopus*[tiab] OR systematic*[tiab] OR "web of knowledge*[tiab] OR "web of science*[tiab])) OR (systematic*[tiab] AND review*[tiab])) NOT ((protocol[ti] AND review[ti]) OR "review protocol"[ti] OR "scoping review"[ti]))
- 20 18 AND (random allocation[mh] OR "randomized controlled trial"[pt] OR "phase 3"[tiab] OR "phase iii"[tiab] OR random*[tiab] OR RCT[tiab] OR "clinical trial"[tiab] OR "clinical study"[tiab] OR "controlled trial"[tiab] OR "controlled study"[tiab])
- 21 19 OR 20
- 22 21 AND (inprocess[SB] OR publisher[SB] OR pubmednotmedline[SB])
- 23 22 AND english[la]

PubMed Syntax

*** = truncation**

[ti] = search in the title field

[tiab] = search in the title and abstract

[la] = search in the language field

[sb] = subset

PsycINFO: 1987 to January 11, 2023 (Note: database does not include records prior to 1987)

- 1 "migraine headache"/ OR migrain*.ti,ab. OR headache*.ti.
- 2 ("drug free" OR non-drug OR nondrug OR non-pharmacologic* OR nonpharmacologic* OR collaborative OR "inter disciplinary" OR interdisciplinary OR "multi disciplinary" OR multidisciplinary OR psych* OR behav* OR cognitive).ti.
- 3 exp psychotherapy/ OR exp "behavior modification"/ OR exp "cognitive behavior therapy"/ OR exp cognitive therapy/ OR exp "cognitive restructuring"/ OR "stress management"/ OR exp "coping behavior"/ OR "parent training"/ OR "family intervention"/ OR exp "parent child communication"/ OR "problem solving"/ OR ((behav* OR cognitive) ADJ2 (intervention* OR modif* OR therap* OR treatment*)).ti,ab. OR (manag* ADJ2 stress).ti,ab. OR coping.ti,ab. OR (cope ADJ3 trigger*).ti,ab. OR ((caregiver* OR mother* OR father* OR parent*) ADJ4 (behav* OR counsel* OR educat* OR intervention* OR mediated OR support* OR train* OR operant* OR therapy)).ti,ab. OR ('parent child interaction therapy' OR PCIT OR 'supportive care').ti,ab. OR (problem ADJ3 (solving OR coping)).ti,ab. OR psychotherap*.ti,ab.
- 4 exp Biofeedback Training/ or exp Biofeedback/ OR neurotherapy/ OR (biofeedback OR 'bio feedback' OR neurofeedback OR 'neuro feedback' OR neurobiofeedback* OR neurotherapy*).ti,ab. OR (Handwarming OR 'hand warming').ti,ab. OR (feedback ADJ5 (thermal OR temperature OR EMG OR electromyograph* OR "heart rate" OR electrocardiogra* OR pulse OR "blood volume" OR respiratory OR respiration OR

- breathing OR electroencephalogra* OR EEG OR ECG OR BVP)).ti,ab. OR (finger* ADJ3 temp*).ti,ab. OR (skin ADJ3 conduct*).ti,ab.
- 5 exp Relaxation/ or exp "relaxation therapy"/ or "muscle relaxation"/ or "guided imagery"/ OR "autogenic training"/ or (Autogenic ADJ3 (feedback or training or exercise)).ti,ab. or ('AFTE' or 'progressive muscle relaxation').ti,ab. or (relaxation ADJ2 (techniques or therapy or training)).ti,ab. or breathing.ti. or relaxation.ti,ab. or (Breathing ADJ4 (exercise* or deep or guided OR diaphragm* OR paced OR belly)).ti,ab. OR ((guided OR visual) ADJ3 imagery).ti,ab.
- 6 meditation/ OR mindfulness/ OR "mindfulness- based interventions"/ OR mind body therapy/ OR (mindfulness* OR 'mind body' OR MBSR OR MBCT OR meditat* OR (guided ADJ3 imagery)).ti,ab.
- 7 exp "Acceptance and Commitment Therapy"/ OR (acceptance ADJ2 commitment)
- 8 exp "dialectical behavior therapy"/ OR "dialectical behav* therap*"
- 9 motivational interviewing/ OR "Stages of Change"/ OR (motivational ADJ2 (enhancement OR interview*)).ti,ab. OR "stages of change".ti,ab. OR (transtheoretical ADJ2 model*).ti,ab.
- 10 "client education"/ OR exp "educational programs"/ OR counseling/ OR "educational counseling"/ OR "psychotherapeutic counseling"/ OR "lifestyle changes"/ OR exp "self-help techniques"/ OR exp "Self-Care"/ OR "journal writing"/ OR (coaching OR counseling OR counselling OR ((education* OR management* OR training) ADJ3 (intervention* OR program*)) OR ((weight OR nutrition* OR lifestyle OR neuroscience OR sleep* OR diet* OR exercis*) ADJ3 (education* OR training* OR coaching OR counseling)) OR "self care" OR "self management" OR (trigger* ADJ3 avoid*) OR motivation OR (goal* ADJ3 set*) OR (diary OR diaries OR journal*)).ti,ab.
- 11 exp Hypnosis/ OR exp hypnotherapy/ OR (hypnosis OR hypnotherap*).ti,ab.
- 12 eye movement desensitization therapy/ OR (EDMR OR "eye movement desensiti*" OR (trauma ADJ3 (informed OR focused))).ti,ab.
- 13 exp Group Psychotherapy/ OR support groups/ or group counseling/ OR (((group OR peer* OR "self help") ADJ2 (counseling OR meeting* OR therap* OR support*)) OR ((mutual OR community OR peer) ADJ2 (help OR group* OR meeting* OR "self help" OR support* OR aid OR led OR assist*))).ti,ab.
- 14 sleep quality/ OR chronotherapy OR (((sleep OR insomnia*) ADJ2 (behav* OR educat* OR habit* OR hygiene OR quality OR specialist* OR therapy OR intervention* OR health*)) OR CBTi).ti,ab.
- 15 *asynchronous learning/ OR exp *Computer Assisted Instruction/ OR *computer mediated communication/ OR *digital interventions/ OR *Internet/ OR *Mobile Health/ OR exp *Online Therapy/ OR exp *Telemedicine/ OR *teleconsultation/ OR exp *telepsychology/ OR *internet/ OR *telerehabilitation/ OR *online therapy/ OR exp *websites/ OR *wireless technologies/ OR *text messaging/ OR exp *mobile devices/ OR exp *mobile phones/ OR *smartphones/ OR exp *Videoconferencing/ OR (((distance OR mobile OR remote OR tele* OR virtual) ADJ3 (care OR counseling OR counselor* OR consult* OR health OR medical OR medicine OR monitor* OR psychiatr* OR psycholog* OR psychotherap* OR therapy OR visit*))).ti.) OR android*.ti. OR app.ti. OR apps.ti. OR asynchronous*.ti. OR Bluetooth*.ti. OR cellphone*.ti. OR "computer based".ti. OR cyber*.ti. OR digital.ti. OR "e health*".ti. OR ehealth*.ti. OR "e therapy".ti. OR etherapy.ti. OR facebook.ti. OR facetime.ti. OR internet.ti. OR ipad.ti.

- OR iphone.ti. OR "lap top*".ti. OR laptop*.ti. OR "m health*".ti. OR mhealth*.ti. OR (((mobil* OR portab*) ADJ1 (computer* OR device* OR health OR tablet*)).ti.) OR "on line".ti. OR online.ti. OR phone.ti. OR phones.ti. OR samsung.ti. OR "short messag* service*".ti. OR smartphone*.ti. OR (((sms OR text) ADJ2 messag*).ti.) OR ((social ADJ1 (media OR network* OR platform*)).ti.) OR software.ti. OR synchronous*.ti. OR teleconsult*.ti. OR telecounsel*.ti. OR telehealth*.ti. OR telemed*.ti. OR telemonitor*.ti. OR telephone*.ti. OR telepsych*.ti. OR teletherapy.ti. OR televisit*.ti. OR texting*.ti. OR video*.ti. OR web.ti. OR website*.ti. OR zoom.ti.
- 16 1 AND (2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15)
- 17 16 NOT (animals/ OR animal models/ OR ((animal OR animals OR canine* OR dog OR dogs OR feline OR hamster* OR lamb OR lambs OR mice OR monkey OR monkeys OR mouse OR murine OR pig OR piglet* OR pigs OR porcine OR primate* OR rabbit* OR rat OR rats OR rodent* OR sheep* OR swine OR veterinar* OR (vitro not vivo)) NOT (human* OR patient*)).ti.)
- 18 17 NOT ((chapter OR "column/opinion" OR "comment/reply" OR dissertation OR editorial OR letter OR review-book).dt. OR (book OR encyclopedia OR "dissertation abstract").pt. OR ("case report" OR comment* OR editorial OR letter OR news).ti. OR ((protocol AND (study OR trial)) NOT ("therapy protocol*" OR "treatment protocol*")).ti.)
- 19 limit 18 to english language
- 20 19 NOT (1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*).pm.
- 21 20 AND (((meta analysis OR systematic review).md. OR meta analysis/ OR systematic review/ OR systematic.ti. OR (cochrane* OR meta analy* OR metaanaly* OR (search* AND (cinahl* OR databases OR ebsco* OR embase* OR psychinfo* OR psycinfo* OR science direct* OR sciencedirect* OR scopus* OR systematic* OR "web of knowledge*" OR "web of science*"))) OR (review* ADJ3 systematic*) OR (systematic* ADJ3 review*)).ti,ab.) NOT ((protocol ADJ3 review) OR review protocol OR scoping review).ti.)
- 22 20 AND (exp randomized controlled trials/ OR random sampling/ OR *Clinical Trials*/ OR (phase 3 OR phase iii or random* OR RCT OR (*control* ADJ3 (trial* or study or studies)*))).ti,ab.)
- 23 21 OR 22

PsycINFO Syntax

**** = truncation***

/= controlled vocabulary

exp = explode to include all terms in the tree

.ti. = search in the title field

.ti,ab. = search in the title and abstract field

.pm. = search in PubMed id field (to identify records that are also included in Medline/PubMed)

ADJ# - search the terms within # of each other in any order

Cochrane Library (Cochrane Database of Systematic Reviews): Inception through January 11, 2023

1 migrain*:ti,ab,kw OR headache*:ti

Cochrane Library Syntax

**** = truncation***

:ti = search in the title field

:ti,ab,kw= search in the title, abstract, and keyword field

ClinicalTrials.gov: March 6, 2023

Advanced Search:

Disease field: Migraine

Intervention field: behavior OR education OR psych OR cognitive OR biofeedback OR neurobiofeedback OR feedback OR meditat OR relax OR device OR mind OR breath OR accept OR commit OR dialect OR motivat OR eye OR sleep OR anxious OR anxiety OR insomnia OR depress OR telehealth OR virtual OR application OR smartphone OR computer OR mhealth OR mobile OR ehealth

Limit to: ongoing trials (Not yet recruiting, recruiting, enrolling by invitation, active (not recruiting))

Appendix B. Excluded Publications

Table B-1. Excluded publications

Reference	Exclusion Reason
Abram Harry 2007 ¹	Does not meet population criteria
Altieri 2009 ²	Does not meet study design criteria
Anderson 1975 ³	Does not evaluate a comparison of interest
Andersson 2003 ⁴	Does not evaluate a comparison of interest
Arina 2022 ⁵	Does not meet population criteria
Azam 2016 ⁶	Does not meet population criteria
Bakhshani 2015 ⁷	Does not meet setting criteria
Balottin 2014 ⁸	Does not meet population criteria
Barry 1997 ⁹	Does not meet population criteria
Basler 1996 ¹⁰	Does not meet population criteria
Bekkelund 2021 ¹¹	Does not meet population criteria
Blanchard 1990 ¹²	Does not evaluate key outcomes of interest
Blanchard 1990 ¹³	Does not evaluate key outcomes of interest
Blanchard 1991 ¹⁴	Does not evaluate key outcomes of interest
Blanchard 1997 ¹⁵	Does not evaluate key outcomes of interest
Bruhn 1979 ¹⁶	Does not meet population criteria
Carlsen 2020 ¹⁷	Does not evaluate a comparison of interest
Cooper 2017 ¹⁸	Does not meet population criteria
Crawford 2020 ¹⁹	Does not evaluate a comparison of interest
Devineni 2005 ²⁰	Does not meet population criteria
Dodick 2005 ²¹	Unable to obtain record
Dowd 2015 ²²	Does not meet population criteria
Eppley 1996 ²³	Does not evaluate a comparison of interest
Feuille 2015 ²⁴	Does not meet minimum follow-up criteria
Fichtel 2004 ²⁵	Does not meet population criteria
Fox 2011 ²⁶	Does not meet population criteria
Friedman 1984 ²⁷	Fewer than 10 patients/arm
Friedman 2019 ²⁸	Does not evaluate a comparison of interest
Gauthier 1981 ²⁹	Fewer than 10 patients/arm
Gauthier 1983 ³⁰	Fewer than 10 patients/arm
Grazzi 2022 ³¹	Does not meet setting criteria
Grazzi 2023 ³²	Does not evaluate a comparison of interest
Griffiths 1996 ³³	Does not meet population criteria
Hagen 2011 ³⁴	Does not meet population criteria
Hart 1984 ³⁵	Does not meet population criteria
Hasan 2023 ³⁶	Does not meet population criteria

Reference	Exclusion Reason
Heriseanu 2023 ³⁷	Does not meet population criteria
Hickman 2015 ³⁸	Does not meet population criteria
Holroyd 1989 ³⁹	Does not evaluate a comparison of interest
Holroyd 1995 ⁴⁰	Does not evaluate a comparison of interest
Ilacqua 1994 ⁴¹	Does not meet minimum follow-up criteria
Jaramillo Guerrero 2022 ⁴²	Not published in English
Jong 2019 ⁴³	Does not meet population criteria
Junker 2004 ⁴⁴	Does not meet study design criteria
Kang 2009 ⁴⁵	Does not evaluate key outcomes of interest
Kaushik 2005 ⁴⁶	Does not meet setting criteria
Khazraee 2023 ⁴⁷	Does not meet setting criteria
Kjeldgaard 2014 ⁴⁸	Does not meet population criteria
Kraft 2008 ⁴⁹	Does not evaluate key outcomes of interest
Kroener-Herwig 2002 ⁵⁰	Does not meet population criteria
Kroner-Herwig 1993 ⁵¹	Does not evaluate key outcomes of interest
Kroner-Herwig 1998 ⁵²	Does not meet population criteria
Lake 1979 ⁵³	Fewer than 10 patients/arm
Largen 1981 ⁵⁴	Fewer than 10 patients/arm
Larsson 1986 ⁵⁵	Does not meet population criteria
Larsson 1987 ⁵⁶	Does not meet population criteria
Larsson 1987 ⁵⁷	Does not meet population criteria
Larsson 1990 ⁵⁸	Does not meet population criteria
Larsson 2005 ⁵⁹	Does not meet population criteria
Launso 1999 ⁶⁰	Does not evaluate a comparison of interest
Law 2015 ⁶¹	Does not meet population criteria
Law 2020 ⁶²	Does not evaluate key outcomes of interest
Lipton 2011 ⁶³	Does not meet study design criteria
Llaneza-Ramos 1989 ⁶⁴	Does not meet population criteria
Mahmoudzadeh 2016 ⁶⁵	Does not meet setting criteria
Majore-Dusele 2021 ⁶⁶	Does not evaluate a comparison of interest
Mansourishad 2017 ⁶⁷	Does not meet setting criteria
Martin 2007 ⁶⁸	Does not meet population criteria
Martin 2014 ⁶⁹	Does not meet population criteria
Martin 2014 ⁷⁰	Does not meet population criteria
Martin 2015 ⁷¹	Does not meet population criteria
Martin 2017 ⁷²	Does not meet population criteria
Martin 2021 ⁷³	Does not meet population criteria
McGeary 2022 ⁷⁴	Does not meet population criteria
McGrady 1994 ⁷⁵	Does not evaluate key outcomes of interest

Reference	Exclusion Reason
McGrath 1988 ⁷⁶	Does not evaluate key outcomes of interest
McGrath 1992 ⁷⁷	Does not evaluate key outcomes of interest
Meise 2023 ⁷⁸	Does not evaluate a comparison of interest
Meyer 2016 ⁷⁹	Does not meet study design criteria
Minen 2020 ⁸⁰	Does not evaluate key outcomes of interest
Mongini 2008 ⁸¹	Does not meet population criteria
Mongini 2009 ⁸²	Does not meet population criteria
Mongini 2012 ⁸³	Does not meet population criteria
Mose 2020 ⁸⁴	Does not meet population criteria
Mose 2022 ⁸⁵	Does not meet population criteria
Moyes 2023 ⁸⁶	Fewer than 10 patients/arm
Mullally 2009 ⁸⁷	Does not meet population criteria
Müller 2016 ⁸⁸	Does not evaluate a comparison of interest
Müller 2017 ⁸⁹	Does not evaluate a comparison of interest
Müller 2017 ⁹⁰	Does not meet population criteria
Müller 2017 ⁹¹	Does not evaluate a comparison of interest
Nabity 2021 ⁹²	Does not meet population criteria
Nabity 2023 ⁹³	Does not evaluate a comparison of interest
Palermo 2009 ⁹⁴	Does not meet population criteria
Pazmiño 2022 ⁹⁵	Does not meet setting criteria
Pijpers 2019 ⁹⁶	Does not evaluate a comparison of interest
Pijpers 2022 ⁹⁷	Does not evaluate a comparison of interest
Rahimi 2022 ⁹⁸	Does not meet setting criteria
Rota 2011 ⁹⁹	Does not meet study design criteria
Sciamanna 2006 ¹⁰⁰	Does not evaluate a comparison of interest
Shagbazyan 2021 ¹⁰¹	Not published in English
Silberstein 2006 ¹⁰²	Not published as a full-length article
Siniatchkin 2011 ¹⁰³	Does not meet study design criteria
Slavin 2013 ¹⁰⁴	Does not meet population criteria
Smelt 2012 ¹⁰⁵	Does not evaluate a comparison of interest
Solbach 1989 ¹⁰⁶	Does not meet population criteria
Soleimanian 2022 ¹⁰⁷	Does not meet setting criteria
Sovak 1981 ¹⁰⁸	Does not evaluate key outcomes of interest
Sprouse 2013 ¹⁰⁹	Does not evaluate a comparison of interest
Stevens 2014 ¹¹⁰	Does not meet population criteria
Ström 2000 ¹¹¹	Does not meet population criteria
Taylor 2014 ¹¹²	Does not meet study design criteria
Ter Kuile 1994 ¹¹³	Does not meet population criteria
Terkuile 1996 ¹¹⁴	Does not meet population criteria

Reference	Exclusion Reason
Thorn 2007 ¹¹⁵	Does not evaluate a comparison of interest
Trautmann 2008 ¹¹⁶	Does not meet population criteria
Trautmann 2010 ¹¹⁷	Does not meet population criteria
Trinka 2002 ¹¹⁸	Does not evaluate a comparison of interest
Vasudeva 2003 ¹¹⁹	Does not evaluate key outcomes of interest
Walach 1997 ¹²⁰	Does not evaluate a comparison of interest
Walter 2020 ¹²¹	Does not meet population criteria
Wang 2005 ¹²²	Not published in English
Wauquier 1995 ¹²³	Does not evaluate key outcomes of interest
Wells 2014 ¹²⁴	Fewer than 10 patients/arm
Winkler 1989 ¹²⁵	Does not meet population criteria
Wisniewski 1988 ¹²⁶	Fewer than 10 patients/arm
Woldeamanuel 2021 ¹²⁷	Does not meet population criteria

Appendix C. Evidence Tables

Table C-1. Study details and patient characteristics

Study Details	Patient Characteristics	Migraine Characteristics
<p>Aguirrezabal 2019¹²⁸ Design: RCT Country: Spain Purpose: To assess the effectiveness of a primary care-based group educational intervention about concepts of pain neuroscience for the management of migraine compared to the routine medical care delivered to patients with this condition, compared to routine medical care. Funding: None Included for: KQ1</p>	<p>Number of participants: 116 randomized Age (years): Category, %: 21-30, 8.8%; 31-40 21.1%; 41-50, 31.6%; 51-60 38.6% Gender (% female): 81.9 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Primary care Inclusion criteria: Diagnosed with migraine (ICD-9-CM Diagnosis Code 346) who had at least one migraine attack per month despite treatment. Exclusion criteria: Patients with mental illness, cognitive impairment or those with difficulties to understand the Spanish language were excluded. Patients that could not attend all sessions of the intervention or had received training as part of the previous pilot study were also excluded.</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICD-9-CM Diagnosis Code 346 Method for establishing baseline frequency: In-person interview about the previous 3 months Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Albers 2015¹²⁹ (MUKIS) Registration: DRKS00003308 Design: Cluster RCT Country: Germany Purpose: to assess the effectiveness of a low-level headache prevention program in the classroom setting to prevent these risk factors. Funding: unrestricted fund of the DMKG (German Headache Society) Included for: KQ1</p>	<p>Number of participants: 1674 randomized; 900 at baseline Age (years): Range 12 to 19 Gender (% female): 59.8 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Schools Inclusion criteria: Participants were restricted to students in the 8th, 9th and 10th grades who answered "yes" to the question 'Did you experience headache within the last 7 days, 3 months or 6 months?' Exclusion criteria: NR</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Questionnaire on recent headache experience Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Allen 1998¹³⁰ Design: RCT Country: USA Purpose: " to evaluate the efficacy of parent-mediated pain behavior management strategies implemented by parents of children undergoing biofeedback treatment for migraine headache. " Funding: This manuscript was supported in part by grant MCJ 319152 from the Maternal and Child Health Bureau, Health Resources Services Administration, and by grant 90 DD 032402 of the Administration on Developmental Disabilities Included for: KQ3</p>	<p>Number of participants: 27 randomized Age (years): Mean 12.2 Gender (% female): 59.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Home and clinic Inclusion criteria: "each child had to have received a diagnosis of migraine headache by their family physician and meet the appropriate diagnostic criteria (as determined by the investigators) for migraine headache based on the criteria established by the International Headache Society (Headache Classification Committee, 1988). Inclusion criteria also included at least 2 migraine headaches a month with a minimum 6-month history of headache activity and stable or increasing headache activity during baseline recording. " Exclusion criteria: NR</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 4.4 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Blanchard 1978^{131,132} Design: RCT Country: USA Purpose: To assess effect of biofeedback training for migraine headaches with adequate controls. Funding: NR Included for: KQ1, KQ2</p>	<p>Number of participants: 37 randomized Age (years): Mean 38.7 Gender (% female): 67.6 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Psychology department Inclusion criteria: "At least 2 migraine headaches per month and meet 3 of 5 following criteria: 1) headaches were predominantly 1 sided; 2) headaches usually accompanied by nausea or vomiting; 3) sensitivity to light 4) positive family history for migraine headaches 5) independent diagnosis by personal physician of migraine or vascular headache." Patients with a mixture of migraine and muscular contraction headache symptoms were included if they could identify 2 migraine headaches per month. Exclusion criteria: "Patients who described their headaches predominantly as 1) occurring almost daily 2) feeling 'like a band around their head and usually bilateral or 3) as a 'dull ache' were excluded"</p>	<p>Migraine type: NR Migraine diagnosis criteria: Independent diagnosis by personal physician of migraine or vascular headache Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: Participants with migraine + tension type headaches were allowed Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Bromberg 2012¹³³ Design: RCT Country: USA Purpose: "Test the clinical efficacy of a web-based intervention designed to increase patient self-efficacy to perform headache self-management activities and symptom management strategies; and reduce migraine-related psychological distress." Funding: Grant support was received from the National Institutes of Health (NIH), the National Institute of Drug Abuse (NIDA No. R44DA023539-02) Included for: KQ1, KQ1a</p>	<p>Number of participants: 189 randomized Age (years): Mean 42.6 Gender (% female): 87.3 Race: 85.2% White, 4.8% Black/African American, 2.1% Asian, 0.5% Native Hawaiian/Other Pacific Islander, 4.8% Other Ethnicity: 2.1% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: Online Inclusion criteria: "Volunteers were eligible for the study if: (1) they were between ages 18–65; (2) they met ICHD-II diagnostic criteria for migraine, with or without aura; (3) their migraines had been present for at least one year; (4) they experienced at least 48 continuous hours of freedom from headache or migraine per month; (5) their age of onset of migraine was less than 50 years; (6) they were able to provide informed consent; (7) they had a migraine at least twice a month; (8) they had daily Internet access with email; and (9) they completed the Daily Headache Record for a minimum of 5 out of 14 days during a 'run-in' period.</p> <p>To validate whether participants met ICHD-II criteria for migraine, all volunteers were first asked: 'Has a doctor diagnosed you with migraine?' Those responding 'no' were screened out. Volunteers who responded 'yes' were screened in, and were then asked through a structured interview conducted by the Research Coordinator, a migraine-specific set of questions corresponding to ICHD criteria. If the Research Coordinator had any questions about the volunteer's responses, these were reviewed on a case-by-case basis with a board certified physician and pain management specialist, before a volunteer was included or excluded from the study. Volunteers who met ICHD-II criteria we included in the study and those not meeting criteria were screened out."</p> <p>Exclusion criteria: "Exclusion criteria were: (1) endorsement of questions indicating that migraine may be indicative of a progressive disease; (2) presence of fibromyalgia or epilepsy; (3) experiencing non-migraine headaches more than six days per month; (4) participants completing less than four entries during the 'run-in' period (explained below); and (5) non-English speaking."</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (2-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Brown 1984¹³⁴ Design: RCT Country: Canada Purpose: Examine the efficacy of two types of imaginal strategy treatments relative to a placebo control group on cold pressor pain and migrain Funding: Carleton University Included for: KQ1, KQ2</p>	<p>Number of participants: 39 randomized Age (years): Mean 38 Gender (% female): 89.7 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Only respondents who reported a regular occurrence of four or more headaches per month, with at least two of the following symptoms associated with their headaches: nausea, vomiting, pulsatile head pain, unilateral onset and sensory prodromata were selected for inclusion in the study. All participants had been previously diagnosed as having migraine by their physician or neurologist. Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Calhoun 2007¹³⁵ Design: RCT Country: USA Purpose: assess the impact of CBT on transformed migraine Funding: National Headache Foundation Included for: KQ4</p>	<p>Number of participants: 43 randomized Age (years): Mean 34.2 Gender (% female): 100 Race: NR Ethnicity: NR Non-headache co-morbidities (%): 39.5% Anxiety, 39.5% Depression Setting: Neurology/Headache clinic Inclusion criteria: nonpregnant, nonlactating adult females with "transformed migraine" diagnosed in accordance with criteria proposed by Silberstein et al 1996 (revised IHS criteria) and no diagnosis of a primary sleep disorder. Headache diagnosis was established or confirmed by a headache specialist at our facility Exclusion criteria: NR</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Patient memory Duration of migraine or headache (years): 10.8 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Connelly 2006¹³⁶ (Headstrong) Design: RCT Country: USA Purpose: "to test a minimal therapist contact treatment for recurrent pediatric headache by using the CD-ROM as a medium for delivering empirically-supported psychological interventions." Funding: This research was supported in part by an educational grant from AstraZeneca LP. The authors wish to acknowledge the late Marilyn Duke-Woodside, MD, and the staff at Children's Mercy Hospital in Kansas City, MO, for their assistance in the recruitment of participants for this study. Included for: KQ1, KQ1a</p>	<p>Number of participants: 37 randomized Age (years): Mean 10 Gender (% female): 48.6 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "Patients were recruited who had clinical diagnosis by a neurologist of a nonmalignant recurrent headache syndrome (migraine with or without aura and tension-type, including chronic migraine and chronic tension-type headache) based on revised International Headache Association classification standards for pediatric headache. Headaches had to occur at an average frequency of at least four times monthly per caregiver or child report and be separated by symptom-free periods. Children were deemed otherwise healthy by means of a medical history, physical examination, and vital-sign measurement." Exclusion criteria: "Exclusion criteria were history of seizure, significant developmental delay per parent report, or psychological impairments determined through interview by psychology research staff to have impeded ability to complete study requirements (e.g., clinical depression). Children having concurrent chronic or acute illness or taking other medication that might confound headache ratings were excluded. Children who were non Englishspeaking were also excluded from participation."</p>	<p>Migraine type: Mixed (75.7% Episodic, 24.3% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (2-week period) Duration of migraine or headache (years): 2.3 Co-morbid headache disorders: NR Non-migraine participants included: NR</p>
<p>Cottrell 2007¹³⁷ Design: RCT Country: USA Purpose: Examine the feasibility and acceptability of administering behavioral migraine management training by telephone to adolescents with episodic migraine Funding: NIH Included for: KQ1, KQ1a</p>	<p>Number of participants: 34 randomized; 30 at baseline Age (years): Mean 14.1 Gender (% female): 50 Race: 86.7% White Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Age 12 to 17 years, and diagnosis of migraine (with or without aura) by the project neurologist based on International Headache Society (IHS) criteria adjusted for adolescents. Participants were required to average between 2 and 6 migraines per month (based on self-report and baseline daily headache diary recordings) with average migraine duration of at least 4 hours to ensure that acute therapy was warranted Exclusion criteria: Current or planned pregnancy or breastfeeding, significant medical problem other than migraine, more than 8 tension or nonmigraine headaches per month, significant ECG abnormality, current or recent history of illicit drug use or alcohol abuse, current psychological treatment, and failure to complete a baseline headache diary</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: Tension type, non migraine, max 8/month</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Cousins 2015¹³⁸ Registration: ISRCTN53460881 Design: RCT Country: UK Purpose: Our pilot trial objectives were i) to calculate recruitment, consent and follow-up rates, ii) to test acceptability of randomisation to participants, iii) to assess treatment fidelity of SHE, and iv) to provide estimates of the mean and standard deviation of the outcomes measures to inform future sample size calculation Funding: National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme [Grant Reference Number PB-PG-0610-22373] Included for: KQ1</p>	<p>Number of participants: 73 randomized Age (years): Mean 39.3 Gender (% female): 82.2 Race: 72.6% White, 16.4% Black/African American, 1.4% Asian, 8.2% Other Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Inclusion criteria were adults (men and aged 18–75 years; diagnosis of migraine headache; onset [6 months previously; and] 3 headache days per month (assessed by headache diary; including both episodic and chronic migraine). Exclusion criteria: Exclusion criteria were physical conditions likely to cause headache (secondary headache); pregnancy; current psychotic illness; substance dependency (not including headache rescue medication); currently undergoing psychological therapy; and inability to complete self-report measures.</p>	<p>Migraine type: Mixed (%s NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Cuneo 2023¹³⁹ Registration: NCT05720819 Design: RCT Country: USA Purpose: To determine if the frequent use of a combined biofeedback-virtual reality device improves headache-related outcomes in chronic migraine. Funding: Osher Center for Integrative Medicine Small Research Project Grant Included for: KQ1, KQ1a</p>	<p>Number of participants: 50 randomized; 36 at baseline Age (years): Mean 42.3 Gender (% female): 83.3 Race: 77.8% White, 2.8% Black/African American, 5.6% Asian Ethnicity: 11.1% Hispanic/Latino Non-headache co-morbidities (%): 80.6% Anxiety, 55.6% Depression, 75% Insomnia Setting: Neurology/Headache clinic Inclusion criteria: Age 18 to 85 years; meet International Classification of Headache Disorders (ICHD-3 beta) criteria for chronic migraine; and the ability to speak English or Spanish Exclusion criteria: Pts w/cognitive impairment, severe psychiatric comorbidities (including active suicidal or homicidal ideation and/or psychosis), hearing/seeing difficulties, epileptic or non-epileptic seizures, and prisoners.</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 26.9 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>D'Souza 2008¹⁴⁰ Design: RCT Country: USA Purpose: We compared the effects of relaxation training and written emotional exposure on people with tension or migraine headaches. Funding: Preparation of this manuscript was supported, in part, by a Clinical Science Award from the Arthritis Foundation, and by NIH grants AR049059 and AG009203 Included for: KQ1, KQ1a</p>	<p>Number of participants: 90 randomized Age (years): Mean 21.4 Gender (% female): 88.9 Race: 58.9% White, 18.9% Black/African American, 6.7% Asian, 1.1% American Indian/Alaska Native, 10% Other Ethnicity: 4.4% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: University Inclusion criteria: After providing written consent, participants were given a structured headache diagnostic interview by a trained interviewer to determine whether they met International Headache Society criteria for either tension or migraine headaches. Exclusion criteria: We excluded people who did not meet such criteria, as well as those whose headaches were suspected as being due to neurologic disease (e.g., a tumor), alcohol abuse, or a primary medical disorder, or who were currently in psychotherapy or counseling.</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Participants asked to recall headache frequency from prior month Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: Tension headache</p>
<p>Day 2014¹⁴¹⁻¹⁴⁴ Registration: NCT01213056 Design: RCT Country: USA Purpose: "To examine the feasibility, tolerability, and patient acceptance of MBCT. To conduct a preliminary examination of the efficacy and clinical utility of MBCT" Funding: This research was supported by grants from the Anthony Marchionne Foundation and the National Headache Foundation. Included for: KQ1</p>	<p>Number of participants: 36 randomized Age (years): Mean 41.7 Gender (% female): 88.9 Race: 86.1% White, 5.5% Black/African American, 2.8% American Indian/Alaska Native, 5.6% Other Ethnicity: 5.6% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "Study inclusion criteria were: (1) 19 years of age or older; (2) At least 3 pain days per month (for the past ≥3 months) due to a primary headache pain type (ie, migraine, tension-type headache, cluster, or other) as defined by the International Headache Society; (3) headache pain was the primary source of pain; (4) if currently using psychotropic or headache medications, use of these medications must have begun at least 4 weeks before baseline assessment; and (5) reading ability was sufficient to comprehend self-monitoring forms." Exclusion criteria: "Study exclusion criteria included the following: (1) human immunodeficiency virus-related pain and cancer pain because these are associated with malignant disease²⁰; (2) history of seizure or facial neuralgia, as these conditions might preclude the accurate diagnosis of headache; (3) significant cognitive impairment, evidenced by a positive screen on the Mini-cog²¹; (4) current participation in other psychological treatments for any pain condition; and (5) schizophrenia, bipolar affective disorder, seizure disorder not adequately controlled by medication, or current substance abuse."</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (1-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: 11.1% tension type headache, 2.8% new daily persistent headache Non-migraine participants included: 11.1% tension type headache, 2.8% new daily persistent headache</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Dindo 2020¹⁴⁵ Registration: NCT02108678 Design: RCT Country: USA Purpose: The current study compared the efficacy of two 1-day (5- to 6-h) interventions for co-occurring migraine and depression: (1) acceptance and commitment therapy plus migraine education (ACT-ED), and (2) support plus migraine education (S-ED). Funding: This work was made possible by grant number K23MH097827 from the National Institute of Mental Health awarded to Lilian N. Dindo and was partially supported by the use and resources of the Houston VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (CIN13-413) Included for: KQ2</p>	<p>Number of participants: 136 randomized; 103 at baseline Age (years): Mean 35.8 Gender (% female): 82.5 Race: 75.7% White Ethnicity: NR Non-headache co-morbidities (%): 100% Depression Setting: NR Inclusion criteria: The screening inventory was completed by 4880 individuals, ages 18–70, with a history of migraine. Of those, 501 individuals met the following screening cutoffs: (1) obtained a score of 2 or more on the ID Migraine, a widely used 3-item screening tool with high positive predictive value for the presence of migraines [16]; (2) reported 4–12 migraine days over the previous month; (3) scored 10 or greater on the Patient Health Questionnaire-8 (PHQ-8) [17]; (4) no history of brain injury; (5) if currently using psychotropic or headache medications, use of these medications must have begun at last 4 weeks before the intake interview; (6) no history of schizophrenia, bipolar affective disorder or current substance abuse. The eligibility criteria for the treatment phase included (1) a diagnosis of current major depressive episode on the Structured Clinical Interview for Diagnostic and Statistical Manual for Mental Disorders – Fourth Edition (SCID-IV; DSM-IV [18, 19]; (2) a score of 17 or greater on the Hamilton Rating Scale for Depression (HRSD) [20]; (3) a medical chart diagnosis of migraine; and (4) no imminent suicidality requiring urgent clinical attention. Exclusion criteria: NR</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: A medical chart diagnosis of migraine Method for establishing baseline frequency: NR Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Dittrich 2008¹⁴⁶ Design: RCT Country: Austria Purpose: To address the influence of an aerobic exercise program combined with relaxation on pain and psychological variables in migraine patients. Funding: NR Included for: KQ1</p>	<p>Number of participants: 30 randomized Age (years): Mean 32.9 Gender (% female): 100 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: NR Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Self-rating of frequency category ("More than once per year"; "Once per month"; "More than once per month"; "Once per week or more") Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Fichtel 2001¹⁴⁷ Design: RCT Country: Sweden Purpose: (1) a standardized relaxation treatment was more effective as compared with a WL condition in reducing overall headache activity in adolescents suffering from migraine; (2) relaxation training would influence frequency, headache-free days, intensity, duration, and medicine consumption in the adolescents; (3) relaxation training would influence migraine or TTH differently; and (4) treatment improvement was maintained for 8 to 12 months after treatment. Funding: NR Included for: KQ1</p>	<p>Number of participants: 37 at baseline Age (years): Range 13 to 18 Gender (% female): 67.6 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Either at school or at a psychology department Inclusion criteria: In addition to being between 13 and 18 years of age, subjects had to have a headache history of at least 6 months, to fulfill the International Headache Society (IHS) diagnostic criteria for migraine or both migraine and TTH, and to experience migraine attacks at least twice a month. Exclusion criteria: At the diagnostic interview, pupils with secondary headache caused by physical or mental disease were excluded</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: TTH in 86% Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Flynn 2019¹⁴⁸ Design: RCT Country: Ireland Purpose: This study was designed to assess the acceptability and potential efficacy of an online hypnosis intervention for migraine with a view to decreasing the disability caused by migraine, the frequency of migraine, and the level of pain catastrophizing in migraine sufferers. Specific objectives were: (1) To evaluate the statistical and clinical significance of the intervention on functional (disability index), psychological (pain catastrophizing), and physiological (pain intensity) indices in a controlled clinical trial; (2) To evaluate the feasibility and efficacy of the intervention using quantitative data; (3) To determine if any treatment effects are maintained at 6-week follow-up. Funding: NR Included for: KQ1, KQ1a</p>	<p>Number of participants: 43 randomized; 40 at baseline Age (years): Category, %: 20-29, 5.9%; 30-39, 0.0%; 40-49, 29.4%; 50-59, 47.1%; 60-69, 11.8%; 70+, 5.9% Gender (% female): 87.5 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Online Inclusion criteria: Inclusion criteria were based on recommendations from the International Association for Study of Pain (IASP). Participants were required to have a formal diagnosis of a headache disorder and have had migraine headaches for at least 3 months. Other inclusion criteria required that participants must be 18 years of age or older, have a willingness to complete all components of the study, and have access to the internet on a daily basis. All participants were required to obtain a letter from their GP or neurologist to establish that they met the study criteria. Exclusion criteria: Exclusion criteria included: substance addiction; participation in other clinical trials; migraine related to menstrual cycle; abuse of migraine medication; and psychological disorders or cognitive impairment that would compromise study adherence.</p>	<p>Migraine type: NR Migraine diagnosis criteria: Formal diagnosis of headache disorder Method for establishing baseline frequency: Headache diary (1-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Fritsche 2010¹⁴⁹ Design: RCT Country: Germany Purpose: comparing the effect of the two treatment methods for prevention of MOH in patients with frequent migraine attacks Funding: German Ministry of Research and Education Grant (BMBF) (O1EM0513) Included for: KQ3</p>	<p>Number of participants: 158 randomized; 150 at baseline Age (years): Mean 48 Gender (% female): 90.7 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: Patients suffering from migraine with and without aura; Patients with combined headache (migraine and tension-type headache (TTH), if migraine was the main headache (as reported by the patient); Age: 18–65 years; One of the following conditions: Intake of triptans on >4 and <10 days per month or intake of analgesics on >7 and <14 days per month during the past three months or combined intake of triptans and analgesics not exceeding 15 intake days, including a maximum of 9 triptan intake days; Agreement to participate in one of two study arms by randomization Exclusion criteria: Significant psychiatric disorder; Additional secondary headache; Additional chronic pain diseases with pharmacological treatment; Insufficient knowledge of the German language; Pregnancy</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 25.2 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Gerber 2010¹⁵⁰ (MIPAS-Family) Design: RCT Country: Germany Purpose: The present study aimed to compare the clinical efficacy of this new multi-modal behavioral education program for children with headaches and their parents. This program was in turn compared to a "benchmark" treatment—Biofeedback. A further aim was to test for improvements in non-pain measures, exploring whether one or both treatment conditions, above the influence of headache parameters, have a positive impact on the child's QoL and the child's ability to take part in daily living activities. Funding: NR Included for: KQ2</p>	<p>Number of participants: 34 at baseline Age (years): Mean 11.8 Gender (% female): 64.5 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: 60 consecutive children and adolescents, ranging from 7 to 16 years of age, and their parents were considered for participation in the study. They were termed eligible if they suffered from migraine without aura, tension-type headache, or the combination of both (fulfilled the inclusion criteria of the International Headache Society classification). Exclusion criteria: Exclusion criteria were the presence of chronic daily headache (≥15 days per month) or drug abuse.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: Combination headache (TTH and migraine)</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Grazzi 2021¹⁵¹⁻¹⁵³ (ACTMigraine) Registration: NCT03461874 Design: RCT Country: Italy Purpose: To study the incremental effects of adding acceptance and commitment therapy (ACT) to pharmacological treatment as usual (TAU) in a sample of patients with high-frequency episodic migraine without aura (HFEM), assessing the impact on a spectrum of measures across multiple domains. Funding: None Included for: KQ1</p>	<p>Number of participants: 35 randomized Age (years): Mean NA Gender (% female): NR Race: NR Ethnicity: NR Non-headache co-morbidities (%): Setting: Neurology/Headache clinic Inclusion criteria: Participants at the Milan site who were adults, 18–65 years old, diagnosed with HFEM (i.e., code 1.1 of the International Classification of Headache Disorders, 3rd edition, migraines without aura), with an average monthly headache frequency between 9 and 14 days in the preceding 3 months (documented by daily diaries). Exclusion criteria: overuse of medications according to the International Classification of Headache Disorders, 3rd edition definition (i.e., regular intake in the previous 3 months of ergotamine, triptans, opioids or combination analgesics on ≥10 days/month, or of nonsteroidal anti-inflammatory drugs on ≥15 days/month); having undergone a withdrawal intervention in the 18 months preceding inclusion in the research protocol; major depression or other psychiatric disorders based on clinical history; psychotherapy in the previous 18 months; known to have epilepsy or idiopathic intracranial hypertension as reported by clinical documentation; previous experience of mindfulness or meditation approaches; or pregnancy or planning to become pregnant in the next 12 months.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Hedborg 2011^{154,155} Design: RCT Country: Sweden Purpose: We hypothesized that both the Internet-administered MBT program and the hand massage would be effective in decreasing the frequency of migraine. Funding: The Erik, Karin, and Gösta Selander Foundation and from the Nursing Research Foundation, Faculty of Medicine and Pharmacy, Uppsala University Included for: KQ1, KQ1a, KQ5</p>	<p>Number of participants: 83 randomized; 76 at baseline Age (years): Mean 47.8 Gender (% female): 68.4 Race: NR Ethnicity: NR Non-headache co-morbidities (%): 23.7% Depression Setting: NR Inclusion criteria: Fulfillment of migraine criteria according to the International Classification of Headache Disorders (30) and at least two migraine attacks monthly Exclusion criteria: NR</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 23.2 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Holroyd 1988^{156,157} Design: RCT Country: USA Purpose: to compare the effectiveness of a home-based behavioral intervention with an abortive pharmacological intervention for treating recurrent migraine and mixed migraine and tension headaches. Funding: NR Included for: KQ1, KQ1a</p>	<p>Number of participants: 41 randomized; 37 at baseline Age (years): Mean 33 Gender (% female): 65 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: University research clinic Inclusion criteria: To be included in this study, patients had to (a) receive a diagnosis of either migraine or mixed migraine and tension headache from a project physician, (b) regularly experience at least one migraine headache per month, and (c) have suffered from recurrent headache problems for at least 1 year. Patients also were re-quired to meet the specific inclusion and exclusion criteria for either migraine or mixed migraine and tension headache used in other studies Exclusion criteria: Participants were required to be free from prophylactic medication for at least 2 months prior to treatment and to be free from abortive medication for at least 1 month prior to treatment.</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 14 Co-morbid headache disorders: 49% mixed headaches and 74% reported a parental history of vascular headache Non-migraine participants included: None</p>
<p>Holroyd 2010¹⁵⁸⁻¹⁶⁰ Registration: NCT00910689 Design: RCT Country: USA Purpose: To determine if the addition of preventive drug treatment (beta blocker), brief behavioral migraine management, or their combination improves the outcome of optimized acute treatment in the management of frequent migraine. Funding: Grant R01-NS-32374 from the National Institutes of Health Included for: KQ1, KQ2</p>	<p>Number of participants: 232 randomized Age (years): Mean 38.2 Gender (% female): 80.2 Race: 83.6% White, 13.4% Black/African American, 0.9% Asian, 0.4% American Indian/Alaska Native, 0.4% Native Hawaiian/Other Pacific Islander, 1.3% Other Ethnicity: 1.3% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Age 18 to 65 years, diagnosis of migraine (with or without aura) according to the International Classification of Headache Disorders criteria at two separate evaluations during the evaluation clinic visit, and diary confirmed criteria for severity of migraine during the optimized acute treatment run-in of at least three migraines with disability per 30 days. Exclusion criteria: Diagnosis of probable medication overuse headache according to the International Classification of Headache Disorders criteria, a pain disorder other than migraine as the primary presenting problem, 20 or more days with headache a month, contraindication or sensitivity to any study drug, current use of migraine preventive drugs (with participant's preference or welfare contraindicating withdrawal), current psychological treatment, psychiatric disorder needing immediate or priority treatment, and inability to read and understand the study materials; for women, current or planned breast feeding or pregnancy or unwillingness to use an established contraceptive method were also exclusion criteria.</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 5.5 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Janssen 1986¹⁶¹ Design: RCT Country: Netherlands Purpose: Compare two forms of relaxation, separately for migraine, TTH, and combined migraine TTH Funding: NR Included for: KQ2</p>	<p>Number of participants: Age (years): Mean 33.4 Gender (% female): NA Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: referred by general practitioner specifically for relaxation treatment. Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: Psychologist diagnosed using patient history Method for establishing baseline frequency: Headache diary (2.5-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: N=10 had only TTH</p>
<p>Kewman 1980¹⁶² Design: RCT Country: USA Purpose: "To assess the relative contribution of specific and nonspecific effects of skin temperature biofeedback upon migraine headache." Funding: The work was supported in part by Rehabilitation Services Administration Grant No. 16-P-56810/5-17 to the University of Minnesota Medical Rehabilitation Research and Training Center and by a grant from the Division of Health Care Psychology, University of Minnesota. Included for: KQ1</p>	<p>Number of participants: 23 randomized Age (years): Mean 40 Gender (% female): 52.2 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: (1) a minimum 3-year history of migraine headache, (2) a minimum history of 72 headaches, (3) a minimum of two headaches per month during the preceding 12 months, (4) a verified diagnosis by their personal physician of migraine headaches, (5) migraine headaches that were unilateral at onset, and (6) a history of nausea or vomiting accompanying the migraine headaches or the prodromal symptoms of the headaches. Exclusion criteria: Patients who were "obviously not naive about biofeedback treatment of migraine headaches and subjects who had scheduling conflicts."</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: Verified diagnosis by their personal physician of migraine headaches Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Klan 2022^{163,164} Registration: DRKS00011111 Design: RCT Country: Germany Purpose: To assess the efficacy of migraine-specific, integrative CBT compared with a standard behavioral intervention for migraine-prophylaxis and a waiting-list control group in a three-armed randomized controlled trial. Funding: German Migraine and Headache Society (DMKG, e.V.); Department of Psychology, Johannes Gutenberg University of Mainz Included for: KQ1, KQ2</p>	<p>Number of participants: 121 randomized; 106 at baseline Age (years): Mean 46.9 Gender (% female): 90.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Psychotherapy clinic Inclusion criteria: (i) Meeting the ICHD-3 beta criteria of either migraine without aura, migraine with aura, or chronic migraine for at least one year; (ii) a minimum of four headache days per month, and a pattern of migraine symptoms stable over the last six months; (iii) psychological factors, such as dysfunctional thoughts (e.g., overambitious achievement orientation), emotions (e.g., attack-related fear), and behavior (e.g., excessive avoidance of triggers), or the experience of emotional distress, were associated with migraine [meeting the DSM-5 criteria (25) of either "somatic symptom disorder" or "psychological factors affecting other medical conditions"]; (iv) fluency in German, Internet access; (v) age of at least 18 years. Exclusion criteria: (i) Diagnosis of medication-overuse headache; (ii) currently taking a headache prophylactic medication (3-month wash-out) or therapy with botulinum toxin or neuromodulation during the trial period; (iii) previous completed or current psychotherapy; (iv) a severe mental disorder or medical comorbidity (which was likely to interfere with the ability to participate in group therapy, e.g., an acute psychosis, a major depressive episode, or an advanced Parkinson's disease); (v) suicidal tendency; and (vi) pregnancy or lactating.</p>	<p>Migraine type: Mixed (96.2% Episodic, 3.8% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 21.9 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Kleiboer 2014¹⁶⁵⁻¹⁶⁷ Design: RCT Country: Netherlands Purpose: To establish the post-treatment effectiveness of online behavioral therapy delivered with minimal guidance for adults with episodic migraine compared to a waitlist control group" Funding: This study was supported by grant # 1871 of the Health Insurers Innovation Foundation (Innovatiefonds Zorgverzekeraars) and by substantial support of the Utrecht University Faculty of Social and Behavioral Sciences. Included for: KQ1, KQ1a</p>	<p>Number of participants: 368 randomized Age (years): Mean 43.6 Gender (% female): 85.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "Inclusion criteria were (1) being aged 18-65 years, (2) meeting the ICHD-II criteria for migraine without (ICD-10NA code G43.0) or with aura (ICD-10NA code G43.1), (3) an attack frequency of 2-6 in the 30 days prior to randomization. " Exclusion criteria: "Exclusion criteria were (1) headache occurring on more than 15 days in the 30 days before randomization, (2) headache due to medication overuse (10 triptans e or analgesics on 15 days e in the 30 days before randomization), (3) a score of 178 or higher on the SCL-90R screening instrument for psychopathology, (4) a migraine duration of less than one year, (5) current or planned pregnancy."</p>	<p>Migraine type: Mixed (%s NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 22 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Kohlenberg 1981¹⁶⁸ Design: RCT Country: USA Purpose: To evaluate self-directed effort, without therapist contact, aimed at reducing the symptoms of migraine. Funding: NR Included for: KQ1</p>	<p>Number of participants: 117 randomized Age (years): Mean 45.4 Gender (% female): 98.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Community Inclusion criteria: n order to qualify for the study, subjects were told the (1) they should have at least two headaches per month; (2) they need to have been diagnosed as having migraine headaches by their doctor and currently be under his or her care; (5) be willing to collect data on their headaches on a daily basis; (6) be willing to collect data for six weeks prior to receiving any of the experimental treatments. Subjects were required to have their physician document all of the above criteria (except #6), in writing. Exclusion criteria: subject to high or low blood pressure; subject to strokes; have any severe psychiatric problems</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 20 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
Kropp 1997 ¹⁶⁹ Design: Crossover RCT Country: Germany Purpose: Ascertain the effects of two behavioral medicine approaches Funding: NR Included for: KQ2	Number of participants: 38 randomized Age (years): Mean 38.2 Gender (% female): 76.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Suffered from migraine, IHS diagnostic criteria (1991) Exclusion criteria: NR	Migraine type: Mixed (%s NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 17.4 Co-morbid headache disorders: NR Non-migraine participants included: None
Labbe 1984 ¹⁷⁰ Design: RCT Country: USA Purpose: To evaluate the effectiveness of autogenic feedback with childhood migraineurs by using a controlled group outcome experimental design. Funding: NR Included for: KQ1	Number of participants: 28 randomized Age (years): Mean 10.7 Gender (% female): 50 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: To be included in the study the child had to (a) receive a secondary diagnosis of vascular or migraine headache by a physician, (b) report at least 2 migraine headaches per month, and (c) meet three of the following six criteria: (a) headaches predominantly one-sided; (b) headaches usually accompanied by nausea or vomiting; (c) relief after rest; (d) positive family history for migraine headaches; (e) pulsating or throbbing pain; (f) visual, sensory, or motor prodromes. Exclusion criteria: NR	Migraine type: Episodic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 4.3 Co-morbid headache disorders: NR Non-migraine participants included: None
Labbe 1995 ¹⁷¹ Design: RCT Country: USA Purpose: To assess the "potency" of the skin temperature biofeedback component in the treatment of childhood migraine. Funding: NR Included for: KQ1, KQ3	Number of participants: 30 at baseline Age (years): Mean 12 Gender (% female): 43.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Laboratory Inclusion criteria: Received a secondary diagnosis of vascular or migraine headache by a physician; reported at least two migraine headaches per month; and met three of the following six criteria: headaches predominantly one-sided; headaches usually accompanied by nausea or vomiting; relief after rest; positive family history for migraine headaches; pulsating or throbbing pain; visual, sensory, or motor prodromes. Exclusion criteria: NR	Migraine type: Episodic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None

Study Details	Patient Characteristics	Migraine Characteristics
<p>Lemstra 2002¹⁷² Design: RCT Country: Canada Purpose: To test the effectiveness of a multidisciplinary management program for migraine treatment in a group, low cost, nonclinical setting. Funding: NR Included for: KQ1</p>	<p>Number of participants: 80 randomized Age (years): Mean 34.5 Gender (% female): 66.2 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Community center Inclusion criteria: Eligible subjects required a referral from their physician indicating a diagnosis of migraine and safety to participate. Subjects were also required to have chronic migraine pain for at least 6 months and to meet the diagnostic criteria for migraine with or without aura in accordance with the International Headache Society. The subjects also had to be 18 years of age or older in order to give written informed consent. Exclusion criteria: Patients were excluded if their pain was of a benign nature. Patients were not excluded for any other comorbidity.</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Neurologist evaluation included obtaining a detailed history Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Matchar 2008¹⁷³ Design: RCT Country: USA Purpose: To determine if patients cared for in a coordinated headache management program would achieve reduced headache disability compared with patients in usual care. Funding: AHRQ) Grant No. 5R01HS10893 Included for: KQ1</p>	<p>Number of participants: 614 at baseline Age (years): Mean 43.5 Gender (% female): 87 Race: NR Ethnicity: NR Non-headache co-morbidities (%): 39.3% Depression, 1.1% Epilepsy, 1.8% Stroke, 23% Hypertension, 5.8% CAD Setting: Neurology/Headache clinic Inclusion criteria: Eligibility was determined through a validated computer-assisted telephone screening interview administered by trained surveyors at Innovative Medical Research (IMR). Eligible subjects had to be 21 years of age or older; have chronic headache thought to be of tension-type, migraine, or mixed etiology; and have a Migraine Disability Assessment (MIDAS) score greater than 5. Their responses on the screening interview had to indicate an intention to continue general medical care at their current locations and to continue their present health insurance coverage for the next 12 months. Exclusion criteria: Subjects were excluded if they were currently receiving treatment from a neurologist or a headache clinic or had received such treatment within the past 6 months.</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: NR Method for establishing baseline frequency: NR Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Mathew 1981¹⁷⁴ Design: RCT Country: USA Purpose: Study comparative on the effects of combinations of propranolol, amitriptyline, and biofeedback training versus individual modalities of treatment. Funding: NR Included for: KQ1, KQ2</p>	<p>Number of participants: 715 randomized Age (years): Mean 38.9 Gender (% female): 88.8 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Adults with a history of migraine or a combination of migraine and muscle contraction headache. Only outcomes for pts with migraine were abstracted. Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: NR Method for establishing baseline frequency: NR Observation period (4 weeks) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Minen 2020a¹⁷⁵ Registration: NCT03183791 Design: RCT Country: USA Purpose: The primary aim was to conduct a pilot feasibility and acceptability study of the RELAX approach in Multiple Sclerosis-migraine patients who visit a Multiple Sclerosis Center. A secondary aim was to assess whether there was any change in migraine disability and Multiple Sclerosis pain related disability. Funding: National Multiple Sclerosis Society; the Doris Duke Charitable Foundation [Fund to Retain Clinical Scientists]; New York University Clinical Translational Science Institute (NYU CTSI); the National Center for Complementary and Integrative Health (NCCIH) [K23 AT009706-01] Included for: KQ1, KQ1a</p>	<p>Number of participants: 62 randomized Age (years): Mean 39.6 Gender (% female): 88.7 Race: 45.2% White, 30.6% Black/African American, 24.2% Other Ethnicity: 33.9% Hispanic/Latino Non-headache co-morbidities (%): 51.6% Anxiety, 56.5% Depression Setting: Neurology/Headache clinic Inclusion criteria: Age 18 to 80; 4+ headache days a month; meets migraine criteria per International Classification of Headache Disorders (ICHD)-3b, (Headache Classification Committee of the International Headache Society (IHS) 2013); speaks English; owns a smartphone; willing to use a smartphone application for migraine treatment Exclusion criteria: Cognitive deficits or other physical problem with the potential to interfere with behavioral therapy Opioid or barbiturate use 10+ days a month; Alcohol or other substance abuse; Have done PMR, cognitive behavioral therapy, biofeedback, or other relaxation therapy for migraine in the past year; Does not own a smartphone; Unable or unwilling to follow a treatment program that relies on written and audio file material</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: NR Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Minen 2020^{176,177} Registration: NCT03183791 Design: RCT Country: USA Purpose: To evaluate if a smartphone-based intervention would be feasible and acceptable, and if those who practiced PMR would have better preliminary migraine efficacy outcomes in terms of migraine disability and headache days Funding: NIH NCCIH [K23AT009706]; the New York University Clinical Translational Science Institute (NYU CTSI) [UL1TR001445]; New York University, Center for Healthcare Innovation and Delivery Science (NYU CHIDS); American Academy of Neurology (AAN); and the American Brain Foundation (ABF); The Doris Duke Charitable Foundation [Fellowship to Retain Clinical Scientists]; NYU Department of Neurology; International Headache Academy (IHA) Included for: KQ1, KQ1a</p>	<p>Number of participants: 169 randomized; 139 at baseline Age (years): Mean 41.7 Gender (% female): 83.5 Race: 54% White, 18.7% Black/African American, 27.3% Other Ethnicity: 27.3% Hispanic/Latino Non-headache co-morbidities (%): 43.2% Anxiety, 39.6% Depression Setting: Primary care Inclusion criteria: Age 18-80, migraine (per the International Classification of Headache Disorders, ICHD3 beta criteria), 4+ headache days/month, own a smartphone, speak English, be willing to try a smartphone-based behavioral therapy for migraine, and not have practiced behavioral therapy (PMR, CBT, biofeedback) to control headaches in the past year. Exclusion criteria: Having a cognitive deficit or other physical problem with the potential to interfere with behavioral therapy, presence of alcohol or other substance abuse as determined by self-report or prior documentation in the medical record, and opioid or barbiturate use 10+ days a month, and being unable or unwilling to follow a treatment program that relies on written and audio file materials</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: NR Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Minen 2021¹⁷⁸ (HeartMath) Registration: NCT04077658 Design: RCT Country: USA Purpose: The current study aimed to evaluate whether an 8-week program of application (app)-based HRV biofeedback (HeartMath) was feasible and acceptable, and attained a significant signal for superiority compared to wait list control in improving migraine quality of life (Migraine-Specific Quality of Life Questionnaire; MSQv2). Funding: This work was supported by the Doris Duke Charitable Foundation (Funds to Retain Clinical Scientists); the NIH NCCIH (K23 AT009706-01). Included for: KQ1, KQ1a</p>	<p>Number of participants: 52 randomized Age (years): Mean 42.2 Gender (% female): 88.5 Race: 78.8% White Ethnicity: 3.8% Hispanic/Latino Non-headache co-morbidities (%): 48.1% Anxiety, 28.8% Depression, 30.8% Insomnia Setting: Neurology/Headache clinic Inclusion criteria: Inclusion criteria included subjects who were 18+, were diagnosed with migraine (in accordance with ICHD3 criteria), had 4–20 headache days/month, had not utilized behavioral therapy for migraine within the past year, had access to a smartphone and wifi, spoke English, reported an education level of high school completion or higher, and agreed to not change migraine preventative treatments during the course of the study period. Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Questionnaire Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Mérelle 2008¹⁷⁹⁻¹⁸¹ Design: RCT Country: Netherlands Purpose: To evaluate behavioral training for reducing attack frequency, increasing feelings of control and self-confidence in attack prevention, and improving patients' quality of life and to reduce migraine-related disability. Funding: Grant no. 940-31-069 from the Netherlands Organization for Health Research and Development (ZonMw), The Hague and financial means provided by the Pain Expertise Centre Rotterdam Included for: KQ1</p>	<p>Number of participants: 129 randomized; 127 at baseline Age (years): Mean 43.5 Gender (% female): 87.6 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: University medical center Inclusion criteria: Patients were included according to the scientific guidelines of the International Headache Society subcommittee on clinical trials. Participants had to be aged 18–65 years, fulfil the IHS criteria for migraine with (G43.1) or without (G43.0) aura and have an attack frequency of one to six per month. Exclusion criteria: Patients with headache occurring on ≥ 15 days per month, a migraine duration of < 1 year, migraine onset at age > 50 years referring to underlying organic disease, and an above average score (> 178) on the Symptom Checklist 90 (SCL-90), indicative of psychopathology.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 19.1 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Odawara 2015¹⁸² Design: RCT Country: Japan Purpose: investigate the feasibility of using computerized ecological momentary assessment (EMA) for evaluating the efficacy of BF treatment for migraine Funding: NR Included for: KQ1</p>	<p>Number of participants: 47 randomized; 27 at baseline Age (years): Mean 39.9 Gender (% female): 96.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: diagnosis of any type of migraine according to the criteria of the International Headache Society (IHS) 2004 Exclusion criteria: either the presence of psychiatric disease at the time of application; history of paranoia, schizophrenia, panic disorder, personality disorders, or severe physical illnesses; or diagnosis of analgesics abuse headache according to the criteria of the IHS 2004.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 19.7 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Pickering 2012¹⁸³ (MIGREL) Registration: NCT00904527 Design: RCT Country: France Purpose: study aims at studying 1-the impact of autogenic training-AT on pain in a homogeneous group of well defined migraine patients and to compare it to waitlist patients, 2-Health-related outcomes and quality of life. Funding: French Ministry of Health Included for: KQ1</p>	<p>Number of participants: 58 randomized; 42 at baseline Age (years): Mean 39 Gender (% female): 83.3 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: Male or female patients, 18 to 60 years old should comply with diagnostic criteria established by the International Headache Society (IHS) in the 2002 International Classification of Headache Disorders (ICHD-I), including paragraphs 1.1 to 1.7 of the IHS classification (ICHD). Patients must have experienced headaches for at least three months occurring 5 to 14 days per month before the first visit. Exclusion criteria: Exclusion criteria were patients with probable or confirmed medication-overuse headache (codes IHS 8.2.6 and IHS 8.2.7), who cannot distinguish migraines from tension headaches, with face vascular algia, or other types of headaches (codes HIS 3, 4 and 5) or with tension headache (code IHS 2.3.1 et 2.3.2) or a combination of tension headache (2.2) and migraines (1.1 ou 1.2) reaching a cumulated number of days of less than 5 or at least 15 days per month. Will also be excluded patients who cannot communicate, who have a major depressive episode, evaluated by the MINI test (12) at the first visit and patients who have already been previously involved in relaxation training or in any migraine clinical trial.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: None Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Powers 2013¹⁸⁴⁻¹⁸⁷ Registration: NCT00389038 Design: RCT Country: USA Purpose: "To determine the benefits of cognitive behavioral therapy (CBT) when combined with amitriptyline vs headache education plus amitriptyline." Funding: "Funding was provided by grant R01NS05036 from the National Institute of Neurological Disorders and Stroke (Dr Powers), grant 8UL1TR000077 from the National Center for Research Resources and the National Center for Advancing Translational Sciences, and grant T32DK063929 from the National Institute of Diabetes and Digestive and Kidney Diseases for some of the post-doctoral fellows who contributed to the trial (Dr Powers, program director). Amitriptyline, which was provided without cost to participants, was purchased using National Institutes of Health grant funds and managed by the investigational pharmacy at Cincinnati Children's Hospital Medical Center." Included for: KQ2</p>	<p>Number of participants: 135 randomized Age (years): Mean 14.4 Gender (% female): 79.3 Race: 88.9% White, 9.6% Black/African American, 0.7% Asian, 0.7% American Indian/Alaska Native Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "Inclusion criteria included a diagnosis of chronic migraine made by a board-certified headache specialist using the International Classification of Headache Disorders, 2nd Edition (ICHD-II) criteria, 5, 16, 15 or more days with headache per month measured by a prospective 28-day headache diary, and Pediatric Migraine Disability Assessment Score (PedMIDAS) of greater than 20 points, indicating at least moderate disability." Exclusion criteria: "Exclusion criteria were (1) medication overuse (ICHD-II criteria 5, 16), (2) current use of amitriptyline or other prophylactic antimigraine medication within a period equivalent to less than 5 half-lives before study screening, (3) other chronic pain condition such as fibromyalgia or complex regional pain syndrome II, (4) abnormal electrocardiogram, (5) severe orthostatic intolerance or dysregulation, (6) documented developmental delay or impairment, (7) severe psychiatric comorbidity eg, psychosis, bipolar disorder, major depressive disorder, (8) PedMIDAS of greater than 140 points (indicating excessive disability and need for multisystemic therapies), (9) pregnancy or being sexually active without use of medically accepted form of contraception (barrier or hormonal methods), and (10) use of disallowed medications including opioids, antipsychotics, antimanics, barbiturates, benzodiazepines, muscle relaxants, sedatives, tramadol, or herbal products."</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: None Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Rapoff 2014¹⁸⁸ Design: RCT Country: USA Purpose: To evaluate the efficacy of a self-guided CD-ROM program ("Headstrong") containing cognitive-behavioral self-management strategies versus an educational CD-ROM program for treating headaches, headache-related disability, and quality of life. Funding: NIH Included for: KQ1, KQ1a</p>	<p>Number of participants: 70 randomized; 35 at baseline Age (years): Mean 10.2 Gender (% female): 71.5 Race: 94% White Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: (a) 7–12 years of age; (b) having migraine occurring on the average at least once per week by parental or child report and separated by symptom-free periods; and (c) having a board-certified neurologist's diagnosis of migraine with or without aura, using International Classification of Headache Disorders [20]. Exclusion criteria: (a) their medical history and/ or neurological exam suggested that theirs were secondary headaches; (b) parents reported the child had been diagnosed with a mental health condition or was receiving concurrent psychotherapy; (c) scores on the internalizing or externalizing scales of the parent-reported Child Behavior Checklist [21] were in the clinical range at baseline; or (d) the baseline headache diaries indicated an average headache frequency of less than one per week (over a 14-day period).</p>	<p>Migraine type: Mixed (%s NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (2-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: 2 of 35 did not have a formal diagnosis of migraine by a board certified neurologist, but they might have nevertheless been having migraines</p>
<p>Rausa 2016¹⁸⁹ Design: RCT Country: Italy Purpose: "The primary outcome was to evaluate the number of patients that return episodic after treatment. Secondly we evaluate the effects of frontal EMG BFB on frequency of headache and analgesic intake. Changes in coping strategies and in EMG frontalis tension were also evaluated." Funding: "sabella SerÀ gnoli Foundation supported this study by a research grant awarded to Dr. Marialuisa Rausa." Included for: KQ1</p>	<p>Number of participants: 47 randomized Age (years): Mean 42.2 Gender (% female): 48.9 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "All consecutive patients attending the Headache Center of IRCCS Institute of Neurological Sciences of Bologna in a range of 2 years (from 2008 to 2010), satisfying inclusion criteria for CM and MOH or CTTH and MOH, and accepting to participate were recruited." "Headache and drug overuse were classified according to the International Classification of Headache Disorders 3rd Edition (beta version)" Exclusion criteria: "Exclusion criteria were: foreign language as mother tongue, pregnancy, secondary headaches, age <18, noncompliance. Secondary headaches were ruled out by clinical examination, biochemical tests, and neuroimaging studies, when indicated."</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: All patients had medication overuse headache; 4 patients (2 in each arm) had TTH + MOH Non-migraine participants included: 4 patients had TTH + Medication Overuse Headache</p>

Study Details	Patient Characteristics	Migraine Characteristics
Reich 1989 ¹⁹⁰ Design: RCT Country: USA Purpose: to assess the long term success of four different non-invasive treatments in reducing the self-reported frequency and self reported intensity of pain from either vascular/ migraine or muscle contraction/tension headaches Funding: NR Included for: KQ2	Number of participants: 392 at baseline Age (years): ≥18 Gender (% female): 63 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Adults aged ≥18 y.o. with vascular/ migraine headache (V/M) or muscle contraction headache (M/C). Only data for pts with V/M were abstracted Exclusion criteria: Pts with mixed diagnostic category patients (vascular/contraction)	Migraine type: Chronic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None
Richardson 1989 ¹⁹¹ Design: RCT Country: Canada Purpose: the purpose of this study was to compare the efficacy and cost-effectiveness of a minimal-therapist-contact cognitive-behavioral treatment of headaches diagnosed as common migraine to the same treatment administered in a traditional clinic-based format. Funding: National Headache Foundation and by a Medical Research Council of Canada Studentship to G. M. Richardson. Dr. P. J. McGrath is supported by a Career Scientist Award of the Ontario Ministry of Health Included for: KQ1, KQ5	Number of participants: 47 at baseline Age (years): Mean 35.7 Gender (% female): 85.1 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Psychology clinic Inclusion criteria: Personal history of paroxysmal headaches plus at least two of the following factors: (a) associated nausea and/or vomiting, (b) throbbing pain, (c) family history of severe chronic headache. Other inclusion criteria were as follows: (a) independent diagnosis of common migraine from the individual's own physician, (b) age 18 to 50 years, (c) recurrent headaches for at least three months occurring with a minimum frequency of two per month. Exclusion criteria: Patients who consistently experienced prodromal symptoms, diagnostic of classic migraine, were excluded in order that subjects would be as homogeneous as possible. Other exclusion criteria: (d) not to be currently on, or to have terminated prophylactic headache medication within the previous one month, (e) not to be suffering from any major neurological or psychiatric disorder (determined by a physician's questionnaire, the Brief Symptom Inventory 16 and the Beck Depression Inventory) (f) not to have received cognitive or behavioral therapy within the previous five years for treatment of headaches, (g) females not to be taking contraceptive or other hormone therapy.	Migraine type: Mixed (%s NR) Migraine diagnosis criteria: Paroxysmal headaches plus at least two of the following factors: (a) associated nausea and/or vomiting, (b) throbbing pain, (c) family history of severe chronic headache. Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 16.7 Co-morbid headache disorders: NR Non-migraine participants included: None

Study Details	Patient Characteristics	Migraine Characteristics
<p>Richter 1986¹⁹² Design: RCT Country: Canada Purpose: to compare the efficacy of two active treatments, relaxation training and cognitive coping, with a non-specific placebo control in the treatment of 42 children and adolescents with migraine. Funding: Ontario Ministry of Health and the Ontario Ministry of Community and Social Services Included for: KQ1, KQ2</p>	<p>Number of participants: 42 at baseline Age (years): Mean 12.9 Gender (% female): NR Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Hospital Inclusion criteria: Participation required confirmation of the diagnosis of classical or common migraine by a project neurologist using the diagnostic criteria of intermittent paroxysmal headache and any 2 out of the following 4 symptoms: throbbing pain, scotomata or related neurologic phenomena, nausea and/or vomiting, and a positive family history. Other inclusion criteria were a minimum headache history of 3 months, an average frequency of once/week, no new prophylactic medication within the previous 2 months, and a minimum I.Q. of 80 on the PPVT. Exclusion criteria: Children with allergic, purely dietary, or menstrual headache were excluded, as were those with unstable emotional or medical problems likely to require other interventions.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: NR Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 2 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Rothrock 2006¹⁹³ Design: RCT Country: USA Purpose: To determine whether implementation of a different system of healthcare delivery would offer an advantage over the traditional paradigm and, specifically, to investigate whether the addition of intensive patient education to routine medical management would improve clinical outcome and reduce utilization of healthcare resources. Funding: Unrestricted educational grant from GlaxoSmithKline Included for: KQ1</p>	<p>Number of participants: 100 randomized Age (years): Mean 42.5 Gender (% female): 92 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "One hundred consecutive patients with episodic, frequent, or daily migraine diagnosed according to existing International Headache Society criteria and, for chronic daily headache patients, criteria proposed by Silberstein et al." Exclusion criteria: NR</p>	<p>Migraine type: Mixed (19% Episodic, 81% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: None Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Sargent 1986^{194,195} Design: RCT Country: USA Purpose: Our controlled, experimental, outcome study had as its primary objective the investigation of this very problem, namely, to determine whether increasing blood flow in the hands at will is specifically effective in the treatment of migraine (Sargent et al., 1978). In addition to the Thermal Biofeedback Group, an Autogenic Phrases Group was included to ascertain if biofeedback supplemented the autogenic phrases used to encourage relaxation and to increase blood flow in the hands (Schultz and Luthe, 1979). Funding: NIMH, National Migraine Foundation and the P. W. Skogmo Foundation Included for: KQ1, KQ2, KQ3</p>	<p>Number of participants: 136 at baseline Age (years): Mean 35.7 Gender (% female): 83.1 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Only subjects with predominately migraine headaches, classical or common, based on criteria established by the Ad Hoc Committee on Classification of Headache (1962) were accepted into the study. Those with both migraine and tension headaches could participate if the headache type could be clearly distinguished clinically and the tension headache activity was minimal. To enhance the validity of the study, patients had to manifest significant disability, defined as (a) at least 4 migraine headache days per month for 6 months of each year for the past 2 years and (b) failure at least once during the year for the past 2 years of the usual medication for acute episodes to relieve symptoms, forcing the patient to go to bed or attend the emergency room. Exclusion criteria: Subjects with serious physical or psychological problems were not accepted into the study.</p>	<p>Migraine type: NR Migraine diagnosis criteria: Determined by internist Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 17 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Sartory 1998¹⁹⁶ Design: RCT Country: Germany Purpose: The aim of the present study was to compare the efficacy of a beta blocker, metoprolol, a prophylactic drug treatment with two psychological treatments of pediatric migraine namely, progressive relaxation training and vasomotor feedback, both combined with stress management training. Funding: Bundesminister für Forschung und Technologie (BMFT; Federal Minister for Research and Technology, Germany) Included for: KQ2</p>	<p>Number of participants: 43 randomized Age (years): Mean 11.3 Gender (% female): 39.5 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Primary care Inclusion criteria: Headache diagnoses were confirmed by the pediatrician author (R.P.) according to the IHS (1988) criteria, i.e., at least 5 headache attacks lasting for 2 to 48 h with two of the following symptoms or more: lateralized headache, pulsing pain of moderate to high intensity, exacerbation by effortful physical activity; nausea or vomiting, in addition to photo- and phonophobia. The minimal duration of the disorder had to be 6 months with at least two attacks having taken place during the last month. Exclusion criteria: Children with secondary headache and also those with a neurological or developmental disorder were excluded</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 4.7 Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Scharff 2002¹⁹⁷ Design: RCT Country: USA Purpose: To evaluate the effectiveness of handwarming biofeedback (HWB) and stress management training in comparison to attention (handcooling, HCB) and wait-list control groups. Funding: This research was supported by grants from the University of Pittsburgh Anesthesiology and Critical Care Foundation, the Raymond and Elizabeth Bloch Educational and Charitable Foundation, and the NIH/NICHD (HD38647). Included for: KQ1</p>	<p>Number of participants: 36 at baseline Age (years): Mean 12.8 Gender (% female): 66.7 Race: NR Ethnicity: NR Non-headache co-morbidities (%): 16.7% Anxiety, 8.3% Depression Setting: Neurology/Headache clinic Inclusion criteria: Children were referred from neurologists at Children's Hospital of Pittsburgh if they (1) were between the ages of 7 and 17 years; (2) qualified for an International Headache Society (IHS; Headache Classification Committee of the International Headache Society, 1988) diagnosis of migraine with or without aura; (3) had no primary medical condition and a negative neurological exam; (4) were not taking daily preventative medication for headaches; and (5) reported an average of at least one migraine per week or 5 days per month with migraine. Exclusion criteria: NR.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (2-week period) Duration of migraine or headache (years): 2.5 Co-morbid headache disorders: 12 children (33.3% of the sample) met IHS criteria for co-existing tension-type headache. Three children (8.3%) described headaches in addition to migraine that did not meet full IHS criteria for tension-type headache Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Seminowicz 2020¹⁹⁸⁻²⁰⁰ Design: RCT Country: USA Purpose: Evaluate the efficacy of an enhanced mindfulness based stress reduction (MBSR+) versus stress management for headache (SMH) Funding: NCCIH/NIH Included for: KQ2</p>	<p>Number of participants: 98 randomized Age (years): Median 36 Gender (% female): 90.8 Race: 72.4% White, 17.3% Black/African American, 9.2% Other Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: 18 to 65 years of age and met International Classification of Headache Disorders criteria for migraine with or without aura. Written informed consent, screening established ≥ 1 year history of a migraine diagnosis. Completed at least 28 days of an electronic daily diary to establish eligibility (4–14 headache days in 28 days) Exclusion criteria: Reported severe or unstable psychiatric symptoms, using opioid medications, had prior experience with mindfulness or concurrent treatment expected to affect mindfulness/stress reduction, pregnant, lactating, or planning to become pregnant, unable to undergo MRI.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Seng 2019^{201,202} Registration: NCT02443519 Design: RCT Country: USA Purpose: evaluate the efficacy of MBCT-M to reduce migraine-related disability in people with migraine. Funding: International Headache Academy, National Center for Advancing Translational Sciences, National Institute of Neurological Disorders and Stroke, Yeshiva University, Hollander Seed Fun Included for: KQ1, KQ5</p>	<p>Number of participants: 60 randomized Age (years): Mean 40.1 Gender (% female): 91.7 Race: 81.7% White, 18.3% Black/African American Ethnicity: 16.7% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: University Psychology departments Inclusion criteria: Inclusion criteria were a) currently meeting International Classification of Headache Disorders (ICHD)-3 beta headache diagnosis for migraine using a semi-structured clinical interview and the validated American Migraine Study/American Migraine Prevalence and Prevention Study migraine diagnostic screener, b) self-reported and prospective diary-confirmed ≥ 6 headache days per month, c) aged 18–65, d) ability to read English, and e) capacity to consent. Exclusion criteria: Exclusion criteria were a) continuous headache over the course of 30 days, b) initiation of a preventative migraine treatment within four weeks of the baseline assessment or a plan to initiate preventive migraine treatment during the duration of the study, c) severe psychiatric illness that would interfere with participation in the treatment such as active suicidality, active psychosis, or failing a cognitive screen, or d) inability to adhere to headache diary during baseline period (recorded fewer than 26/30 days).</p>	<p>Migraine type: Mixed (48.3% Episodic, 51.7% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Simshäuser 2022²⁰³ Registration: DRKS00007477 Design: RCT Country: Germany Purpose: to evaluate the migraine-specific adaptation of the Mindfulness-Based Cognitive Therapy (MBCT) program for feasibility and effectiveness in a randomized controlled trial. Funding: Research Council of the Medical Faculty of the University of Freiburg Included for: KQ1</p>	<p>Number of participants: 54 randomized Age (years): Mean 45.2 Gender (% female): 88.9 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: University medical center Inclusion criteria: (1) aged 18–65 years, (2) diagnosis of migraine with or without aura by the trial physician in accordance with the diagnostic criteria of the International Headache Society [28], (3) at least two migraine attacks per month on average, and (4) in case of a medical prophylaxis maintaining a stable dose for at least 3 months prior to inclusion until the end of the trial Exclusion criteria: (1) chronic migraine with more than 15 migraine days per month, (2) taking headache analgesics on more than 15 days or migraine-specific triptans on more than 10 days per month, (3) regular practice of meditation (> 1 × per week) or yoga (> 2 × per week), (4) plans to start psychotherapy or any other migraine treatments during the course of the trial, (5) prior participation in a mindfulness training, (6) participation in other clinical studies throughout the study duration, and (7) presence of a life-threatening disease or a mental disorder that might severely hinder interpersonal contacts.</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Smitherman 2016^{204,205} Design: RCT Country: USA Purpose: Pilot-test the efficacy of a brief behavioral insomnia intervention for adults with CM and comorbid insomnia Funding: Migraine Research Foundation Included for: KQ4</p>	<p>Number of participants: 32 randomized; 31 at baseline Age (years): Mean 30.8 Gender (% female): 90.4 Race: 80.6% White, 16.1% Black/African American, 3.2% Other Ethnicity: 3.2% Hispanic/Latino Non-headache co-morbidities (%): 100% Insomnia Setting: Neurology/Headache clinic Inclusion criteria: Adults, from June 2011 to March 2013 they either presented for treatment a local neurology clinic or were identified as having chronic migraine through their completion of an electronic headache diagnostic at a large southeastern university. Meeting revised ICHD-II criteria for CM without medication overuse headache (MOH) and ICSD-3 criteria for insomnia (eg, sleep onset or maintenance insomnia or nonrefreshing sleep, plus daytime impairment). Exclusion criteria: Presence of a secondary headache disorder including MOH, pregnancy or breastfeeding, being unable to read or speak English at a 6th grade level, untreated sleep apnea, active alcohol or substance abuse or dependence, active bipolar disorder, psychiatric hospitalization within the last year, employment involving rotating shift work schedule, and recent or expected change in preventive headache pharmacotherapy (ie, starting a new preventive medication within 3 weeks of enrollment or expecting to start a new medication during the 3-month study duration).</p>	<p>Migraine type: Chronic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (2-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>
<p>Sorbi 1984²⁰⁶ Design: RCT Country: Netherlands Purpose: "Examine the therapeutic necessity of thermal feedback training in a multimodal treatment program for migraine headache" Funding: Dep of Psychology, University of Utrecht Included for: KQ3</p>	<p>Number of participants: 21 at baseline Age (years): Mean 40.8 Gender (% female): 76.2 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: Referred by general practitioners, migraine diagnosis confirmed by one of the authors Exclusion criteria: Insufficient motivation to participate, too much anxiety, starting another therapy at the same time</p>	<p>Migraine type: Episodic Migraine diagnosis criteria: Ad Hoc Committee on Classification of Headache criteria; Criteria by Passchier and van der Helm-Hylkema; a diagnostic questionnaire developed at St Lucas Hospital in Amsterdam Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Sorbi 1986^{207,208} Design: RCT Country: Netherlands Purpose: measure the differential effectiveness of relaxation training and stress coping training Funding: Faculty of the Social Sciences, Univ of Utrecht Included for: KQ2</p>	<p>Number of participants: 32 randomized; 29 at baseline Age (years): Mean 35.8 Gender (% female): 82.8 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: NR Inclusion criteria: Age 18+, migraines for at least one year, at least 2 per month. if egotamine being consumed, it had to be less than 2 tablets or suppositories per week (NR dose maximum) Exclusion criteria: NR</p>	<p>Migraine type: NR Migraine diagnosis criteria: Ad Hoc Committee on Classification of Headache criteria Method for establishing baseline frequency: NR Duration of migraine or headache (years): 17.3 Co-morbid headache disorders: 3 also had "muscle contraction headache" Non-migraine participants included: None</p>
<p>Underwood 2022²⁰⁹⁻²¹¹ (CHESS) Registration: ISRCTN79708100 Design: RCT Country: UK Purpose: To test the effectiveness of a group educational and supportive self-management programme for people living with chronic headaches. Funding: National Institute for Health Research (NIHR) Programme Grants for Applied Research programme (RP-PG-1212-20018). Included for: KQ1, KQ1a, KQ5</p>	<p>Number of participants: 727 at baseline Age (years): Mean 47.4 Gender (% female): 83.1 Race: 80.6% White, 5.8% Black/African American, 8.3% Asian, 5.4% Other Ethnicity: NR Non-headache co-morbidities (%): 52.5% Anxiety, 21.9% Depression Setting: Primary care Inclusion criteria: Adults meeting an epidemiological definition of chronic headaches (≥ 15 headache days per month for at least three months) with migraine or tension type headaches. For reporting we identified three phenotypes, people with: 1) ICHD-3 criteria for chronic migraine, i.e., at least eight days per month with a migraine attack with or without aura (2) less than eight migraine attacks per month, or any number of attacks meeting ICHD -3 criteria for episodic migraine and chronic tension type headache, and 3) chronic tension type headache. In each group we included those with and without medication overuse headache. Exclusion criteria: Unable to attend the group self-management sessions, without access to a telephone, not fluent in English, or unable to participate in the group intervention for health reasons.</p>	<p>Migraine type: Mixed (45.5% Episodic, 54.5% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (period NR) Duration of migraine or headache (years): NR Co-morbid headache disorders: Episodic migraine patients also had chronic tension-type headache. Around half of participants also had medication-overuse headache. Non-migraine participants included: Nine participants had chronic tension-type headache without migraine and were excluded from analyses</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Varkey 2011²¹² Design: RCT Country: Sweden Purpose: To evaluate the effects of exercise in migraine prevention. Funding: The Swedish Research Council (Vetenskapsrådet) (DNR: 2009-376), the Gothenburg Research and Development Council (VGFOUGSB-6147), Praktikertjänst, Stockholm, Sweden, the Minnesfonden at the Swedish Association of Registered Physiotherapists, the Renee Eander fund (Renee Eanders hjälpfond), The Neurological Research Foundation (Insamlingsstiftelsen för neurologisk forskning), the Olle Engkvists Byggnadsstare Foundation (Stiftelsen Olle Engkvist Byggnadsstare), GlaxoSmithKlein, and AstraZeneca. Included for: KQ2</p>	<p>Number of participants: 91 randomized Age (years): Mean 44.3 Gender (% female): 90.1 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: The inclusion criteria stated that the participants must: be aged between 18 and 65 years old; have migraine with or without aura with a frequency of 2–8 attacks per month, and have had migraine for at least 1 year before participating in the study and before the age of 50. Exclusion criteria: The exclusion criteria were: interval headaches not distinguishable from migraine; medication-overuse headache; regular exercise (once or more per week during the 12 weeks prior to the study); earlier regular practice of relaxation; pregnancy; breastfeeding; use of daily migraine prophylaxis in the 12 weeks prior to the study; inability to understand Swedish; use of antipsychotic or antidepressive medication in the 12 weeks prior to the study; drug or alcohol abuse; and topiramate intolerance.</p>	<p>Migraine type: Mixed (98.9% Episodic, 1.1% Chronic) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 25.4 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Vasiliou 2021^{213,214} Registration: NCT02734992 Design: RCT Country: Cyprus Purpose: To compare an ACT-based group headache-specific intervention to wait-list control, in a randomized clinical trial, on disability, distress, medical utilization, functioning, and quality of life. Funding: "This work was part of a larger project supported by the European Union Structural Funds and National Funds [K3_01_06] via the collaborative program between Greece and Cyprus to Maria Karekla, PhD, Principal investigator." Included for: KQ1</p>	<p>Number of participants: 94 randomized Age (years): Mean 43.9 Gender (% female): 83.6 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: "1) meeting diagnostic criteria for Primary Headache based on the International Classification of Headache Disorders-II- ICHD-II30;2) older than 18 years; 3) sufficient Greek reading ability; and 4) stable pharmacotherapy and headache experience (both remained unchanged for 4 weeks prior to assessment)." Exclusion criteria: "1) had an active psychotic spectrum condition or manic episode, suicidal ideation/intent or substance use problems (particularly misuse of prescription head pain relievers) within the past 6 months; 2) had a history of seizure, facial neuralgia, or other secondary headache diagnoses (ie, conditions that might preclude the accuracy of primary headache diagnosis); 3) scored <20 on the Mini-Mental Status Examination suggesting significant cognitive impairment; 4) were living in nursing homes; 5) had multiple pain sides (pain experienced in multiple body sides or groups of muscles); 6) took part in other psychological interventions or counseling (particularly for managing headache) over the last 2 years; and 7) were pregnant or lactating."</p>	<p>Migraine type: Mixed (%s NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: NR Duration of migraine or headache (years): 18.4 Co-morbid headache disorders: NR Non-migraine participants included: 13% tension type headache; 6.5% other primary headaches</p>

Study Details	Patient Characteristics	Migraine Characteristics
<p>Wachholtz 2008²¹⁵⁻²¹⁷ Design: RCT Country: USA Purpose: To test whether including spiritual content into a meditative phrase represents a critical ingredient to the meditation process. To compare spiritual meditation to three contrasting conditions: relaxation and two types of secular meditation, a secular meditation that focused on an internally focused secular phrase and a secular meditation that focused on an externally focused phrase." Funding: Dissertation Fellowship from Bowling Green State University to AW and by an NIH-NIDA grant (#K23DA030397) Included for: KQ2</p>	<p>Number of participants: 92 randomized; 83 at baseline Age (years): Mean 19.1 Gender (% female): 90.4 Race: 73.5% White, 10.8% Black/African American, 1.2% American Indian/Alaska Native, 16.9% Other Ethnicity: 6% Hispanic/Latino Non-headache co-morbidities (%): NR Setting: College campus Inclusion criteria: "All participants met the criteria for vascular headache (migraine; mixed migraine + tension headache) based on the criteria of the International Headache Society (2004). Participants were at least 18 years old, and experienced at least two migraine headaches in the previous month." Exclusion criteria: "Participants could have no history of diabetes or Raynaud's syndrome diagnosis."</p>	<p>Migraine type: NR Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Participants asked to recall headache frequency from prior month Duration of migraine or headache (years): NR Co-morbid headache disorders: Migraine + Tension Type Headache Non-migraine participants included: NR</p>
<p>Wells 2021²¹⁸ Registration: NCT02695498 Design: RCT Country: USA Purpose: To determine if MBSR improves migraine outcomes and affective/cognitive processes compared with headache education. Funding: American Pain Society Grant from the Sharon S. Keller Chronic Pain Research Program, as well as the National Center for Complementary and Integrative Health K23AT008406, R21-AT010352, K99-R00 AT008238, and R01AT009693. Included for: KQ2</p>	<p>Number of participants: 96 randomized; 89 at baseline Age (years): Mean 44 Gender (% female): 92.1 Race: 88.8% White, 11.2% Black/African American Ethnicity: 6.7% Hispanic/Latino Non-headache co-morbidities (%): 38.2% Anxiety, 42.7% Depression Setting: Neurology/Headache clinic Inclusion criteria: Diagnosis of Migraine by ICHD-2a criteria; 4 to 20 migraines/month; ≥1 year of migraine (excluding medication overuse headache); ≥ 18 years old; Available for 8 weekly in-person classes Exclusion criteria: Regular mind-body practice; Unstable medical/psychiatric condition; Severe clinical depression (with Patient Health Questionnaire PHQ-9 >20); Non-migraine chronic pain; Active medication overuse headache MOH; Current/planned pregnancy; New migraine medication within 4 weeks; Unable to maintain stable medications; Failure to complete baseline headache logs; Absence of pain ratings to noxious (49°C) stimuli</p>	<p>Migraine type: Mixed (% NR) Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): 24 Co-morbid headache disorders: NR Non-migraine participants included: None</p>

Study Details	Patient Characteristics	Migraine Characteristics
Wittchen 1983 ²¹⁹ Design: RCT Country: Purpose: Assess the effectiveness of a biobehavioral treatment program Funding: NR Included for: KQ1	Number of participants: 20 randomized Age (years): Mean 39 Gender (% female): 115 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Medically oriented pain clinic Inclusion criteria: Referred by their general practitioners or other specialists, because they were suffering from severe long-term migraine attacks. Exclusion criteria: NR	Migraine type: NR Migraine diagnosis criteria: Neurological exam Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: 7 were also having tension type Non-migraine participants included: None
de Tommaso 2017 ²²⁰ Design: RCT Country: Italy Purpose: to test the efficacy of biofeedback training based on learning of habituation of the NBR (NBR biofeedback) compared with pharmacological (topiramate) treatment and NBR biofeedback plus topiramate treatment in a cohort of migraine without aura patients eligible for prophylaxis Funding: NR Included for: KQ2	Number of participants: 33 randomized Age (years): Mean 40.7 Gender (% female): 72.7 Race: NR Ethnicity: NR Non-headache co-morbidities (%): NR Setting: Neurology/Headache clinic Inclusion criteria: A diagnosis of migraine without aura (Headache Classification Committee, 2004) and eligibility for migraine prophylaxis (≥ 4 disabling migraine attacks per month or, if < 4 per month, in the case of poor response to symptomatic treatment), Exclusion criteria: general medical problems (including kidney stones) and psychiatric and other neurological diseases, psychoactive drug intake in the previous three months	Migraine type: Episodic Migraine diagnosis criteria: ICHD Method for establishing baseline frequency: Headache diary (4-week period) Duration of migraine or headache (years): NR Co-morbid headache disorders: NR Non-migraine participants included: None

Abbreviations: ACT=acceptance and commitment therapy; AHRQ=Agency for Healthcare Research and Quality; CAD=coronary artery disease; CBT=cognitive behavioral therapy; DSM=Diagnostic and Statistical Manual for Mental Disorders; HRSD= Hamilton Rating Scale for Depression; ICHD=International Classification of Headache Disorders; IHS=International Headache Society; KQ=key question; MBCT=mindfulness-based cognitive therapy; MIDAS=Migraine Disability Assessment; MIPAS=Migraine-Patient-Seminar program; MOH=medication overuse headache; NBR=nociceptive blink reflex; NCCIH=National Center for Complementary and Integrative Health; NIH=National Institutes of Health; NR=not reported; PHQ-9=patient health questionnaire; RCT=randomized controlled trial; SCID=Structured Clinical Interview for DSM; TAU=treatment-as-usual; TTH=tension-type headache; USA=United States of America

Table C-2. Treatment characteristics

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
Aguirrezabal 2019 ¹²⁸	Neuroscience education therapy (Education) 5 education sessions lasting 1 hour and 45 minutes: 4 given once a week and then 5th one month after the 4th session. Neuroscience-based information on the neurophysiology of pain and migraine were provided by means of audio–visual support.	No intervention/TAU	-	-	-	-	-	-
Albers 2015 ¹²⁹	Relaxation training+CBT+ Education Headache prevention lesson lasting 60 minutes included CBT, relaxation (muscle relaxation techniques), and education. Asked to also practice	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	exercises at home at least once a day.							
Allen 1998 ¹³⁰	<p>Thermal biofeedback (Biofeedback)</p> <p>6 sessions of thermal biofeedback lasting 40 minutes. The sessions were spaced at weekly intervals. A session consisted of 4 phases. First treatment session included a brief ""desensitization"" session in which the equipment was explained and attached. Asked to practice at home at least once daily (2 practices were recommended) for 10 minutes.</p>	<p>Thermal biofeedback+Education (Biofeedback+ Education)</p> <p>6 sessions of thermal biofeedback lasting 40 minutes. The sessions were spaced at weekly intervals. A session consisted of 4 phases. First treatment session included a brief ""desensitization"" session in which the equipment was explained and attached. Asked to practice at home at least once daily (2 practices were recommended) for 10 minutes.</p> <p>Parents received guideline asking them to</p>	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
		minimize their responses to pain behavior and to insist upon active participation in normal daily activities. They were also encouraged to praise and support practice of biofeedback and to encourage others to do the same.						
Blanchard 1978 ¹³¹	Thermal biofeedback+Autogenic training (Biofeedback+Relaxation training) 12 sessions lasting 50 minutes of thermal biofeedback and autogenic training conducted twice weekly over 6 weeks. Instructed to practice autogenic exercises and biofeedback for 5-10 minutes 2-3	PMR (Relaxation training) 12 sessions lasting 50 minutes of PMR conducted twice weekly over 6 weeks. Asked to practice relaxation exercises daily 20-30 minutes.	No intervention/TAU	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	times a day. Instructions were repeated for the first 2-3 sessions and then brief reminders.							
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education (Biofeedback+Relaxation training+CBT+Education) Website: Interactive instructions for pain management, graphic and interactive learning for problem solving, self assessments, text, audio and video advice 8 sessions (20 minutes each) over 4 weeks At least 5 sessions (20 minutes) over the following month. (Weeks 4 to 8) . Weekly checklist reminders	No intervention/TAU	-	-	-	-	-	-
Brown 1984 ¹³⁴	Guided imagery-1	Guided imagery-5	Sham (Attention)	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	hr/week for 4 weeks, using relaxing statements (MBSR) Guided imagery 1 hr/week for 4 weeks, using relaxing statements	hours over 4 weeks, imaging details of the scene (MBSR) Guided imagery 1 hr/week for 4 weeks, using relaxing statements	control/sham/p placebo) sham imagery					
Calhoun 2007 ¹³⁵	Sleep counseling (Education) 1 session of sleep counseling lasting approximately 20 minutes	Sham (Attention control/sham/p placebo) Participants given one-time sham instructions: 1. Schedule consistent supertime that varies <1 hr from day to day. 2. Perform acupressure as instructed for 2 minutes twice daily. 3. Record liquid consumption for 3 consecutive days. 4. Do 5 minutes of gentle range of motion exercises every morning. 5. Have 1	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
		protein serving at breakfast						
Connelly 2006 ¹³⁶	Relaxation training+CBT+ Education CD-ROM: 1 module per week for 4 weeks; modules took approximately 1 hour to complete and had homework Telephone: Weekly call to address questions and encourage reporting of headache frequency	No intervention/TA U	-	-	-	-	-	-
Cottrell 2007 ¹³⁷	Thermal biofeedback+E ducation+PMR +SMT+Activity pacing (Biofeedback+ Relaxation training+CBT+ Education) Intervention: Telephone calls (30 minutes) for education with counselor to review STOP migraine manual Control:	Attention control and education (Attention control/sham/p lacebo) Triptan rescue medications only plus some headache/med ication education	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	initiation with triptan therapy, in person visits at baseline, 1, 3, 8 months Both arms received weekly telephone calls							
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing (Relaxation training+CBT) CBT and relaxation (deep breathing and PMR training) carried out over 5 weeks in 3 face-to-face sessions lasting for 60 minutes, alternating with two phone calls. Given a copy of a patient manual and asked to complete headache and thought diaries at home. Also asked to practice relaxation at home with a CD for 15 minutes each day.	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
Cuneo 2023 ¹³⁹	Biofeedback	No intervention/TAU	-	-	-	-	-	-
D'Souza 2008 ¹⁴⁰	Written emotional disclosure (Other) Written emotional disclosure: given standard instructions for writing; 4 sessions (20 minutes each) over 2 weeks	Relaxation training Audiotape: for relaxation; were given audiotapes at the end to continue at home. 4 sessions (20 minutes each) over 2 weeks	Attention control (Attention control/sham/placebo) Time management writing control	-	-	-	-	-
Day 2014 ¹⁴¹	MBCT 8 group MBCT sessions of 2 hours once a week. Instructed to practice meditation in between group sessions for 45 minutes, 6 days per week. Completed a daily online meditation practice diary. Weekly reminders and graphs summarizing headache activity were sent by email.	No intervention/TAU	-	-	-	-	-	-
Dindo 2020 ¹⁴⁵	Education+ACT	Relaxation training+Educa	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	ACT-ED workshops lasted 5–6 hours and involved training in ACT and education about migraine.	tion The S-ED workshop also lasted about 5–6 hours. The same educational topics listed above about migraine were presented. Diaphragmatic breathing was taught and practiced; and a passive progressive relaxation exercise (approximately 30 min) was completed.						
Dittrich 2008 ¹⁴⁶	PMR+Exercise (Relaxation training+Other) Twice-weekly 60 minute indoor aerobic exercise program over 6 weeks. Included 45 minutes of gymnastics with music and 15 minutes of PMR.	No intervention/TA U	-	-	-	-	-	-
Fichtel 2001 ¹⁴⁷	PMR (Relaxation training)	No intervention/TA U	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	8-10 sessions of relaxation, including PMR, lasting 45 minutes each. Both individual and group formats. Sessions conducted in 10 sequential steps.							
Flynn 2019 ¹⁴⁸	Hypnotherapy Website: patients logged on to listen to an MP track 3 times per week (for 4 weeks) Telephone: 10 minute introduction Email - reminders	No intervention/TAU	-	-	-	-	-	-
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR (Relaxation training+CBT+Education) 5 sessions lasting 2 hours of CBT, PMR, and education. Asked to complete a daily headache diary and PMR between sessions and after each	Education+PMR (Relaxation training+Education) Received brochures including detailed information on the physiological and psychological aspects of migraine and migraine	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	session. Also given topic-related homework. At the end of the 5th session, received brochures including detailed information on the physiological and psychological aspects of migraine and migraine medication.	medication. Instructions for exercises to minimize drug consumption and instructions for PMR were included.						
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback (Biofeedback+Relaxation training+Education) Children received 20 sessions (for a total of 900 minutes) of simultaneous EMG and thermal biofeedback, along with other strategies (identification	CBT+Education+PMR (Relaxation training+CBT+Education) MIPAS-Family program sessions (described as sensory coping training [SCT]) divided into three modules: diagnostic, education, and behavioral training. Child training: 8 sessions, 90 minutes each Parent training: 4 sessions, 120	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	of psychophysiological relationships, relaxation, etc.).	minutes each Child and parent components were alternated.						
Grazzi 2021 ¹⁵¹	ACT 6 weekly group sessions lasting 90 minutes of ACT, as well as 2 supplementary booster sessions conducted at 2 and 4 weeks after the last session. Also received TAU.	No intervention/TAU	-	-	-	-	-	-
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management (Relaxation training+Education) Website: Treatment program and diary 53 pages on stress physiology, physical activity, diet, emotions,	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy (Relaxation training+Education+Other) Website: Treatment program and diary 53 pages on stress physiology, physical	Minimal intervention A CD containing a 15-minute program for muscular relaxation	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	attitudes; practice muscle relaxation program (provided on CD). Patients asked to enter diary data daily or transfer from paper to online within 1 week. No requirements for amount of time spent	activity, diet, emotions, attitudes; practice muscle relaxation program (provided on CD). Patients asked to enter diary data daily or transfer from paper to online within 1 week. No requirements for amount of time spent. Patients received adjunctive hand massages for 15 minutes per session.						
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+R relaxation training (Biofeedback+ Relaxation training) In person visits: Introduced relaxation, thermal biofeedback with 2 visits early on; 1 final visit performed at	Attention control and education (Attention control/sham/p placebo) Abortive medication (ergotamine tartrate) accompanied by compliance training.	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	end of trial. Audiotapes: provided for home use Telephone: Brief consultations at the end of 2nd and 6th week of treatment							
Holroyd 2010 ¹⁵⁸	<p>Propranolol (Pharmacologi c)</p> <p>Started with one capsule (60 mg long acting propranolol hydrochloride) and increased to three capsules (180 mg) at week 12 as tolerated. If at least two capsules not tolerated, switched to nadolol and initially received a single 40mg capsule. The dose was increased at the next visit to two capsules (80 mg) as tolerated. At week 12, the</p>	<p>CBT+PMR+Pr eference- based/tailored (Relaxation training+CBT+ Tailored)</p> <p>Started with one capsule (propranolol- matched placebo) and increased to three capsules at week 12 as tolerated. If at least two capsules not tolerated, switched to nadaol- matched placebo. Initially received a capsule of matched placebo. The dose was increased at the next visit to two capsules</p>	<p>Propranolol+C BT+PMR+Pref erence- based/tailored (Relaxation training+Phar macologic+CB T+Tailored)</p> <p>Started with one capsule (60 mg long acting propranolol hydrochloride) and increased to three capsules (180 mg) at week 12 as tolerated. If at least two capsules not tolerated, switched to nadolol and initially received a single 40mg capsule. The dose was increased at</p>	<p>Placebo (Attention control/sham/p lacebo)</p> <p>Started with one capsule (60 mg long acting propranolol- matched placebo) and increased to three capsules at week 12 as tolerated. If at least two capsules not tolerated, switched to nadolol- matched placebo and initially received a single capsule. The dose was increased at the next visit to two capsules as tolerated. At week 12, the</p>	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	dose was stabilized at the highest tolerated level. During evaluation, an increase to four capsules of long acting propranolol hydrochloride (240 mg) or three capsules of nadolol (120 mg) was permitted. Instructional handouts and three monthly phone calls also provided.	as tolerated. At week 12, the dose was stabilized at the highest tolerated level. In the evaluation phase, an increase to four capsules of propranolol-matched placebo or three capsules of nadolol-matched placebo was permitted. Instructional handouts and three monthly phone calls also provided. Behavioral migraine management: delivered over four clinic visits. Relaxation skills are taught in first session; CBT is introduced in the second; and the third allows for choice between continuing with previously learned skills,	the next visit to two capsules (80 mg) as tolerated. At week 12, the dose was stabilized at the highest tolerated level. During evaluation, an increase to four capsules of long acting propranolol hydrochloride (240 mg) or three capsules of nadolol (120 mg) was permitted. Instructional handouts and three monthly phone calls also provided. Behavioral migraine management: delivered over four clinic visits. Relaxation skills are taught in first session; CBT is introduced in the second; and the third allows for choice between continuing with	dose was stabilized at the highest tolerated level. During evaluation, an increase to four capsules of propranolol-matched placebo or three capsules of nadolol-matched placebo was permitted. Instructional handouts and three monthly phone calls also provided.				

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
		introducing cognitive-behavioral stress management, or introducing thermal biofeedback Accompanied by a workbook and 10 audio lessons.	previously learned skills, introducing cognitive-behavioral stress management, or introducing thermal biofeedback Accompanied by a workbook and 10 audio lessons.					
Janssen 1986 ¹⁶¹	PMR (Relaxation training) 12 weekly sessions using the method of Bernstein 1973	Autogenic training (Relaxation training) 12 weekly sessions using the method of Schultz 1932	-	-	-	-	-	-
Kewman 1980 ¹⁶²	Thermal biofeedback (Biofeedback) 10 weekly laboratory sessions of skin temperature biofeedback during a 9 week + 1 day period. Participants were reminded to send in their diaries and were instructed to practice at	Sham (Attention control/sham/p placebo) 10 weekly laboratory sessions of temperature cooling (sham) biofeedback during a 9 week +1 day period. Participants were reminded to send in their diaries and were instructed to	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	home and at the onset of migraine symptoms.	practice at home and at the onset of migraine symptoms.						
Klan 2022 ¹⁶³	PMR (Relaxation training) 7 sessions of PMR. Encouraged to practice on their own. From the 3rd session onward, given logs to document weekly practice (not mandatory, but recommended) .	Relaxation training+CBT+ Education A mix of behavioral approaches (CBT, relaxation, and education) provided across 7 sessions that each focused on an aspect of migraine management. At the end of each session, a brief relaxation method was taught.	No intervention/TA U	-	-	-	-	-
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+ Education Website: Online portal with videos, interactive exercises, and homework 8 Lessons (1 hour each) 2 relaxation exercises per day (30	No intervention/TA U	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	minutes each) 1-2 hours of cognitive behavioral homework Telephone: Coaching for behavioral therapy by trained coach (post graduate psychologist or masters level psychology student supervised by clinical psychologist). On average 90-120 minutes total, delivered weekly or biweekly							
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+R elaxation training+CBT+ Meditation (Biofeedback+ Relaxation training+CBT+ MBSR) Treatment book including instructions on cognitive restructuring, thermal biofeedback, and a relaxation	Attention control (Attention control/sham/p lacebo) Book about about symptoms, diagnosis, and treatment of headaches	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	exercise which combines components of meditation and progressive relaxation.							
Kropp 1997 ¹⁶⁹	Biofeedback 10 biofeedback sessions over 3 months. Patients were taught to auto-regulate the blood-volume-pulse activity of the superficial temporal artery.	Relaxation training+CBT 10 CBT group sessions over 3 months. 3-4 patients per group and two therapists. Participants were taught to cope with stress using relaxation techniques.	-	-	-	-	-	-
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training (Biofeedback+Relaxation training) Autogenic training: 10 sessions lasting 40 minutes over 7 weeks. 2 sessions per week for the first 3 weeks, one per week for the last 4 weeks. First 9 sessions were divided into 3	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	phases. 10th session was posttreatment self-control. Biofeedback: 15 minutes of skin temperature biofeedback during 3rd phase							
Labbe 1995 ¹⁷¹	Thermal biofeedback+Autogenic training (Biofeedback+Relaxation training) Biofeedback: 10 sessions lasting 45 minutes over 7 weeks. 2 sessions per week for the first 3 weeks, then one per week for the last 4 weeks. Given autogenic training instructions. Instructions about biofeedback and autogenic training were repeated during the first 4 sessions. Headache	Autogenic training (Relaxation training) Given autogenic training instructions. Instructions about autogenic training were repeated during the first 4 sessions then briefly mentioned during the remainder of the sessions.	No intervention/TAU	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	booklets were reviewed and home practice was discussed.							
Lemstra 2002 ¹⁷²	<p>Relaxation training+CBT+ Education+Exercise+Massage therapy+Physical therapy (Relaxation training+CBT+ Education+Other)</p> <p>A neurologist intake, physical therapist intake, 18 group-supervised exercise therapy sessions with an exercise therapist, 2 group lectures with a registered psychologist, 1 group lecture with a dietitian, 2 massage therapy sessions, and a neurologist and physical therapist discharge.</p>	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
Matchar 2008 ¹⁷³	<p>Relaxation training+Education</p> <p>Individual or group headache education session that included materials on relaxation techniques. Also taught how to use a headache diary. Follow-up visits (in-person or phone) at 1, 3, and 6 months.</p>	No intervention/TAU	-	-	-	-	-	-
Mathew 1981 ¹⁷⁴	<p>Relaxation training+Biofeedback (Biofeedback+Relaxation training)</p> <p>Biofeedback: 10 one-hour sessions of combined electromyographic and temperature regulation training. Given relaxation tapes, autogenic phrases and skin</p>	<p>Relaxation training+Amitriptyline+Biofeedback (Biofeedback+Relaxation training+Pharmacologic)</p> <p>Amitriptyline was combined with biofeedback training.</p>	<p>Relaxation training+Propranolol+Amitriptyline+Biofeedback (Biofeedback+Relaxation training+Pharmacologic)</p> <p>Propranolol, amitriptyline, and biofeedback were used concomitantly.</p>	<p>Relaxation training+Propranolol+Biofeedback (Biofeedback+Relaxation training+Pharmacologic)</p> <p>Propranolol was combined with biofeedback training.</p>	<p>Propranolol (Pharmacologic)</p> <p>Propranolol 20 mg three times a day to start with and increased to 40 mg three times a day or four times a day within the first month of therapy depending on individual tolerance.</p>	<p>Amitriptyline (Pharmacologic)</p> <p>Amitriptyline 25 mg at bedtime for the first two weeks, increased to 50-75 mg at bedtime in the first month according to individual tolerance and side effects.</p>	<p>Propranolol+Amitriptyline (Pharmacologic)</p> <p>Propranolol was combined concomitantly with amitriptyline.</p>	<p>No intervention/TAU</p> <p>Oral or rectal ergotamine with or without anti-nausea medications</p>

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	temperature monitoring finger bands and instructed to practice biofeedback at least once a day for a minimum of 30 minutes.							
Minen 2020a ¹⁷⁵	PMR (Relaxation training) RELAXaHEAD app Instructed to perform PMR at least 20 minutes daily for 90 days	No intervention/TAU	-	-	-	-	-	-
Minen 2020b ¹⁷⁶	PMR (Relaxation training) RELAXaHEAD app Instructed to perform PMR at least 15 minutes daily for 90 days	No intervention/TAU	-	-	-	-	-	-
Minen 2021 ¹⁷⁸	HRV biofeedback (Biofeedback) HeartMath Sensor attached to earlobe transmits data to app Instructed to	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	do biofeedback at least 2x per day for five minutes, or once a day for ten minutes daily for 60 days. Email: reminders (every 3 days) for adherence.							
Mérelle 2008 ¹⁷⁹	<p>Autogenic training+Educa tion (Relaxation training+Educa tion)</p> <p>7 behavioral training sessions (autogenic training and education) lasting 2 hours over 10 weeks. Received a written manual, an organizer for homework assignments, diary ratings and self-evaluations, and a CD-ROM with auditory relaxation exercises.</p>	No intervention/TA U	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
Odawara 2015 ¹⁸²	Thermal biofeedback+PMR+EMG biofeedback (Biofeedback+Relaxation training) 8 guided sessions of EMG, temperature biofeedback, and PMR lasting 30 minutes accompanied by home practice of PMR for 10 weeks.	No intervention/TAU	-	-	-	-	-	-
Pickering 2012 ¹⁸³	Relaxation training 8 weekly sessions of relaxation techniques lasting for 60 minutes over 2 months.	No intervention/TAU Only background intervention—Pharmacoprevention (betablockers OR oxyton)	-	-	-	-	-	-
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback (Biofeedback+Relaxation training+Pharmacologic+CB	Amitriptyline+Education (Pharmacologic+Education) 8 weekly, 1-hour individual education sessions, followed by monthly	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	<p>T)</p> <p>8 weekly, 1-hour individual modified CBT sessions, followed by monthly booster sessions of similar duration at weeks 12 and 16, and at the 3-, 6-, and 9-month follow-up points. CBT had a biofeedback component that included thermal and electromyographic monitoring of the relaxation response. Amitriptyline was titrated to a goal dose of 1 mg/kg/d in a standardized protocol over the first 8 weeks, then held at this maintenance dose from week 8 to week 20. The dose was increased by 0.25 mg/kg at</p>	<p>booster sessions of similar duration at weeks 12 and 16, and at the 3-, 6-, and 9-month follow-up points. Included discussion of headache-related education topics and nonspecific support along with equal time and attention from a trained therapist. Amitriptyline was titrated to a goal dose of 1 mg/kg/d in a standardized protocol over the first 8 weeks, then held at this maintenance dose from week 8 to week 20. The dose was increased by 0.25 mg/kg at weeks 0, 2, 4, and 6.</p>						

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	weeks 0, 2, 4, and 6.							
Rapoff 2014 ¹⁸⁸	<p>Relaxation training+CBT+ Education+ Pain management education (Relaxation training+CBT+ Education)</p> <p>CD ROM: 1 lesson per day for 4 weeks, simple quizzes to assess processing of information; homework assignments required. Telephone: Weekly call to encourage record keeping</p>	<p>Education control (Minimal intervention)</p> <p>Acute medications or preventative medications for participants with frequency of headache greater than one per week as prescribed by treating neurologist. General educational CD provided.</p>	-	-	-	-	-	-
Rausa 2016 ¹⁸⁹	<p>EMG biofeedback (Biofeedback)</p> <p>2 assessment sessions, 9 weekly sessions of EMG biofeedback divided into 3 phases, and a reassessment session. All sessions lasted 60 minutes.</p>	<p>Attention control (Attention control/sham/placebo)</p> <p>9 weekly sessions with a psychologist in which participants were interviewed about their previous week's headaches, their mood,</p>	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
		and their analgesic intake.						
Reich 1989 ¹⁹⁰	<p>Thermal biofeedback (Biofeedback)</p> <p>Received thermal biofeedback. Subjects were subdivided into one of two groups: those receiving 15 treatment sessions or less and those receiving over 15 treatments. Each treatment session was administered once per week. Asked to practice training procedures at home three times per day for ten minutes at a time.</p>	<p>Micro-electrical therapy (Other)</p> <p>Received either traditional TENS or electrical neurotransmitter modulation, either singly or in combination once per week. Subjects were subdivided into one of two groups: those receiving 15 treatment sessions or less and those receiving over 15 treatments. Each treatment session was administered once per week. Administered treatments prophylactically once daily for 1/2 hour according to the specific electrode placements/uni</p>	<p>Relaxation training</p> <p>Received either cognitively oriented psychotherapy, hypnosis, or autogenic training/progressive muscle relaxation training, either singly or in combination. Subjects were subdivided into one of two groups: those receiving 15 treatment sessions or less and those receiving over 15 treatments. Each treatment session was administered once per week. Asked to practice training procedures at home three times per day for ten minutes at a time.</p>	<p>Preference-based/tailored (Tailored)</p> <p>Received a combination of two of the following interventions: "Relaxation" (cognitively oriented psychotherapy, hypnosis, or autogenic training/progressive muscle relaxation training, either singly or in combination), "Biofeedback" (thermal biofeedback), "Micro-electrical therapy" (traditional TENS or electrical neurotransmitter modulation, either singly or in combination). Subjects were subdivided into one of two groups: those receiving 15</p>	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
		t settings used in treatment.		treatment sessions or less and those receiving over 15 treatments. Each treatment session was administered once per week. Asked to practice training procedures at home three times per day for ten minutes at a time.				
Richardson 1989 ¹⁹¹	CBT+PMR- Clinic format (Relaxation training+CBT) 8 weekly sessions of a clinic-based program that included CBT and PMR lasting 60 minutes. Homework was assigned weekly, including audio tapes for PMR.	CBT+PMR- Self-administered (Relaxation training+CBT) CBT and PMR delivered via a self-help manual and audiotapes. Seen for 30 minutes before beginning treatment and again during the 5th week of treatment. Homework was assigned.	No intervention/TAU	-	-	-	-	-
Richter 1986 ¹⁹²	CBT "Thinking straight" program that	PMR+Deep breathing (Relaxation training)	Attention control (Attention control/sham/placebo)	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	emphasized altering maladaptive thought processes. Used elements of cognitive restructuring, the cognitive control of pain, fantasy, simple problem solving, and stress-inoculation training. Personalized cards containing coping statements were prepared for each subject.	Taught sequential relaxation with and without tensing and the use of deep breathing to achieve total body relaxation. Instructed to practice daily.	"Stress reduction training" providing general education and sham "coping skills"					
Rothrock 2006 ¹⁹³	Education 3 education ("headache school") classes lasting 90 minutes	Education control (Minimal intervention) Participants provided general educational materials.	-	-	-	-	-	-
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback (Biofeedback+ Relaxation training) Relaxation with autogenic	Thermal biofeedback+Relaxation training (Biofeedback+ Relaxation training) Relaxation	Relaxation training Relaxation with autogenic phrases	No intervention/TAU No treatment	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	phrases plus EMG biofeedback	with autogenic phrases plus thermal biofeedback						
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse (Biofeedback+ CBT) Multiple sessions of stress management training and biofeedback. Asked to complete diaries and homework assignments.	Metoprolol (Pharmacologic) Metoprolol-50-100 mg daily depending on weight	PMR+SMT (Relaxation training+CBT) Multiple sessions of stress management training and PMR. Asked to complete diaries and homework assignments.	-	-	-	-	-
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT (Biofeedback+ Relaxation training+CBT) 4 sessions of HWB over 6 weeks, consisting of cognitive-behavioral stress management training and 30 minutes of thermal biofeedback, as well as PMR, imagery training, and	Sham (Attention control/sham/placebo) 4 sessions of HCB over 6 weeks. Participants were trained in handcooling strategies such as imagery of cold places and peripheral vasoconstriction.	No intervention/TAU	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	deep breathing techniques. Asked to practice for at least 15 minutes daily and were provided with a portable biofeedback monitor. Home practice was recorded on a daily monitoring sheet.							
Seminowicz 2020 ¹⁹⁸	Education+SM T (CBT+Education) Stress management training included 12 sessions over 4 months focused on didactic content about the role of stress and other triggers in headaches	Education+MBSR 8 weekly sessions of MBSR+ lasting 2 hours, then bi-weekly sessions for another 8 weeks (12 sessions over 4 months).	-	-	-	-	-	-
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR (CBT+Education+MBSR) 8 weekly sessions of	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	MBCT-M lasting 75-minute over 8–10 weeks. Also completed a daily headache diary and mindfulness log.							
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR (CBT+MBSR) 8 weekly groups sessions of MBCT lasting 2.5 hours. A booster session was held after 6 months. Encouraged to practice at home 30-45 minutes daily.	No intervention/TAU	-	-	-	-	-	-
Smitherman 2016 ²⁰⁴	Non-headache CBT Behavioral insomnia treatment (CBTi) that included four instructions in stimulus control and one in sleep restriction. At subsequent sessions, sleep diaries from the prior	Sham (Attention control/sham/placebo) Sham control involving acupuncture, stretching, general sleep/diet advice	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	2 weeks were reviewed.							
Sorbi 1984 ²⁰⁶	<p>Thermal biofeedback+CBT+PMR (Biofeedback+Relaxation training+CBT)</p> <p>Cognitive behavioral therapy was administered as combined cognitive and social skill program with 9 weekly sessions of 1 hour. Relaxation training consisted of autogenic suggestions directed successively at body parts from the feet upwards to the head evoking heaviness, warmth, heaviness and warmth. Participants were provided with tapes, and home practice was required at least twice a day. Biofeedback</p>	<p>CBT+PMR (Relaxation training+CBT)</p> <p>Cognitive behavioral therapy was administered as combined cognitive and social skill program with 9 weekly sessions of 1 hour. Relaxation training consisted of autogenic suggestions directed successively at body parts from the feet upwards to the head evoking heaviness, warmth, heaviness and warmth. Participants were provided with tapes, and home practice was required at least twice a day.</p>	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	was administered as once a week finger skin temperature trials, immediately after the relaxation training given that same week.							
Sorbi 1986 ²⁰⁷	Education+SM T (CBT+Education) 9 weekly sessions of stress coping training	Autogenic training+Education (Relaxation training+Education) 9 weekly sessions of autogenic training based on the method by Schultz 1932	-	-	-	-	-	-
Underwood 2022 ²⁰⁹	Education Telephone: 1 on 1 visit with nurse who provided education on drug management lifestyle change and goal setting In person: 2 group sessions (8-10 persons) 1 week apart.	Minimal intervention	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
Varkey 2011 ²¹²	Exercise (Other) Group exercise training with a registered physiotherapist 3 times a week for 40 minutes.	Topiramate (Pharmacologic) Topiramate: dosage was slowly increased by 25 mg every week until the dosage reached the highest dose that the individual could tolerate, with a maximum of 200 mg/day. Given written information about the drug and were allowed to call the neurologist during the treatment period and schedule a visit if needed.	Relaxation training Relaxation program based on common forms of relaxation, breathing, and stress-management techniques and included a series of 6 exercises Individual appointment with a registered physiotherapist once a week. Asked to practice at home every day with a CD.	-	-	-	-	-
Vasiliou 2021 ²¹³	ACT 8 weekly group sessions of ACT (lead by a treatment guide) lasting 1.5 hours.	No intervention/TAU	-	-	-	-	-	-
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation (MBSR)	Meditation-Internal secular meditation (MBSR)	Meditation-External secular meditation (MBSR)	PMR (Relaxation training) Taught PMR	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
	Taught spiritual meditation and asked to practice for 20 minutes daily for 30 days	Taught internal secular meditation and asked to practice for 20 minutes daily for 30 days	Taught external secular meditation and asked to practice for 20 minutes daily for 30 days	and asked to practice 20 minutes daily for 30 days.				
Wells 2021 ²¹⁸	Education 8 weekly classes that included education lasting 2 hours, plus a 1 day optional "retreat." Content included education about migraine pathophysiology, headache triggers, stress.	MBSR 8 weekly classes that included MBSR lasting 2 hours, plus a 1 day optional "retreat." Given the same standard guided electronic audio recordings and encouraged to practice at home for 30 minutes per day, at least 5 additional days per week.	-	-	-	-	-	-
Wittchen 1983 ²¹⁹	Relaxation training+CBT+ Education 10 sessions of treatment including aspects of CBT, relaxation, and education	No intervention/TAU	-	-	-	-	-	-

Study	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Intervention 5	Intervention 6	Intervention 7	Intervention 8
de Tommaso 2017 ²²⁰	Biofeedback NBR habituation biofeedback sessions 3 times a week for 3 months.	Biofeedback+T opiramate (Biofeedback+ Pharmacologic) Topiramate 50 mg (b.i.d.) over 3 months. NBR habituation biofeedback sessions 3 times a week for 3 months.	Topiramate (Pharmacologi c) Topiramate 50 mg (b.i.d.) over 3 months	-	-	-	-	-

Abbreviations: ACT=acceptance and commitment therapy; CBT=cognitive behavioral therapy; CD-ROD=compact disc read-only memory; EMG=electromyography; MBSR=mindfulness-based stress reduction; PMR=progressive muscle relaxation; SMT=stress management therapy; TAU=treatment-as-usual

Table C-3. Outcomes and results

Reference	Intervention Group and Outcome	Results
Aguirrezabal 2019 ¹²⁸	Neuroscience education therapy Functional status: MIDAS	Change from baseline: 12 month(s) The MIDAS scores of the five questions related to the level of disability decreased by at least 50% in 68.9% (n = 37) of patients in the intervention group., n=53
Aguirrezabal 2019 ¹²⁸	No intervention/TAU Functional status: MIDAS	Change from baseline: 12 month(s) The MIDAS scores of the five questions related to the level of disability decreased by at least 50% in 34.6% of those in the control group (n = 18)., n=52
Aguirrezabal 2019 ¹²⁸	Neuroscience education therapy Other headache: Other: Reduction of headache duration by ≥50%	Reducing the duration of the headache (in days) by ≥50% from baseline to 12mos: 71.9%
Aguirrezabal 2019 ¹²⁸	No intervention/TAU Other headache: Other: Reduction of headache duration by ≥50%	Reducing the duration of the headache (in days) by ≥50% from baseline to 12mos: 22.4%
Aguirrezabal 2019 ¹²⁸	Neuroscience education therapy Other headache: Other: Reduction of headache intensity by ≥50%	Reducing the intensity of the headache by ≥50% from baseline to 12mos: 24.6%
Aguirrezabal 2019 ¹²⁸	No intervention/TAU Other headache: Other: Reduction of headache intensity by ≥50%	Reducing the intensity of the headache by ≥50% from baseline to 12mos: 3.4%
Aguirrezabal 2019 ¹²⁸	Neuroscience education therapy Other headache: Other: Reduction of medication intake by ≥50%	Reducing the medication intake by ≥50% from baseline to 12mos: 73.7%
Aguirrezabal 2019 ¹²⁸	No intervention/TAU Other headache: Other: Reduction of medication intake by ≥50%	Reducing the medication intake by ≥50% from baseline to 12mos: 22.8%
Albers 2015 ¹²⁹	Relaxation training+CBT+Education Adverse events: Other: drop out	286/813
Albers 2015 ¹²⁹	No intervention/TAU Adverse events: Other: drop out	311/861

Reference	Intervention Group and Outcome	Results
Allen 1998 ¹³⁰	Thermal biofeedback	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 4.2, SD: 2.4, n=13
Allen 1998 ¹³⁰	Thermal biofeedback+Education	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 4.1, SD: 2.2, n=14
Allen 1998 ¹³⁰	Thermal biofeedback	Follow-up: 10 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 3.4, SD: 2.9, n=13
Allen 1998 ¹³⁰	Thermal biofeedback+Education	Follow-up: 10 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 0.9, SD: 1.9, n=14
Allen 1998 ¹³⁰	Thermal biofeedback	Follow-up: 18 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 2.2, SD: 1.4, n=13
Allen 1998 ¹³⁰	Thermal biofeedback+Education	Follow-up: 18 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 0.8, SD: 0.9, n=14
Allen 1998 ¹³⁰	Thermal biofeedback	Follow-up: 58 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 1.6, SD: 1.6, n=10
Allen 1998 ¹³⁰	Thermal biofeedback+Education	Follow-up: 58 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 0.9, SD: 0.9, n=11
Blanchard 1978 ¹³¹	Thermal biofeedback+Autogenic training	Baseline
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 3.2, Precision NR, n=11
Blanchard 1978 ¹³¹	PMR	Baseline
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 2.7, Precision NR, n=11
Blanchard 1978 ¹³¹	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 2.9, Precision NR, n=15
Blanchard 1978 ¹³¹	Thermal biofeedback+Autogenic training	Follow-up: 6 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 1.4, Precision NR, n=10
Blanchard 1978 ¹³¹	PMR	Follow-up: 6 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 0.5, Precision NR, n=10
Blanchard 1978 ¹³¹	No intervention/TAU	Follow-up: 6 week(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 1.7, Precision NR, n=10

Reference	Intervention Group and Outcome	Results
Blanchard 1978 ¹³¹	Thermal biofeedback+Autogenic training Other headache: Other: Medication Index	Medication Index defined as: Amount of medication used and relative potency: all medications rated for potency on a scale ranging from 1 to 7; medication index calculated by multiplying potency by number of pills taken. Biofeedback: Baseline: 14; 6 weeks: 4.6
Blanchard 1978 ¹³¹	PMR Other headache: Other: Medication Index	Medication Index defined as: Amount of medication used and relative potency: all medications rated for potency on a scale ranging from 1 to 7; medication index calculated by multiplying potency by number of pills taken. Relaxation Baseline: 10.3; 6 weeks: 0.1
Blanchard 1978 ¹³¹	No intervention/TAU Other headache: Other: Medication Index	Medication Index defined as: Amount of medication used and relative potency: all medications rated for potency on a scale ranging from 1 to 7; medication index calculated by multiplying potency by number of pills taken. Wait list Baseline: 12.7; 6 weeks: 9.3
Bromberg 2012 ¹³³	No intervention/TAU Adverse events: Other: No measurement	The study states no adverse events were reported
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Adverse events: Other: No measurement	The study states no adverse events were reported
Bromberg 2012 ¹³³	No intervention/TAU Anxiety, depression, or sleep: Other: Depression/Anxiety/Stress Scale (DASS)	Depression/Anxiety/Stress Scale: Anxiety: Baseline 19.52 (SE 0.83) 8 weeks: 19.8 (SE 0.76) 12 weeks: 19.6 (SE 0.8) 24 weeks: 19.4 (SE 0.5) Depression: Baseline : 21.4 (SE 1) 8 weeks: 21.4 (SE 0.9) 12 weeks: 21.4 (SE 0.84) 24 weeks: 22.03

Reference	Intervention Group and Outcome	Results
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Anxiety, depression, or sleep: Other: Depression/Anxiety/Stress Scale (DASS)	Depression/Anxiety/Stress Scale: Anxiety: Baseline : 20.42 (SE 0.8) 8 weeks: 18.9 (SE 0.8) 12 weeks: 18.5 (SE 0.86) 24 weeks: 18.7 (SE 1) Depression: Baseline : 22.8 (SE 1) 8 weeks: 20.4 (SE 1) 12 weeks: 18.6 (SE 1) 24 weeks: 19.7 (SE 1.2)
Bromberg 2012 ¹³³	No intervention/TAU Functional status: MIDAS	Baseline Mean: 51.6, SE: 4.7, n=91
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Functional status: MIDAS	Baseline Mean: 48.7, SE: 4.8, n=89
Bromberg 2012 ¹³³	No intervention/TAU Functional status: MIDAS	Follow-up: 3 month(s) Mean: 42.5, SE: 5.3, n=73
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Functional status: MIDAS	Follow-up: 3 month(s) Mean: 42.2, SE: 5.8, n=51
Bromberg 2012 ¹³³	No intervention/TAU Functional status: MIDAS	Follow-up: 4 week(s) Mean: 46, SE: 4.8, n=87
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Functional status: MIDAS	Follow-up: 4 week(s) Mean: 42.5, SE: 5.1, n=68
Bromberg 2012 ¹³³	No intervention/TAU Functional status: MIDAS	Follow-up: 6 month(s) Mean: 39.5, SE: 4.9, n=74
Bromberg 2012 ¹³³	Relaxation training+Biofeedback+CBT+Education Functional status: MIDAS	Follow-up: 6 month(s) Mean: 36.1, SE: 5.8, n=46
Brown 1984 ¹³⁴	Guided imagery-1 hr/week for 4 weeks, using relaxing statements Migraine frequency: Count: Headache(s)-Total-days-1	Percent CfB: 12 week(s) Mean: -36.69, SE: 14.55, n=13

Reference	Intervention Group and Outcome	Results
Brown 1984 ¹³⁴	Guided imagery-5 hours over 4 weeks, imaging details of the scene Migraine frequency: Count: Headache(s)-Total-days-1	Percent CfB: 12 week(s) Mean: -45.69, SE: 10.58, n=13
Brown 1984 ¹³⁴	Sham Migraine frequency: Count: Headache(s)-Total-days-1	Percent CfB: 12 week(s) Mean: -10.69, SE: 17.46, n=13
Brown 1984 ¹³⁴	Guided imagery-1 hr/week for 4 weeks, using relaxing statements Other headache: Other: % improvement in headache intensity	N=13 in this group. At 12 weeks after the start of treatment (what the authors called followup), the % improvement in headache intensity was 1.15% (SE 5.97%). Did not report whether this specific outcome differed between groups (the authors only performed MANOVA for all outcomes simultaneously)
Brown 1984 ¹³⁴	Guided imagery-5 hours over 4 weeks, imaging details of the scene Other headache: Other: % improvement in headache intensity	N=13 in this group. At 12 weeks after the start of treatment (what the authors called followup), the % improvement in headache intensity was 0.54% (SE 6.74%). Did not report whether this specific outcome differed between groups (the authors only performed MANOVA for all outcomes simultaneously)
Brown 1984 ¹³⁴	Sham Other headache: Other: % improvement in headache intensity	N=13 in this group. At 12 weeks after the start of treatment (what the authors called followup), the % improvement in headache intensity was -20.31% indicating that on average intensity worsened (SE 10.96%). Did not report whether this specific outcome differed between groups (the authors only performed MANOVA for all outcomes simultaneously)
Calhoun 2007 ¹³⁵	Sleep counseling Migraine frequency: Count: Headache(s)-Total-month	Baseline Mean: 24.2, Precision NR, n=23
Calhoun 2007 ¹³⁵	Sham Migraine frequency: Count: Headache(s)-Total-month	Baseline Mean: 23.2, Precision NR, n=23
Calhoun 2007 ¹³⁵	Sleep counseling Migraine frequency: Count: Headache(s)-Total-month	Follow-up: 6 week(s) Mean: 17.4, Precision NR, n=20
Calhoun 2007 ¹³⁵	Sham Migraine frequency: Count: Headache(s)-Total-month	Follow-up: 6 week(s) Mean: 23.9, Precision NR, n=16
Connelly 2006 ¹³⁶	Relaxation training+CBT+Education Functional status: PedMIDAS	Baseline Mean: 14.2, SD: 8.2, n=17
Connelly 2006 ¹³⁶	No intervention/TAU Functional status: PedMIDAS	Baseline Mean: 15.1, SD: 16.1, n=20

Reference	Intervention Group and Outcome	Results
Connelly 2006 ¹³⁶	Relaxation training+CBT+Education	Follow-up: 1 month(s)
	Functional status: PedMIDAS	Mean: 12.2, SD: 9.9, n=14
Connelly 2006 ¹³⁶	No intervention/TAU	Follow-up: 1 month(s)
	Functional status: PedMIDAS	Mean: 10.7, SD: 11.6, n=17
Connelly 2006 ¹³⁶	Relaxation training+CBT+Education	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 3.8, SD: 1.7, n=17
Connelly 2006 ¹³⁶	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 4.3, SD: 2.1, n=20
Connelly 2006 ¹³⁶	Relaxation training+CBT+Education	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 2.3, SD: 1.8, n=14
Connelly 2006 ¹³⁶	No intervention/TAU	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 3.7, SD: 1.8, n=17
Connelly 2006 ¹³⁶	Relaxation training+CBT+Education	Measured on VAS ranging from 0 to 6 (this is a nonstandard range)
	Other headache: Other: Intensity/Episode	Baseline: 3.3 (SD 0.96); 1 month: 2.7 (SD 1.2)
Connelly 2006 ¹³⁶	No intervention/TAU	Measured on VAS ranging from 0 to 6 (this is a nonstandard range)
	Other headache: Other: Intensity/Episode	Baseline: 2.8 (SD 1.1); 1 month: 2.9 (SD 1.0)
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	hours disabled + 0.5*(hours disabled from daily diary). Scaled as hours/month. Baseline in this group (N=15) was mean 10.5 (SD 11.9). At 2 months, change score mean 8.4 95% CI 0.9 to 15.7. At 7 months change score mean 9.4 with 95% CI 0.8 to 17.9. All Ns were 15.
	Functional status: Other: Unique calculation see notes	
Cottrell 2007 ¹³⁷	Attention control and education	hours disabled + 0.5*(hours disabled from daily diary). Scaled as hours/month. Baseline in this group (N=15) was mean 9.8 (SD 14.2). At 2 months, change score mean 6.1 95% CI 1.7 to 10.5. At 7 months, change score mean 7.2 95% CI 2.1 to 12.2. All Ns were 15.
	Functional status: Other: Unique calculation see notes	
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Baseline
	Migraine QOL: MSQ-LA	Mean: 40.8, SD: 12.7, n=15
Cottrell 2007 ¹³⁷	Attention control and education	Baseline
	Migraine QOL: MSQ-LA	Mean: 37.5, SD: 11.9, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Change from baseline: 2 month(s)
		Mean: -17.9, 95% CI: -25.3 to -10.6, n=15

Reference	Intervention Group and Outcome	Results
	Migraine QOL: MSQOL-A	
Cottrell 2007 ¹³⁷	Attention control and education	Change from baseline: 2 month(s)
	Migraine QOL: MSQOL-A	Mean: -6.7, 95% CI: -15.3 to 1.8, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Change from baseline: 7 month(s)
	Migraine QOL: MSQOL-A	Mean: -19.5, 95% CI: -27.1 to -11.9, n=15
Cottrell 2007 ¹³⁷	Attention control and education	Change from baseline: 7 month(s)
	Migraine QOL: MSQOL-A	Mean: -10.2, 95% CI: -17.9 to -2.6, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 3.7, SD: 2.3, n=15
Cottrell 2007 ¹³⁷	Attention control and education	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 3.4, SD: 1.4, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Change from baseline: 2 month(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: -2, 95% CI: -3.5 to -0.5, n=15
Cottrell 2007 ¹³⁷	Attention control and education	Change from baseline: 2 month(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: -1.7, 95% CI: -2.5 to -0.9, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Change from baseline: 7 month(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: -2.7, 95% CI: -4.4 to -1, n=15
Cottrell 2007 ¹³⁷	Attention control and education	Change from baseline: 7 month(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: -1.6, 95% CI: -2.6 to -0.7, n=15
Cottrell 2007 ¹³⁷	Thermal biofeedback+Education+PMR+SMT+Activity pacing	Headache severity (1 = Mild, 2 = Moderate, 3 = Severe). Baseline (N=15) mean 2.3 sd 0.5. At 2 months, change score mean -0.7 95% CI -1.5 to +0.1. At 7 months, change score mean -0.8 95% CI -2.3 to +0.7. All Ns were 15.
	Other headache: Other: intensity on a 1-3 scale (see notes)	
Cottrell 2007 ¹³⁷	Attention control and education	Headache severity (1 = Mild, 2 = Moderate, 3 = Severe). Baseline (N=15) mean 2.2 sd 0.5. At 2 months, change score mean -0.9 95% CI -1.8 to -0.2. At 7 months, change score mean -1.1 95% CI -1.8 to -0.4. All Ns were 15.
	Other headache: Other: intensity on a 1-3 scale (see notes)	

Reference	Intervention Group and Outcome	Results
Cousins 2015 ¹³⁸	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: HADS	Mean: 9.32, SD: 3.55, n=37
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Baseline
	Anxiety, depression, or sleep: HADS	Mean: 7.78, SD: 4.01, n=36
Cousins 2015 ¹³⁸	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: HADS	Mean: 5.68, SD: 3.09, n=37
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Baseline
	Anxiety, depression, or sleep: HADS	Mean: 5.83, SD: 4.61, n=36
Cousins 2015 ¹³⁸	No intervention/TAU	Follow-up: 17 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 7.96, SD: 4.37, n=27
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Follow-up: 17 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 5.76, SD: 4.45, n=29
Cousins 2015 ¹³⁸	No intervention/TAU	Follow-up: 17 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 4.52, SD: 3.51, n=27
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Follow-up: 17 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 4.24, SD: 4.6, n=29
Cousins 2015 ¹³⁸	No intervention/TAU	Baseline
	Functional status: HIT-6	Mean: 65.97, SD: 4.41, n=37
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Baseline
	Functional status: HIT-6	Mean: 66.5, SD: 5.88, n=36
Cousins 2015 ¹³⁸	No intervention/TAU	Follow-up: 17 week(s)
	Functional status: HIT-6	Mean: 60.85, SD: 8.4, n=27
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Follow-up: 17 week(s)
	Functional status: HIT-6	Mean: 59.17, SD: 8.19, n=29
Cousins 2015 ¹³⁸	No intervention/TAU	Baseline
	Functional status: MIDAS	Mean: 65.78, SD: 46.79, n=37
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Baseline
	Functional status: MIDAS	Mean: 51.03, SD: 43.68, n=36

Reference	Intervention Group and Outcome	Results
Cousins 2015 ¹³⁸	No intervention/TAU	Follow-up: 17 week(s)
	Functional status: MIDAS	Mean: 53.85, SD: 78.49, n=27
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Follow-up: 17 week(s)
	Functional status: MIDAS	Mean: 33.86, SD: 34.93, n=29
Cousins 2015 ¹³⁸	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 11.54, SD: 6.64, n=37
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 12.03, SD: 8.7, n=36
Cousins 2015 ¹³⁸	No intervention/TAU	Follow-up: 17 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.68, SD: 6.28, n=25
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	Follow-up: 17 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9, SD: 7.27, n=28
Cousins 2015 ¹³⁸	No intervention/TAU	7.08 at baseline (SD 5.87, N=37) down to 17 week FU at 6.2 (SD 4.86 N=25)
	Other headache: Other: number of rescue med days per month	
Cousins 2015 ¹³⁸	CBT+PMR+Deep breathing	6.69 at baseline (SD 5.3, N=36) down to 17 week FU at 5.86 (SD 5.12 N=28)
	Other headache: Other: number of rescue med days per month	
Cuneo 2023 ¹³⁹	Biofeedback	-
	Adverse events: Other: discontinuation	
Cuneo 2023 ¹³⁹	No intervention/TAU	-
	Adverse events: Other: discontinuation	
Cuneo 2023 ¹³⁹	Biofeedback	Change from baseline: 12 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 3.64, SD: 5.24, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Change from baseline: 12 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: -0.45, SD: 4.67, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Follow-up: 4 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 7.9, SD: 4.9, n=14

Reference	Intervention Group and Outcome	Results
Cuneo 2023 ¹³⁹	No intervention/TAU	Follow-up: 4 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 7.15, SD: 3.45, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 6.5, SD: 5.3, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 7.45, SD: 3.4, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Baseline
	Functional status: MIDAS	Mean: 100.36, SD: 72.76, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Baseline
	Functional status: MIDAS	Mean: 77.55, SD: 64.7, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Change from baseline: 12 week(s)
	Functional status: MIDAS	Mean: 27.72, SD: 57.49, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Change from baseline: 12 week(s)
	Functional status: MIDAS	Mean: 18.05, SD: 52.2, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 23.71, SD: 5.58, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 25.41, SD: 5.8, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 15.64, SD: 7.91, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 17.77, SD: 9.45, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Follow-up: 4 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 18, IQR: 9.5 to 26.9, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU	Follow-up: 4 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 17.3, IQR: 5.8 to 31.8, n=22
Cuneo 2023 ¹³⁹	Biofeedback	Follow-up: 8 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 19.2, IQR: 2.8 to 28.9, n=14

Reference	Intervention Group and Outcome	Results
Cuneo 2023 ¹³⁹	No intervention/TAU Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 8 week(s) Mean: 19.2, IQR: 2.8 to 28.9, n=14
Cuneo 2023 ¹³⁹	Biofeedback Other headache: Number of acute headache medications used	Change from baseline: 12 week(s) Mean: 13.36, SD: 10.72, n=14
Cuneo 2023 ¹³⁹	No intervention/TAU Other headache: Number of acute headache medications used	Change from baseline: 12 week(s) Mean: 3.91, SD: 12.47, n=22
D'Souza 2008 ¹⁴⁰	Relaxation training Functional status: MIDAS	Baseline Mean: 12.11, SD: 8.88, n=28
D'Souza 2008 ¹⁴⁰	Attention control Functional status: MIDAS	Baseline Mean: 15.35, SD: 12.25, n=31
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Functional status: MIDAS	Baseline Mean: 13.35, SD: 11.83, n=31
D'Souza 2008 ¹⁴⁰	Relaxation training Functional status: MIDAS	Follow-up: 14 week(s) Mean: 9.89, SD: 12.91, n=28
D'Souza 2008 ¹⁴⁰	Attention control Functional status: MIDAS	Follow-up: 14 week(s) Mean: 10.13, SD: 11.49, n=31
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Functional status: MIDAS	Follow-up: 14 week(s) Mean: 9.87, SD: 8.79, n=31
D'Souza 2008 ¹⁴⁰	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 9.86, SD: 6.21, n=28
D'Souza 2008 ¹⁴⁰	Attention control Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 11.77, SD: 7.58, n=31
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 9.65, SD: 6.46, n=31
D'Souza 2008 ¹⁴⁰	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 14 week(s) Mean: 9.36, SD: 6.13, n=28

Reference	Intervention Group and Outcome	Results
D'Souza 2008 ¹⁴⁰	Attention control Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 14 week(s) Mean: 8.97, SD: 6.14, n=31
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 14 week(s) Mean: 9, SD: 5.81, n=31
D'Souza 2008 ¹⁴⁰	Relaxation training Other headache: Other: Headache severity	Participants rated how painful the headaches were, on average, during the past month on a scale of 0 to 10 (0 = no pain at all, and 10 = pain as bad as it can be). Mean (SD):Baseline - 6.57 (1.57)Follow-up - 4.68 (2.13)Adjusted follow-up mean (SE) - 4.60 (0.36)
D'Souza 2008 ¹⁴⁰	Attention control Other headache: Other: Headache severity	Participants rated how painful the headaches were, on average, during the past month on a scale of 0 to 10 (0 = no pain at all, and 10 = pain as bad as it can be). Mean (SD):Baseline - 6.35 (1.14)Follow-up - 5.55 (1.69)Adjusted follow-up mean (SE) - 5.60 (0.34)
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Other headache: Other: Headache severity	Participants rated how painful the headaches were, on average, during the past month on a scale of 0 to 10 (0 = no pain at all, and 10 = pain as bad as it can be). Mean (SD):Baseline - 6.39 (1.52)Follow-up - 5.23 (2.28)Adjusted follow-up mean (SE) - 5.25 (0.34)
D'Souza 2008 ¹⁴⁰	Relaxation training Other headache: Other: Symptom Checklist-90-R	Participants reported general physical symptoms on the 12-item Somatization subscale of the Symptom Checklist-90-R (36). Symptoms were rated from 0 (not at all) to 4 (extremely) regarding the past month, and ratings were totaled.Mean (SD):Baseline - 15.50 (8.32)Follow-up - 13.32 (7.82)Adjusted follow-up mean (SE) - 12.15 (1.08)
D'Souza 2008 ¹⁴⁰	Attention control Other headache: Other: Symptom Checklist-90-R	Participants reported general physical symptoms on the 12-item Somatization subscale of the Symptom Checklist-90-R (36). Symptoms were rated from 0 (not at all) to 4 (extremely) regarding the past month, and ratings were totaled.Mean (SD):Baseline - 13.48 (5.16)Follow-up - 10.61 (5.37)Adjusted follow-up mean (SE) - 10.78 (1.02)
D'Souza 2008 ¹⁴⁰	Written emotional disclosure Other headache: Other: Symptom Checklist-90-R	Participants reported general physical symptoms on the 12-item Somatization subscale of the Symptom Checklist-90-R (36). Symptoms were rated from 0 (not at all) to 4 (extremely) regarding the past month, and ratings were totaled.Mean (SD):Baseline - 12.39 (4.94)Follow-up - 11.26 (7.61)Adjusted follow-up mean (SE) - 12.15 (1.02)
Day 2014 ¹⁴¹	MBCT Migraine frequency: Count: Headache(s)-Total-week	Change from baseline: 7 week(s) Mean: -1.08, SD: 1.71, n=17

Reference	Intervention Group and Outcome	Results
Day 2014 ¹⁴¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Total-week	Change from baseline: 7 week(s) Mean: -1, SD: 1.58, n=17
Day 2014 ¹⁴¹	No intervention/TAU Other headache: Number of acute headache medications used	Change from baseline: 7 week(s) Mean: -65.6, SD: 1279.9, n=17
Day 2014 ¹⁴¹	MBCT Other headache: Number of acute headache medications used	Change from baseline: 7 week(s) Mean: -1015.9, SD: 2597.6, n=17
Day 2014 ¹⁴¹	MBCT Other headache: Number of acute headache medications used	Change from baseline: 7 week(s) Mean: 2.17, SD: 9.78, n=17
Day 2014 ¹⁴¹	No intervention/TAU Other headache: Number of acute headache medications used	Change from baseline: 7 week(s) Mean: -9.16, SD: 44, n=17
Day 2014 ¹⁴¹	MBCT Other headache: VAS	Change from baseline: 7 week(s) Mean: -0.25, SD: 1.63, n=17
Day 2014 ¹⁴¹	No intervention/TAU Other headache: VAS	Change from baseline: 7 week(s) Mean: -0.3, SD: 0.96, n=17
Dindo 2020 ¹⁴⁵	Education+ACT Anxiety, depression, or sleep: HDRS	Baseline Mean: 19.8, SE: 0.6, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education Anxiety, depression, or sleep: HDRS	Baseline Mean: 19.7, SE: 0.6, n=65
Dindo 2020 ¹⁴⁵	Relaxation training+Education Anxiety, depression, or sleep: HDRS	Change from baseline: 3 month(s) Mean: -9.5, 95% CI: -12.1 to -6.8, n=69
Dindo 2020 ¹⁴⁵	Education+ACT Anxiety, depression, or sleep: HDRS	Change from baseline: 3 month(s) Mean: -7.1, 95% CI: -9.9 to -4.4, n=65
Dindo 2020 ¹⁴⁵	Education+ACT Anxiety, depression, or sleep: HDRS	Change from baseline: 6 month(s) Mean: -9.4, 95% CI: -12.2 to -6.6, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education Anxiety, depression, or sleep: HDRS	Change from baseline: 6 month(s) Mean: -6, 95% CI: -8.9 to -3, n=65

Reference	Intervention Group and Outcome	Results
Dindo 2020 ¹⁴⁵	Education+ACT	Follow-up: 3 month(s)
	Anxiety, depression, or sleep: HDRS	Mean: 10.3, SE: 1, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Follow-up: 3 month(s)
	Anxiety, depression, or sleep: HDRS	Mean: 12.5, SE: 1, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HDRS	Mean: 10.4, SE: 1, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HDRS	Mean: 13.7, SE: 1.1, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Baseline
	Functional status: HDI	Mean: 63.8, SE: 2.2, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Baseline
	Functional status: HDI	Mean: 61.4, SE: 2.3, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Change from baseline: 3 month(s)
	Functional status: HDI	Mean: -18.2, 95% CI: -25.4 to -10.9, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Change from baseline: 3 month(s)
	Functional status: HDI	Mean: -8.9, 95% CI: -16.7 to -1.1, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Change from baseline: 6 month(s)
	Functional status: HDI	Mean: -22.3, 95% CI: -29.7 to -14.8, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Change from baseline: 6 month(s)
	Functional status: HDI	Mean: -11.8, 95% CI: -20 to -3.6, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Follow-up: 3 month(s)
	Functional status: HDI	Mean: 45.6, SE: 3.2, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Follow-up: 3 month(s)
	Functional status: HDI	Mean: 52.9, SE: 3.6, n=65
Dindo 2020 ¹⁴⁵	Education+ACT	Follow-up: 6 month(s)
	Functional status: HDI	Mean: 41.5, SE: 3.3, n=69
Dindo 2020 ¹⁴⁵	Relaxation training+Education	Follow-up: 6 month(s)
	Functional status: HDI	Mean: 49.6, SE: 3.6, n=65

Reference	Intervention Group and Outcome	Results
Dittrich 2008 ¹⁴⁶	PMR+Exercise	Baseline
	Anxiety, depression, or sleep: BDI	Mean: 5.5, SD: 4.3, n=15
Dittrich 2008 ¹⁴⁶	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: BDI	Mean: 6.9, SD: 6, n=15
Dittrich 2008 ¹⁴⁶	PMR+Exercise	Baseline
	Anxiety, depression, or sleep: BDI	Mean: 4.5, SD: 4.6, n=15
Dittrich 2008 ¹⁴⁶	PMR+Exercise	Baseline
	Anxiety, depression, or sleep: BDI	Mean: 6.9, SD: 5.7, n=15
Fichtel 2001 ¹⁴⁷	PMR	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 4.15, SD: 2.6, n=21
Fichtel 2001 ¹⁴⁷	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 3.4, SD: 1.9, n=16
Fichtel 2001 ¹⁴⁷	PMR	Time point NR
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 3.24, SD: 3.1, n=20
Fichtel 2001 ¹⁴⁷	No intervention/TAU	Time point NR
	Migraine frequency: Count: Headache(s)-Total-week	Mean: 2.61, SD: 1.8, n=16
Fichtel 2001 ¹⁴⁷	PMR	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.85, SD: 2.1, n=21
Fichtel 2001 ¹⁴⁷	No intervention/TAU	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.1, SD: 0.8, n=21
Fichtel 2001 ¹⁴⁷	PMR	Time point NR
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.07, SD: 1.8, n=21
Fichtel 2001 ¹⁴⁷	No intervention/TAU	Time point NR
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 0.77, SD: 0.7, n=21
Fichtel 2001 ¹⁴⁷	PMR Other headache: Other: single highest intensity rating 1 week	At baseline (N=21), the average max headache intensity rating (0-5 scale where 5 is worst) was 3.35 (SD 0.7) and after treatment (N=20) it was 2.43 (SD 1.2). Specifically for migraines, these numbers were 3.35 (SD 0.7) and 2.43 (SD 1.2). Interestingly the TTH numbers (not extracted) were different, which makes it nonsensical that the overall and migraine means were the same as each other.

Reference	Intervention Group and Outcome	Results
Fichtel 2001 ¹⁴⁷	No intervention/TAU Other headache: Other: single highest intensity rating 1 week	At baseline (N=16), the average max headache intensity rating (0-5 scale where 5 is worst) was 3.25 (SD 0.8) and after treatment (N=16) it was 3.33 (SD 1.5). Specifically for migraines, these numbers were 2.45 (SD 1.1) and 1.8 (SD 1.2).
Fichtel 2001 ¹⁴⁷	PMR Other headache: Other: single highest intensity rating 1 week	At baseline (N=21), the # of tablets per week was 0.79 (SD 1) and after treatment (N=20) it was 0.88 (SD 1.5).
Fichtel 2001 ¹⁴⁷	No intervention/TAU Other headache: Other: single highest intensity rating 1 week	At baseline (N=16), the # of tablets per week was 0.9 (SD 1.9) and after treatment (N=16) it was 1.19 (SD 1.4).
Flynn 2019 ¹⁴⁸	Hypnotherapy Functional status: HDI	Baseline Mean: 62.7, SD: 17.4, n=22
Flynn 2019 ¹⁴⁸	No intervention/TAU Functional status: HDI	Baseline Mean: 68.9, SD: 19.4, n=18
Flynn 2019 ¹⁴⁸	Hypnotherapy Functional status: HDI	Follow-up: 10 week(s) Mean: 25.4, SD: 20.9, n=22
Flynn 2019 ¹⁴⁸	No intervention/TAU Functional status: HDI	Follow-up: 10 week(s) Mean: 61.9, SD: 24.6, n=18
Flynn 2019 ¹⁴⁸	Hypnotherapy Migraine frequency: Count: Migraine(s)-Total-week	Baseline Median: 2, IQR: 1.1 to 2.9, n=22
Flynn 2019 ¹⁴⁸	No intervention/TAU Migraine frequency: Count: Migraine(s)-Total-week	Baseline Median: 2, IQR: 1.1 to 2.9, n=18
Flynn 2019 ¹⁴⁸	Hypnotherapy Migraine frequency: Count: Migraine(s)-Total-week	Follow-up: 10 week(s) Median: 1, IQR: 0 to 2, n=22
Flynn 2019 ¹⁴⁸	No intervention/TAU Migraine frequency: Count: Migraine(s)-Total-week	Follow-up: 10 week(s) Median: 1, IQR: 0.25 to 1.75, n=18
Flynn 2019 ¹⁴⁸	Hypnotherapy Other headache: Other: Medication Index Score (MIS)	Median (IQR) Baseline:175 (998.8) 10 weeks: 0(250)
Flynn 2019 ¹⁴⁸	No intervention/TAU Other headache: Other: Medication Index Score (MIS)	Median (IQR) Baseline: 750 (1732.8) 10 weeks: 50(850)

Reference	Intervention Group and Outcome	Results
Flynn 2019 ¹⁴⁸	Hypnotherapy Other headache: Other: Migraine duration, hours	Median (IQR)Baseline: 12(19.8)10 weeks: 2(9.0); Table reports n=22, but only n=19 completed the follow-up questionnaire
Flynn 2019 ¹⁴⁸	No intervention/TAU Other headache: Other: Migraine duration, hours	Median (IQR)Baseline: 12(17.5)10 weeks: 8(10.5); Table reports n=18, but only n=16 completed the follow-up questionnaire
Flynn 2019 ¹⁴⁸	Hypnotherapy Other headache: Other: Migraine severity	n (%) Baseline (N=22): Little=0 (0) Mild= 7 (31.8) Moderate= 10 (45.5) Severe= 5 (22.7) 10 weeks (N=19): Little=9 (50) Mild= 6 (33.3) Moderate= 2 (11.1) Severe= 2 (11.1)
Flynn 2019 ¹⁴⁸	No intervention/TAU Other headache: Other: Migraine severity	n (%)Baseline (N=18):Little=0 (0)Mild= 4 (22.2)Moderate= 11 (61.1)Severe= 3 (16.7)10 weeks (N=15):Little=5 (33.3)Mild= 3 (20)Moderate= 4 (26.7)Severe= 3 (20)
Flynn 2019 ¹⁴⁸	Hypnotherapy Other headache: Other: Pain Catastrophizing Scale (PCS)	Mean (SD)Baseline: 21.4(11.5)10 weeks: 7.6(9.1) Table reports n=22, but only n=19 completed the follow-up questionnaire
Flynn 2019 ¹⁴⁸	No intervention/TAU Other headache: Other: Pain Catastrophizing Scale (PCS)	Mean(SD) Baseline: 24.8 (12.2) 10 weeks: 25.5 (17.0) Table reports n=18, but only n=16 completed the follow-up questionnaire
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Anxiety, depression, or sleep: Other: HADS-A	n = 60 vs. 57 T0 5,90 (1,91) T1 6,70 (2,53) T2 6,18 (2,31) T3 5,87 (3,75)
Fritsche 2010 ¹⁴⁹	Education+PMR Anxiety, depression, or sleep: Other: HADS-A	n = 60 vs. 57 T0 5,84 (2,49) T1 6,51 (2,22) T2 6,35 (2,24) T3 6,19 (4,09)
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Anxiety, depression, or sleep: Other: HADS-D	n = 60 vs. 57 T0 4,40 (1,55) T1 4,65 (1,16) T2 4,78 (1,17) T3 4,77 (4,18)

Reference	Intervention Group and Outcome	Results
Fritsche 2010 ¹⁴⁹	Education+PMR Anxiety, depression, or sleep: Other: HADS-D	n = 60 vs. 57 T0 4,56 (1,07) T1 4,54 (1,18) T2 4,75 (1,30) T3 4,91 (3,99)
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Functional status: Other: headache disability (0-10 scale)	(n = 59 vs. 55) baseline 4.46 (1.80) 5 weeks 4.49 (2.01) 3 months 4.61 (1.97) 12 months 4.39 (2.16)
Fritsche 2010 ¹⁴⁹	Education+PMR Functional status: Other: headache disability (0-10 scale)	(n = 59 vs. 55) baseline 4.16 (1.56) 5 weeks 4.13 (1.97) 3 months 4.25 (1.88) 12 months 4.40 (1.73)
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 7.23, SD: 3.7, n=60
Fritsche 2010 ¹⁴⁹	Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 7.27, SD: 3.82, n=55
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 12 month(s) Mean: 6.15, SD: 4.02, n=60
Fritsche 2010 ¹⁴⁹	Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 12 month(s) Mean: 5.84, SD: 3.76, n=55
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 3 month(s) Mean: 6.15, SD: 3.97, n=60
Fritsche 2010 ¹⁴⁹	Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 3 month(s) Mean: 5.45, SD: 3.16, n=55
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 5 week(s) Mean: 5.6, SD: 3.79, n=60
Fritsche 2010 ¹⁴⁹	Education+PMR Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 5 week(s) Mean: 5.78, SD: 4.01, n=55
Fritsche 2010 ¹⁴⁹	CBT+Education+PMR Other headache: Other: acute medication days	(n = 60 vs. 55) T0 5.27 (2.25) T1 4.30 (2.76)

Reference	Intervention Group and Outcome	Results
		T2 4.83 (3.00) T3 5.03 (3.52)
Fritsche 2010 ¹⁴⁹	Education+PMR Other headache: Other: acute medication days	(n = 60 vs. 55) T0 6.25 (2.98) T1 5.04 (3.11) T2 4.75 (2.82) T3 55.02 (2.78)
Gerber 2010 ¹⁵⁰	CBT+Education+PMR General QOL: Other: KINDL	The ANOVA of the Total Score of the QoL questionnaire KINDL revealed a significant main effect for time ($F(27,1) = 5.527$, $p = .029$) but not for the group factor ($F(27,1) = 0.120$, $p = .732$) or interaction (group 9 time interaction) ($F(27,1) = 3.370$, $p = .08$). Regarding the specific dimensions of the KINDL, which seem to be most relevant for headache, we found the following results: A significant effect for group ($F(1,27) = 4.908$, $p = .036$) and time ($F(1,24) = 4.619$, $p = .041$), but no interaction effect for the dimension Physical Well-Being was found. In addition, the Wilcoxon test revealed significant Post 1 to Post 2 improvements in the dimensions Psychological Well-Being ($z = 2.388$, $p = .017$) and Self-Esteem ($z = 2.266$, $p = .023$). For all other dimensions, no significant effects were found. Thus, the improvements in QoL of the children were restricted mainly to the physical realm. Mean (SD)s of all of the subscales are also reported.
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback General QOL: Other: KINDL	The ANOVA of the Total Score of the QoL questionnaire KINDL revealed a significant main effect for time ($F(27,1) = 5.527$, $p = .029$) but not for the group factor ($F(27,1) = 0.120$, $p = .732$) or interaction (group 9 time interaction) ($F(27,1) = 3.370$, $p = .08$). Regarding the specific dimensions of the KINDL, which seem to be most relevant for headache, we found the following results: A significant effect for group ($F(1,27) = 4.908$, $p = .036$) and time ($F(1,24) = 4.619$, $p = .041$), but no interaction effect for the dimension Physical Well-Being was found. In addition, the Wilcoxon test revealed significant Post 1 to Post 2 improvements in the dimensions Psychological Well-Being ($z = 2.388$, $p = .017$) and Self-Esteem ($z = 2.266$, $p = .023$). For all other dimensions, no significant effects were found. Thus, the improvements in QoL of the children were restricted mainly to the physical realm. Mean (SD)s of all of the subscales are also reported.
Gerber 2010 ¹⁵⁰	CBT+Education+PMR Migraine frequency: Other: Frequency (1 = daily headache,	The mean percentages of headache frequency prior to treatment were 56.2% 2 days per the week, 21.1% 1 day per week and 23.7% 1–3 days per month for the MIPAS-Family group. Mean (SD) Baseline = 2.42 (1.07) Post 1-6 months = 3.61 (1.14) Post 2-12

Reference	Intervention Group and Outcome	Results
	2 = several times per week, 3 = once per week, 4 = 1–3 times per week, 5 = once per month)	months = 3.63 (1.09). The children of the MIPAS-Family group reported highly significant reductions of the headache frequencies (Pre–Post 1: $z = -2.841$, $p = .004$; Pre–Post 2: $z = -3.126$, $p = .002$), whereas the children of the Biofeedback group only showed a significant improvement for the Pre–Post 1 comparison ($z = -2.333$, $p = .02$). The ANOVA revealed a significant course effect ($F(1,27) = 19.283$, $p = .000$) and a significant group effect ($F(1,27) = 4.722$, $p = .039$) but no interaction effect. Effect sizes for general effectiveness (Cohen's d): Pre-post 1-6months: 0.88 Pre-post 2-12 months: 1.12
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback Migraine frequency: Other: Frequency (1 = daily headache, 2 = several times per week, 3 = once per week, 4 = 1–3 times per week, 5 = once per month)	The mean percentages of headache frequency prior to treatment were 40% 2 days per week, 33.3% 1 day per week and 27.3% 1–3 days per month for the Biofeedback group. Mean (SD): Baseline = 1.87 (1.06) Post 1-6 months = 2.50 (1.51) Post 2-12 months = 2.58 (1.68). The children of the Biofeedback group only showed a significant improvement for the Pre–Post 1 comparison ($z = -2.333$, $p = .02$). Effect sizes for general effectiveness (Cohen's d): Pre-post 1-6months: 0.49 Pre-post 2-12 months: 0.51
Gerber 2010 ¹⁵⁰	CBT+Education+PMR Other headache: Other: Duration, hrs/wk	Mean (SD) Baseline: 5.56 (6.05) Post 1-6 months: 2.96 (3.65) Post 2-12 months: 5.29 (7.60) Only the comparison of Pre–Post conditions ($z = -2.092$, $p = .036$) based on child report revealed a significant reduction in the headache duration. Effect sizes for general effectiveness (Cohen's d): Pre-post 1-6months: 0.52 Pre-post 2-12 months: 0.04
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback Other headache: Other: Duration, hrs/wk	Mean (SD) Baseline: 10.07 (9.32) Post 1-6 months: 9.60 (10.60) Post 2-12 months: 11.75 (11.91). No significant differences with respect to headache duration across the different measurement points were found. Effect sizes for general effectiveness (Cohen's d): Pre-post 1-6months: 0.05 Pre-post 2-12 months: 0.16
Gerber 2010 ¹⁵⁰	CBT+Education+PMR Other headache: VAS	Baseline Mean: 2.24, SD: 2.42, $n=19$

Reference	Intervention Group and Outcome	Results
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback Other headache: VAS	Baseline Mean: 3.27, SD: 2.24, n=15
Gerber 2010 ¹⁵⁰	CBT+Education+PMR Other headache: VAS	Follow-up: 12 month(s) Mean: 1.78, SD: 1.89, n=NR
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback Other headache: VAS	Follow-up: 12 month(s) Mean: 2.71, SD: 2.26, n=NR
Gerber 2010 ¹⁵⁰	CBT+Education+PMR Other headache: VAS	Follow-up: 6 month(s) Mean: 2.71, SD: 2.32, n=NR
Gerber 2010 ¹⁵⁰	Thermal biofeedback+Relaxation training+Education+EMG biofeedback Other headache: VAS	Follow-up: 6 month(s) Mean: 2.4, SD: 2.85, n=NR
Grazzi 2021 ¹⁵¹	ACT Adverse events: Other: Any	0
Grazzi 2021 ¹⁵¹	No intervention/TAU Adverse events: Other: Any	0
Grazzi 2021 ¹⁵¹	ACT Adverse events: Other: drop out	6 months: 0/18 12 months: 0/18
Grazzi 2021 ¹⁵¹	No intervention/TAU Adverse events: Other: drop out	6 months: 1/17; 12 months: 3/17
Grazzi 2021 ¹⁵¹	No intervention/TAU Anxiety, depression, or sleep: HADS	Follow-up: 12 month(s) Mean: 6, 95% CI: 4.7 to 7.3, n=17
Grazzi 2021 ¹⁵¹	ACT Anxiety, depression, or sleep: HADS	Follow-up: 12 month(s) Mean: 8.2, 95% CI: 6.6 to 9.7, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU Anxiety, depression, or sleep: HADS	Follow-up: 12 month(s) Mean: 3.4, 95% CI: 2.1 to 4.7, n=17
Grazzi 2021 ¹⁵¹	ACT Anxiety, depression, or sleep: HADS	Follow-up: 12 month(s) Mean: 5.8, 95% CI: 4.3 to 7.3, n=18

Reference	Intervention Group and Outcome	Results
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HADS	Mean: 6.1, 95% CI: 4.6 to 7.5, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HADS	Mean: 8.4, 95% CI: 6.7 to 10.1, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HADS	Mean: 4.7, 95% CI: 3.2 to 6.2, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 6 month(s)
	Anxiety, depression, or sleep: HADS	Mean: 7, 95% CI: 5.2 to 8.8, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Baseline
	Functional status: HIT-6	Mean: 60.4, 95% CI: 56 to 64.8, n=17
Grazzi 2021 ¹⁵¹	ACT	Baseline
	Functional status: HIT-6	Mean: 62.8, 95% CI: 60.2 to 65.3, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 12 month(s)
	Functional status: HIT-6	Mean: 53.7, 95% CI: 49.4 to 58, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 12 month(s)
	Functional status: HIT-6	Mean: 61.2, 95% CI: 58.3 to 64.2, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 6 month(s)
	Functional status: HIT-6	Mean: 56.6, 95% CI: 51.8 to 61.3, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 6 month(s)
	Functional status: HIT-6	Mean: 60.2, 95% CI: 57 to 63.4, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Baseline
	Functional status: MIDAS	Mean: 26.3, 95% CI: 13.7 to 38.9, n=17
Grazzi 2021 ¹⁵¹	ACT	Baseline
	Functional status: MIDAS	Mean: 41.6, 95% CI: 25.4 to 57.7, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 12 month(s)
	Functional status: MIDAS	Mean: 16, 95% CI: 7.2 to 24.9, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 12 month(s)
	Functional status: MIDAS	Mean: 35.7, 95% CI: 17.5 to 53.8, n=18

Reference	Intervention Group and Outcome	Results
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 6 month(s)
	Functional status: MIDAS	Mean: 17.9, 95% CI: 5.7 to 30.1, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 6 month(s)
	Functional status: MIDAS	Mean: 33.1, 95% CI: 15.4 to 50.8, n=18
Grazzi 2021 ¹⁵¹	ACT	Change from baseline: 12 month(s)
	Migraine frequency: 50% responder rate: Headache(s)-Days-month	Responders/events: 11, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Change from baseline: 12 month(s)
	Migraine frequency: 50% responder rate: Headache(s)-Days-month	Responders/events: 5, n=17
Grazzi 2021 ¹⁵¹	ACT	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 10.6, 95% CI: 9.6 to 11.6, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.1, 95% CI: 7.6 to 10.5, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 12 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.1, 95% CI: 3.8 to 8.4, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 12 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.7, 95% CI: 4.8 to 8.5, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 3 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7, 95% CI: 5.4 to 8.6, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 3 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 10, 95% CI: 7.4 to 12.6, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 6 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.6, 95% CI: 5.6 to 9.5, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU	Follow-up: 6 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 8.7, 95% CI: 6.3 to 11.1, n=17
Grazzi 2021 ¹⁵¹	ACT	Follow-up: 12 month(s)
	Other headache: Number of acute headache medications used	Mean: 5.6, 95% CI: 3.1 to 8, n=18

Reference	Intervention Group and Outcome	Results
Grazzi 2021 ¹⁵¹	No intervention/TAU Other headache: Number of acute headache medications used	Follow-up: 12 month(s) Mean: 7, 95% CI: 34.91 to 9.2, n=17
Grazzi 2021 ¹⁵¹	ACT Other headache: Number of acute headache medications used	Follow-up: 3 month(s) Mean: 5.8, 95% CI: 4.1 to 7.5, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU Other headache: Number of acute headache medications used	Follow-up: 3 month(s) Mean: 9.4, 95% CI: 6.6 to 12.2, n=17
Grazzi 2021 ¹⁵¹	ACT Other headache: Number of acute headache medications used	Follow-up: 6 month(s) Mean: 6.5, 95% CI: 4.4 to 8.6, n=18
Grazzi 2021 ¹⁵¹	No intervention/TAU Other headache: Number of acute headache medications used	Follow-up: 6 month(s) Mean: 7.8, 95% CI: 5.4 to 10.3, n=17
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Adverse events: Other: drop out	2/27 at 9 months of f/u
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Adverse events: Other: drop out	4/28 at 9 months of f/u
Hedborg 2011 ¹⁵⁴	Minimal intervention Adverse events: Other: drop out	1/28 at 6 months f/u
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Anxiety, depression, or sleep: MADRS	Baseline Mean: 7.8, SD: 6.6, n=23
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Anxiety, depression, or sleep: MADRS	Baseline Mean: 9.3, SD: 6.4, n=23
Hedborg 2011 ¹⁵⁴	Minimal intervention Anxiety, depression, or sleep: MADRS	Baseline Mean: 6.6, SD: 4.6, n=25

Reference	Intervention Group and Outcome	Results
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Anxiety, depression, or sleep: MADRS	Follow-up: 3 month(s) Mean: 8.1, SD: 7.3, n=23
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Anxiety, depression, or sleep: MADRS	Follow-up: 3 month(s) Mean: 8.9, SD: 6.5, n=23
Hedborg 2011 ¹⁵⁴	Minimal intervention Anxiety, depression, or sleep: MADRS	Follow-up: 3 month(s) Mean: 6.8, SD: 5.2, n=25
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Anxiety, depression, or sleep: MADRS	Follow-up: 6 month(s) Mean: 5.8, SD: 6.1, n=23
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Anxiety, depression, or sleep: MADRS	Follow-up: 6 month(s) Mean: 8.9, SD: 6.9, n=23
Hedborg 2011 ¹⁵⁴	Minimal intervention Anxiety, depression, or sleep: MADRS	Follow-up: 6 month(s) Mean: 5.8, SD: 7.7, n=25
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Anxiety, depression, or sleep: MADRS	Follow-up: 9 month(s) Mean: 6.9, SD: 7.1, n=23
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Anxiety, depression, or sleep: MADRS	Follow-up: 9 month(s) Mean: 8.7, SD: 7.5, n=23
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy General QOL: Other: PQ23	See table 5. No between A and C group comparison; however, presents values at different f/ups
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management General QOL: Other: PQ23	See table 5. No between B and C group comparison; however, presents values at different f/ups
Hedborg 2011 ¹⁵⁴	Minimal intervention General QOL: Other: PQ23	See table 5. No between B and C group comparison; however, presents values at different f/ups

Reference	Intervention Group and Outcome	Results
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Migraine frequency: Count: Migraine(s)-Days-days-56	Baseline Mean: 10.1, 95% CI: 7.2 to 12.9, n=25
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Migraine frequency: Count: Migraine(s)-Days-days-56	Baseline Mean: 13.9, 95% CI: 10.2 to 17.6, n=24
Hedborg 2011 ¹⁵⁴	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-days-56	Baseline Mean: 10, 95% CI: 7.2 to 12.9, n=27
Hedborg 2011 ¹⁵⁴	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-days-56	Follow-up: 6 month(s) Median: 8.9, IQR: 5 to 13.8, n=27
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy Migraine frequency: Count: Migraine(s)-Days-days-56	Follow-up: 9 month(s) Median: 4.8, IQR: 2 to 12, n=25
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Migraine frequency: Count: Migraine(s)-Days-days-56	Follow-up: 9 month(s) Median: 6, IQR: 4 to 14.6, n=24
Hedborg 2011 ¹⁵⁴	Minimal intervention Other headache: Other: drug doses/subject	8.3 at baseline; 8.9 at 6 months f/u See ancillary publication for details and gender differences
Hedborg 2011 ¹⁵⁴	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management Other headache: Other: drug doses/subject	Authors combined two intervention groups for this analysis. See ancillary publication for details and gender differences; n=49). 13.0 at baseline; 10.1 at 6 months of f/u.
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Adverse events: Other: dropouts	2/21
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Adverse events: Other: dropouts	2/20
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Anxiety, depression, or sleep: BDI	Follow-up: 4 month(s) Mean: 6.33, SD: 4.27, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Anxiety, depression, or sleep: BDI	Follow-up: 4 month(s) Mean: 8.25, SD: 6.36, n=18

Reference	Intervention Group and Outcome	Results
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Anxiety, depression, or sleep: Other: State-Trait Personality Inventory (STPI)	Anxiety: Baseline (mean [SD]): 19.75 (6.09) 4 months (mean [SD]): 19.00 (5.03)
Holroyd 1988 ¹⁵⁶	Attention control and education Anxiety, depression, or sleep: Other: State-Trait Personality Inventory (STPI)	Anxiety: Baseline (mean [SD]): 20.63 (4.28); 4 months (mean [SD]): 20.00 (7.02)
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Functional status: Other: Wahler Physical Symptom Checklist (WPSC)	Baseline (m, SD): 61.42 (16.17); 4 months f/u: 52.30 (26.36)
Holroyd 1988 ¹⁵⁶	Attention control and education Functional status: Other: Wahler Physical Symptom Checklist (WPSC)	Baseline (m, SD): 52.94 (24.20); 4 months f/u: 42.50 (24.70)
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Migraine frequency: Count: Headache(s)-Days-week	Baseline Mean: 3.81, SD: 2.27, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Migraine frequency: Count: Headache(s)-Days-week	Baseline Mean: 3.65, SD: 1.71, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 1 month(s) Mean: 3.67, SD: 2.39, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 1 month(s) Mean: 3, SD: 2.02, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 2 month(s) Mean: 3.53, SD: 2.45, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 2 month(s) Mean: 2.78, SD: 2.1, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 4 month(s) Mean: 2.62, SD: 2.52, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Migraine frequency: Count: Headache(s)-Days-week	Follow-up: 4 month(s) Mean: 2.58, SD: 1.75, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training	Follow-up: 1 month(s) Mean: 3.7, SD: 4.42, n=19

Reference	Intervention Group and Outcome	Results
	Other headache: Number of acute headache medications used	
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: Number of acute headache medications used	Follow-up: 1 month(s) Mean: 9.85, SD: 21.74, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Other headache: Number of acute headache medications used	Follow-up: 2 month(s) Mean: 2.55, SD: 4.01, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: Number of acute headache medications used	Follow-up: 2 month(s) Mean: 12.53, SD: 33.91, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Other headache: Number of acute headache medications used	Follow-up: 4 month(s) Mean: 2.48, SD: 4.87, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: Number of acute headache medications used	Follow-up: 4 month(s) Mean: 14.53, SD: 39.93, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Other headache: VAS	Follow-up: 1 month(s) Mean: 6.07, SD: 2.74, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: VAS	Follow-up: 1 month(s) Mean: 5.4, SD: 2.11, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Other headache: VAS	Follow-up: 2 month(s) Mean: 5.54, SD: 2.61, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: VAS	Follow-up: 2 month(s) Mean: 4.85, SD: 2.35, n=18
Holroyd 1988 ¹⁵⁶	Thermal biofeedback+Relaxation training Other headache: VAS	Follow-up: 4 month(s) Mean: 4.4, SD: 2.91, n=19
Holroyd 1988 ¹⁵⁶	Attention control and education Other headache: VAS	Follow-up: 4 month(s) Mean: 5.4, SD: 2.74, n=18
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored Migraine QOL: MSQoL v2.1	Baseline Mean: 39.4, SD: 11.9, n=69

Reference	Intervention Group and Outcome	Results
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Baseline
	Migraine QOL: MSQoL v2.1	Mean: 38.5, SD: 12.4, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Baseline
	Migraine QOL: MSQoL v2.1	Mean: 40.3, SD: 13.4, n=53
Holroyd 2010 ¹⁵⁸	Placebo	Baseline
	Migraine QOL: MSQoL v2.1	Mean: 40.3, SD: 13.4, n=55
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored	Change from baseline: 10 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -13, 95% CI: -13.5 to -12.5, n=69
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Change from baseline: 10 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -8.6, 95% CI: -8.9 to -8.2, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Change from baseline: 10 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -7.1, 95% CI: -7.7 to -6.6, n=53
Holroyd 2010 ¹⁵⁸	Placebo	Change from baseline: 10 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -7.1, 95% CI: -7.8 to -6.3, n=55
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored	Change from baseline: 16 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -15.2, 95% CI: -16 to -14.4, n=69
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Change from baseline: 16 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -9.6, 95% CI: -10.3 to -9, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Change from baseline: 16 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -8.5, 95% CI: -9.4 to -7.6, n=53
Holroyd 2010 ¹⁵⁸	Placebo	Change from baseline: 16 month(s)
	Migraine QOL: MSQoL v2.1	Mean: -8.8, 95% CI: -9.5 to -8.1, n=55
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored	Baseline
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: 8.7, SD: 4, n=69
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Baseline
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: 8.1, SD: 3.4, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Baseline
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: 8.6, SD: 3.3, n=53

Reference	Intervention Group and Outcome	Results
Holroyd 2010 ¹⁵⁸	Placebo	Baseline
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: 8.4, SD: 3.5, n=55
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored	Change from baseline: 10 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -5.4, 95% CI: -5.6 to -5.2, n=69
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Change from baseline: 10 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -3.3, 95% CI: -3.7 to -2.9, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Change from baseline: 10 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -3.9, 95% CI: -4.2 to -3.5, n=53
Holroyd 2010 ¹⁵⁸	Placebo	Change from baseline: 10 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -3.3, 95% CI: -3.6 to -3, n=55
Holroyd 2010 ¹⁵⁸	Propranolol+CBT+PMR+Preference-based/tailored	Change from baseline: 16 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -6.1, 95% CI: -6.6 to -5.6, n=69
Holroyd 2010 ¹⁵⁸	CBT+PMR+Preference-based/tailored	Change from baseline: 16 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -4.1, 95% CI: -4.5 to -3.8, n=55
Holroyd 2010 ¹⁵⁸	Propranolol	Change from baseline: 16 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -4.5, 95% CI: -5.1 to -4, n=53
Holroyd 2010 ¹⁵⁸	Placebo	Change from baseline: 16 month(s)
	Migraine frequency: Count: Migraine(s)-Days-days-30	Mean: -3.9, 95% CI: -4.3 to -3.5, n=55
Janssen 1986 ¹⁶¹	PMR	Follow-up: 13 week(s)
	Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Migraine	Mean: 0.75, Precision NR, n=NR
Janssen 1986 ¹⁶¹	Autogenic training	Follow-up: 13 week(s)
	Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Migraine	Mean: 0.6, Precision NR, n=NR
Janssen 1986 ¹⁶¹	PMR	Follow-up: 26 week(s)
	Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Migraine	Mean: 0.32, Precision NR, n=NR
Janssen 1986 ¹⁶¹	Autogenic training	Follow-up: 26 week(s)
	Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Migraine	Mean: 0.54, Precision NR, n=NR

Reference	Intervention Group and Outcome	Results
Janssen 1986 ¹⁶¹	PMR Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Mix headache (migraine TH)	Follow-up: 13 week(s) Mean: 0.96, Precision NR, n=NR
Janssen 1986 ¹⁶¹	Autogenic training Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Mix headache (migraine TH)	Follow-up: 13 week(s) Mean: 0.63, Precision NR, n=NR
Janssen 1986 ¹⁶¹	PMR Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Mix headache (migraine TH)	Follow-up: 26 week(s) Mean: 0.82, Precision NR, n=NR
Janssen 1986 ¹⁶¹	Autogenic training Migraine frequency: Count: Migraine(s)-NR-NR; Subgroup: Mix headache (migraine TH)	Follow-up: 26 week(s) Mean: 0.56, Precision NR, n=NR
Janssen 1986 ¹⁶¹	PMR Other headache: Other	Pain intensity (scale NR) mean for the migraine patients was 1.26 at 13 weeks and 1.04 at 26 weeks (no dispersion or statistical tests reported). For the combined migraine-TTh patients it was 1.17 at 13 weeks and 0.81 at 26 weeks (no dispersion or statistical tests reported).
Janssen 1986 ¹⁶¹	Autogenic training Other headache: Other	Pain intensity (scale NR) mean for the migraine patients was 1.11 at 13 weeks and 0.78 at 26 weeks (no dispersion or statistical tests reported). For the combined migraine-TTh patients it was 0.94 at 13 weeks and 0.84 at 26 weeks (no dispersion or statistical tests reported).
Kewman 1980 ¹⁶²	Thermal biofeedback Migraine frequency: Count: Migraine(s)-Days-week	Baseline Mean: 0.98, SD: 0.74, n=11
Kewman 1980 ¹⁶²	Sham Migraine frequency: Count: Migraine(s)-Days-week	Baseline Mean: 0.68, SD: 0.47, n=12
Kewman 1980 ¹⁶²	Thermal biofeedback Migraine frequency: Count: Migraine(s)-Days-week	Follow-up: 15 week(s) Mean: 0.85, SD: 1.72, n=11
Kewman 1980 ¹⁶²	Sham Migraine frequency: Count: Migraine(s)-Days-week	Follow-up: 15 week(s) Mean: 0.54, SD: 0.56, n=12
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Adverse events: Other: Participants experiencing adverse events	"Nine participants (miCBT: four; RLX: five) reported a total of 13 adverse events on the session evaluation form. All reported events were classified as temporary and not serious."

Reference	Intervention Group and Outcome	Results
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Follow-up: 59 week(s)
	Adverse events: Withdrawal due to adverse events	Responders/events: 0, n=51
Klan 2022 ¹⁶³	PMR	Follow-up: 59 week(s)
	Adverse events: Withdrawal due to adverse events	Responders/events: 0, n=49
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	DASS is Depression, Anxiety and Stress Scales Table 2: 7 weeks: CfB Mean -2.83 (SE 1.33), n = 36 Supplementary Table 5: 7 weeks + 4 months: CfB Mean -1.71 (SE 1.14), n = 51 7 weeks + 12 months: CfB Mean -3.10 (SE 1.25), n = 51 Group N inferred from combined N of 104, 36 in CBT group at baseline, 15 randomized from waitlist to CBT, 39 in PMR group at baseline, and 14 randomized from waitlist to PMR.
	Anxiety, depression, or sleep: Other: DASS	
Klan 2022 ¹⁶³	PMR	DASS is Depression, Anxiety and Stress Scales Table 2: 7 weeks: CfB Mean -2.22 (SE 1.28), n = 39 Supplementary Table 5: 7 weeks + 4 months: CfB Mean -2.34 (SE 1.14), n = 49 7 weeks + 12 months: CfB Mean -2.65 (SE 1.24), n = 49 Group N inferred from combined N of 104, 36 in CBT group at baseline, 15 randomized from waitlist to CBT, 39 in PMR group at baseline, and 14 randomized from waitlist to PMR.
	Anxiety, depression, or sleep: Other: DASS	
Klan 2022 ¹⁶³	No intervention/TAU	DASS is Depression, Anxiety and Stress Scales Table 2: 7 weeks: CfB Mean -0.43 (SE 1.44), n = 31
	Anxiety, depression, or sleep: Other: DASS	
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Baseline
	Functional status: HDI	Mean: 50.15873016, SE: 2.486772487, n=51
Klan 2022 ¹⁶³	PMR	Baseline
	Functional status: HDI	Mean: 51.95767196, SE: 2.433862434, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Change from baseline: 23 week(s)
	Functional status: HDI	Mean: -7.99, SE: 1.74, n=51
Klan 2022 ¹⁶³	PMR	Change from baseline: 23 week(s)
	Functional status: HDI	Mean: -8.82, SE: 1.74, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Change from baseline: 59 week(s)
	Functional status: HDI	Mean: -11.3, SE: 2.06, n=51

Reference	Intervention Group and Outcome	Results
Klan 2022 ¹⁶³	PMR Functional status: HDI	Change from baseline: 59 week(s) Mean: -12.27, SE: 2.06, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Functional status: HDI	Change from baseline: 7 week(s) Mean: -5.01, SE: 1.7, n=36
Klan 2022 ¹⁶³	PMR Functional status: HDI	Change from baseline: 7 week(s) Mean: -2.51, SE: 1.63, n=39
Klan 2022 ¹⁶³	No intervention/TAU Functional status: HDI	Change from baseline: 7 week(s) Mean: -6.03, SE: 1.85, n=31
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Functional status: HIT-6	Change from baseline: 23 week(s) Mean: -1.84, SE: 0.74, n=51
Klan 2022 ¹⁶³	PMR Functional status: HIT-6	Change from baseline: 23 week(s) Mean: -3.03, SE: 0.73, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Functional status: HIT-6	Change from baseline: 59 week(s) Mean: -3.73, SE: 0.78, n=51
Klan 2022 ¹⁶³	PMR Functional status: HIT-6	Change from baseline: 59 week(s) Mean: -3.86, SE: 0.78, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Functional status: HIT-6	Change from baseline: 7 week(s) Mean: -0.59, SE: 0.75, n=36
Klan 2022 ¹⁶³	PMR Functional status: HIT-6	Change from baseline: 7 week(s) Mean: -3.21, SE: 0.72, n=39
Klan 2022 ¹⁶³	No intervention/TAU Functional status: HIT-6	Change from baseline: 7 week(s) Mean: -1.23, SE: 0.81, n=31
Klan 2022 ¹⁶³	Relaxation training+CBT+Education Migraine frequency: Count: Headache(s)-Days-days-28	Baseline Mean: 9, SD: 5.1, n=36
Klan 2022 ¹⁶³	PMR Migraine frequency: Count: Headache(s)-Days-days-28	Baseline Mean: 8.6, SD: 4.5, n=39
Klan 2022 ¹⁶³	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-days-28	Baseline Mean: 7.4, SD: 3.1, n=31

Reference	Intervention Group and Outcome	Results
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Change from baseline: 23 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -1.67, SE: 0.62, n=51
Klan 2022 ¹⁶³	PMR	Change from baseline: 23 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -1.98, SE: 0.62, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Change from baseline: 59 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -1.75, SE: 0.59, n=51
Klan 2022 ¹⁶³	PMR	Change from baseline: 59 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -2.6, SE: 0.58, n=53
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Change from baseline: 7 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -0.72, SE: 0.66, n=36
Klan 2022 ¹⁶³	PMR	Change from baseline: 7 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: -1.47, SE: 0.63, n=39
Klan 2022 ¹⁶³	No intervention/TAU	Change from baseline: 7 week(s)
	Migraine frequency: Count: Headache(s)-Days-days-28	Mean: 0.33, SE: 0.7, n=31
Klan 2022 ¹⁶³	Relaxation training+CBT+Education	Table 2: 7 weeks: CfB Mean -0.67 (SE 0.62), n = 36
	Other headache: Other: Medication days	Supplementary Table 5: 7 weeks + 4 months: CfB Mean -1.21 (SE 0.49), n = 51 7 weeks + 12 months: CfB Mean -1.26 (SE 0.52), n = 51 Group N inferred from combined N of 104, 36 in CBT group at baseline, 15 randomized from waitlist to CBT, 39 in PMR group at baseline, and 14 randomized from waitlist to PMR.
Klan 2022 ¹⁶³	PMR	Table 2: 7 weeks: CfB Mean -0.70 (SE 0.58), n = 39
	Other headache: Other: Medication days	Supplementary Table 5: 7 weeks + 4 months: CfB Mean -1.17 (SE 0.49), n = 53 7 weeks + 12 months: CfB Mean -1.50 (SE 0.49), n = 53 Group N inferred from combined N of 104, 36 in CBT group at baseline, 15 randomized from waitlist to CBT, 39 in PMR group at baseline, and 14 randomized from waitlist to PMR.
Klan 2022 ¹⁶³	No intervention/TAU	Table 2: 7 weeks: CfB Mean 0.45 (SE 0.65), n = 31
	Other headache: Other: Medication days	
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Baseline
	Functional status: MIDAS	Mean: 35.2, SD: 23.5, n=137

Reference	Intervention Group and Outcome	Results
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Baseline
	Functional status: MIDAS	Mean: 32.1, SD: 23.4, n=148
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 13 week(s)
	Functional status: MIDAS	Mean: 27, SD: 22.4, n=137
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 13 week(s)
	Functional status: MIDAS	Mean: 27.7, SD: 26.6, n=148
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 37 week(s)
	Functional status: MIDAS	Mean: 27.1, SD: 30.2, n=137
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 37 week(s)
	Functional status: MIDAS	Mean: 26.6, SD: 25.5, n=122
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Baseline
	Migraine QOL: MSQoL	Mean: 53.8, SD: 8.9, n=195
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Baseline
	Migraine QOL: MSQoL	Mean: 55.5, SD: 8.3, n=173
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 13 week(s)
	Migraine QOL: MSQoL	Mean: 53, SD: 7.8, n=137
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 13 week(s)
	Migraine QOL: MSQoL	Mean: 53.9, SD: 8.3, n=148
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 37 week(s)
	Migraine QOL: MSQoL	Mean: 57.7, SD: 8.2, n=116
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 37 week(s)
	Migraine QOL: MSQoL	Mean: 56.6, SD: 9.6, n=122
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.9, SD: 3.3, n=195
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.7, SD: 3.6, n=173
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 13 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.6, SD: 4.3, n=137

Reference	Intervention Group and Outcome	Results
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 13 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.6, SD: 4.1, n=148
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Follow-up: 37 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.7, SD: 1.7, n=116
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Follow-up: 37 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.9, SD: 1.7, n=122
Kleiboer 2014 ¹⁶⁵	Relaxation training+CBT+Education	Values taken from Table 2 in secondary analysis:
	Other headache: Other: Acute analgesic use (in days/month)	<p>Analgesic use (days/month)</p> <p>Baseline: 2.9 (SD 3.1) days/month</p> <p>13 weeks: 2.6 (SD 3.5)</p> <p>37 weeks: 2.7 (SD 2.9)</p> <p>Triptan use (days/month)</p> <p>Baseline: 4.3 (SD 3.3)</p> <p>13 weeks: 3.5 (SD 3.1)</p> <p>37 weeks: 3.6 (SD 3.4)</p>
Kleiboer 2014 ¹⁶⁵	No intervention/TAU	Values taken from Table 2 in secondary analysis: Analgesic use (days/month)
	Other headache: Other: Acute analgesic use (in days/month)	<p>Baseline: 2.4 (SD 2.7)</p> <p>13 weeks: 2.4 (SD 2.8)</p> <p>37 weeks: 2.6 (SD 3.1)</p> <p>Triptan use (days/month)</p> <p>Baseline: 4.0 (SD 3.2),</p> <p>13 weeks: 4.0 (SD 3.3)</p> <p>37 weeks: 2.6 (SD 3.1)</p>
Kohlenberg 1981 ¹⁶⁸	Attention control	30/59 at 8 months
	Adverse events: Other: drop out	
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	36/58 at 8 months
	Adverse events: Other: drop out	
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.95, Precision NR, n=58
Kohlenberg 1981 ¹⁶⁸	Attention control	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 2.05, Precision NR, n=59

Reference	Intervention Group and Outcome	Results
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 5 month(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 0.95, Precision NR, n=22
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 5 month(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.55, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 8 month(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 0.7, Precision NR, n=22
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 8 month(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 1.6, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 5 month(s)
	Other headache: Number of acute headache medications used	Mean: 2.2, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 5 month(s)
	Other headache: Number of acute headache medications used	Mean: 4.1, Precision NR, n=22
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 8 month(s)
	Other headache: Number of acute headache medications used	Mean: 2.2, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 8 month(s)
	Other headache: Number of acute headache medications used	Mean: 2.9, Precision NR, n=22
Kohlenberg 1981 ¹⁶⁸	Attention control	Migraine duration (mean hours)
	Other headache: Other: Headache Duration (hours)	Baseline: 10.0; 5 months: 9.25; 8 months: 13.0; Data frames from Figure 2
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Migraine duration (mean hours)Baseline: 13.25;5 months: 6.27;8 months: 5.5;Data frames from Figure 2
	Other headache: Other: Headache Duration (hours)	
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 5 month(s)
	Other headache: VAS	Mean: 1.9, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 5 month(s)
	Other headache: VAS	Mean: 2.3, Precision NR, n=22

Reference	Intervention Group and Outcome	Results
Kohlenberg 1981 ¹⁶⁸	Attention control	Follow-up: 8 month(s)
	Other headache: VAS	Mean: 1.1, Precision NR, n=29
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+Relaxation training+CBT+Meditation	Follow-up: 8 month(s)
	Other headache: VAS	Mean: 2.1, Precision NR, n=22
Kropp 1997 ¹⁶⁹	Biofeedback	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 7.7, SD: 8.6, n=19
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 11.4, SD: 16.6, n=19
Kropp 1997 ¹⁶⁹	Biofeedback	Follow-up: 10 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 4.5, SD: 3.7, n=19
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	Follow-up: 10 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 8, SD: 6, n=19
Kropp 1997 ¹⁶⁹	Biofeedback	Follow-up: 18 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 4.5, SD: 2.4, n=19
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	Follow-up: 18 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 6.5, SD: 6.6, n=19
Kropp 1997 ¹⁶⁹	Biofeedback	8 of 19 patients in the biofeedback group had reduced their medication use by 10 weeks after treatment start. At 18 weeks, it was 7 of 19 patients.
	Other headache: Other: Reduction in medication	
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	2 of 19 patients in the CBT+relaxation group had reduced their medication use by 10 weeks after treatment start. At 18 weeks it was 7 of 19.
	Other headache: Other: Reduction in medication	
Kropp 1997 ¹⁶⁹	Biofeedback	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 3.6, SD: 1.9, n=19
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 4.6, SD: 1.2, n=19
Kropp 1997 ¹⁶⁹	Biofeedback	Follow-up: 18 week(s)
	Other headache: VAS	Mean: 4, SD: 1.6, n=19
Kropp 1997 ¹⁶⁹	Relaxation training+CBT	Follow-up: 18 week(s)
	Other headache: VAS	Mean: 4.5, SD: 1.2, n=19

Reference	Intervention Group and Outcome	Results
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Baseline
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.59, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.64, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 11 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 0.91, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 11 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.57, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 7 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 0.89, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 7 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.68, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	7 weeks f/u; n=5/14; 11 weeks f/u; n=3/14
	Migraine frequency: Other: Zero headaches	
Labbe 1984 ¹⁷⁰	No intervention/TAU	7 weeks f/u; n=0/14; 11 weeks f/u; n=0/14
	Migraine frequency: Other: Zero headaches	
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	7 weeks f/u=0.21 11 weeks f/u = 0.07
	Other headache: Other: Medication index	Medication index—index was computed by multiplying the number of pills taken by the potency rating. A scale adapted from Sargent, Green, and Walters (1973) for rating potency of medication was employed.
Labbe 1984 ¹⁷⁰	No intervention/TAU	7 weeks f/u=3.43 11 weeks f/u = 4.30
	Other headache: Other: Medication index	Medication index—index was computed by multiplying the number of pills taken by the potency rating. A scale adapted from Sargent, Green, and Walters (1973) for rating potency of medication was employed.
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 11 week(s)
	Other headache: VAS	Mean: 1.04, Precision NR, n=14

Reference	Intervention Group and Outcome	Results
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 11 week(s)
	Other headache: VAS	Mean: 3.23, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 11 week(s)
	Other headache: VAS	Mean: 0.88, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 11 week(s)
	Other headache: VAS	Mean: 2.84, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 7 week(s)
	Other headache: VAS	Mean: 1.14, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 7 week(s)
	Other headache: VAS	Mean: 3.43, Precision NR, n=14
Labbe 1984 ¹⁷⁰	Thermal biofeedback+Autogenic training	Follow-up: 7 week(s)
	Other headache: VAS	Mean: 1.07, Precision NR, n=14
Labbe 1984 ¹⁷⁰	No intervention/TAU	Follow-up: 7 week(s)
	Other headache: VAS	Mean: 3.05, Precision NR, n=14
Labbe 1995 ¹⁷¹	Thermal biofeedback+Autogenic training	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.71, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Autogenic training	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 3.67, Precision NR, n=NR
Labbe 1995 ¹⁷¹	No intervention/TAU	Baseline
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 3.18, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Thermal biofeedback+Autogenic training	Follow-up: 11 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 0.05, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Autogenic training	Follow-up: 11 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 0.38, Precision NR, n=NR
Labbe 1995 ¹⁷¹	No intervention/TAU	Follow-up: 11 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.17, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Thermal biofeedback+Autogenic training	Follow-up: 35 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 0.12, Precision NR, n=NR

Reference	Intervention Group and Outcome	Results
Labbe 1995 ¹⁷¹	Autogenic training	Follow-up: 35 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 0.42, Precision NR, n=NR
Labbe 1995 ¹⁷¹	No intervention/TAU	Follow-up: 35 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.52, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Thermal biofeedback+Autogenic training	Follow-up: 7 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 0.6, Precision NR, n=NR
Labbe 1995 ¹⁷¹	Autogenic training	Follow-up: 7 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 1, Precision NR, n=NR
Labbe 1995 ¹⁷¹	No intervention/TAU	Follow-up: 7 week(s)
	Migraine frequency: Count: Migraine(s)-Total-month	Mean: 2.35, Precision NR, n=NR
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Baseline
	Anxiety, depression, or sleep: BDI-II	Mean: 16.05, SD: 10.47, n=44
Lemstra 2002 ¹⁷²	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: BDI-II	Mean: 17.53, SD: 9.82, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 4.5 month(s)
	Anxiety, depression, or sleep: BDI-II	Mean: -10.61, SE: 1.25, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 4.5 month(s)
	Anxiety, depression, or sleep: BDI-II	Mean: -1.17, SE: 0.46, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 6 week(s)
	Anxiety, depression, or sleep: BDI-II	Mean: -9.77, SE: 1.23, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 6 week(s)
	Anxiety, depression, or sleep: BDI-II	Mean: -1.17, SE: 0.46, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change in functional status measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD)
	Functional status: Other: VAS	6 wks: 34.77 (4.75) 4.5 months: 51.59 (7.71)

Reference	Intervention Group and Outcome	Results
Lemstra 2002 ¹⁷²	No intervention/TAU Functional status: Other: VAS	Change in functional status measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 wks: -0.56 (2.03) 4.5 months: -0.56 (2.03)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Functional status: Other: Work status	Change in work status (%): No change (90.9%) Back to work (9.1%) Off work (0%)
Lemstra 2002 ¹⁷²	No intervention/TAU Functional status: Other: Work status	Change in work status (%): No change (100%)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Functional status: PDI	Baseline Mean: 32.95, SD: 12.92, n=44
Lemstra 2002 ¹⁷²	No intervention/TAU Functional status: PDI	Baseline Mean: 34.19, SD: 16.06, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Functional status: PDI	Change from baseline: 4.5 month(s) Mean: -18.8, SE: 2.23, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU Functional status: PDI	Change from baseline: 4.5 month(s) Mean: -1.72, SE: 0.96, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Functional status: PDI	Change from baseline: 6 week(s) Mean: -14.5, SE: 2.13, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU Functional status: PDI	Change from baseline: 6 week(s) Mean: -1.72, SE: 0.96, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy General QOL: Other: Self-rated health	Before and after blinded measurements were taken for the following: health status rated from 1 (excellent health) to 5 (poor health). Baseline Mean (SD): 3.60 (1.03), N=44 Change in health status at 6 wks, Mean (SD): 0.73 (0.12), N=41
Lemstra 2002 ¹⁷²	No intervention/TAU General QOL: Other: Self-rated health	Before and after blinded measurements were taken for the following: health status rated from 1 (excellent health) to 5 (poor health). Baseline Mean (SD): 3.67 (0.89), N=36 Change in health status at 6 wks, Mean (SD): -0.05 (0.03), N=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change in quality of life measured with a Visual Analogue Scale that included values from 100% worse to 100%

Reference	Intervention Group and Outcome	Results
	General QOL: Other: VAS	improvement. Mean (SD) 6 wks:35.34 (5.03) 4.5 months: 57.05 (8.17)
Lemstra 2002 ¹⁷²	No intervention/TAU General QOL: Other: VAS	Change in quality of life measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 wks: -1.94 (1.94) 4.5 months: -1.94 (1.94)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: Other: Change in pain duration	Change in pain duration measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 weeks: 28.75 (5.17) 4.5 months: 47.16 (8.33)
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: Other: Change in pain duration	Change in pain duration measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 weeks: -5.0 (2.91) 4.5 months: -5.0 (2.91)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: Other: Change in pain frequency	Change in pain frequency measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 weeks:33.64 (5.29) 4.5 months: 56.93 (9.13)
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: Other: Change in pain frequency	Change in pain frequency measured with a Visual Analogue Scale that included values from 100% worse to 100% improvement. Mean (SD) 6 weeks: -2.22 (2.22) 4.5 months: -2.22 (2.22)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: Other: Days and hours in pain	Days in pain and hours in pain without relief in the last 30 days. Mean (SD) Baseline days, 20.20 (8.07) Baseline hours, 162.27 (207.68) 6 wks change in days, 9.50 (1.41) 6 wks change in hours, 95.86 (28.66)
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: Other: Days and hours in pain	Days in pain and hours in pain without relief in the last 30 days. Mean (SD) Baseline days, 21.08 (8.33) Baseline hours, 166.14 (29.45)

Reference	Intervention Group and Outcome	Results
		6 wks change in days, 1.31 (0.36) 6 wks change in hours, 4.53 (3.05)
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Baseline Mean: 7.34, SD: 1.87, n=44
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Baseline Mean: 9.05, SD: 1.33, n=44
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Baseline Mean: 3.68, SD: 3.24, n=44
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: VAS	Baseline Mean: 7.14, SD: 2.02, n=36
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: VAS	Baseline Mean: 9.11, SD: 1.35, n=36
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: VAS	Baseline Mean: 3.03, SD: 2.97, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Change from baseline: 4.5 month(s) Mean: -3.25, SE: 0.49, n=41
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Change from baseline: 4.5 month(s) Mean: -2.53, SE: 0.44, n=41
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy Other headache: VAS	Change from baseline: 4.5 month(s) Mean: -2.47, SE: 0.47, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: VAS	Change from baseline: 4.5 month(s) Mean: -0.15, SE: 0.17, n=36
Lemstra 2002 ¹⁷²	No intervention/TAU Other headache: VAS	Change from baseline: 4.5 month(s) Mean: -0.03, SE: 0.14, n=36

Reference	Intervention Group and Outcome	Results
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 4.5 month(s)
	Other headache: VAS	Mean: 0.28, SE: 0.3, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 4.5 month(s)
	Other headache: VAS	Mean: -38.18, SE: 8.54, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 4.5 month(s)
	Other headache: VAS	Mean: 2.78, SE: 1.98, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: -19.55, SE: 5.61, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: 2.78, SE: 1.98, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: -2.29, SE: 0.39, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: -0.15, SE: 0.17, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: -1.57, SE: 0.35, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: 0.28, SE: 0.3, n=36
Lemstra 2002 ¹⁷²	Relaxation training+CBT+Education+Exercise+Massage therapy+Physical therapy	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: -1.55, SE: 0.38, n=41
Lemstra 2002 ¹⁷²	No intervention/TAU	Change from baseline: 6 week(s)
	Other headache: VAS	Mean: 0.28, SE: 0.3, n=36
Matchar 2008 ¹⁷³	No intervention/TAU	64/309 at 6 months
	Adverse events: Other: drop out	

Reference	Intervention Group and Outcome	Results
Matchar 2008 ¹⁷³	Relaxation training+Education Adverse events: Other: drop out	98/305 at 6 months
Matchar 2008 ¹⁷³	No intervention/TAU Anxiety, depression, or sleep: PHQ-9	Follow-up: 6 month(s) Mean: 6.6, SD: 5.3, n=236
Matchar 2008 ¹⁷³	Relaxation training+Education Anxiety, depression, or sleep: PHQ-9	Follow-up: 6 month(s) Mean: 5.6, SD: 5.2, n=201
Matchar 2008 ¹⁷³	No intervention/TAU Functional status: MIDAS	Baseline Mean: 30.6, SD: 42.2, n=236
Matchar 2008 ¹⁷³	Relaxation training+Education Functional status: MIDAS	Baseline Mean: 30.8, SD: 37.1, n=201
Matchar 2008 ¹⁷³	No intervention/TAU Functional status: MIDAS	Follow-up: 6 month(s) Mean: 23.6, SD: 37.6, n=236
Matchar 2008 ¹⁷³	Relaxation training+Education Functional status: MIDAS	Follow-up: 6 month(s) Mean: 15.9, SD: 24.2, n=236
Matchar 2008 ¹⁷³	No intervention/TAU General QOL: SF-36	Follow-up: 6 month(s) Mean: 45, SD: 8.4, n=236
Matchar 2008 ¹⁷³	Relaxation training+Education General QOL: SF-36	Follow-up: 6 month(s) Mean: 47.6, SD: 7.7, n=201
Matchar 2008 ¹⁷³	No intervention/TAU General QOL: SF-36	Follow-up: 6 month(s) Mean: 43.9, SD: 11.6, n=236
Matchar 2008 ¹⁷³	Relaxation training+Education General QOL: SF-36	Follow-up: 6 month(s) Mean: 45.4, SD: 11.6, n=201
Mathew 1981 ¹⁷⁴	No intervention/TAU Adverse events: Other: Drop out (any reason)	26/94
Mathew 1981 ¹⁷⁴	Propranolol Adverse events: Other: Drop out (any reason)	16/76
Mathew 1981 ¹⁷⁴	Amitriptyline Adverse events: Other: Drop out (any reason)	23/86

Reference	Intervention Group and Outcome	Results
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback Adverse events: Other: Drop out (any reason)	38/100
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Adverse events: Other: Drop out (any reason)	14/88
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Adverse events: Other: Drop out (any reason)	15/82
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Adverse events: Other: Drop out (any reason)	14/89
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Adverse events: Other: Drop out (any reason)	17/84
Mathew 1981 ¹⁷⁴	No intervention/TAU Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 13, n=94
Mathew 1981 ¹⁷⁴	Propranolol Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 4, n=92
Mathew 1981 ¹⁷⁴	Amitriptyline Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 7, n=86
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 1, n=100
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 4, n=88
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 5, n=82
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 6, n=89
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events	Change from baseline: 6 month(s) Responders/events: 7, n=84
Mathew 1981 ¹⁷⁴	No intervention/TAU Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 4, n=45

Reference	Intervention Group and Outcome	Results
Mathew 1981 ¹⁷⁴	Propranolol Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 1, n=44
Mathew 1981 ¹⁷⁴	Amitriptyline Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 4, n=42
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 0, n=48
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 2, n=41
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 2, n=39
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 2, n=43
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Migraine	Change from baseline: 6 month(s) Responders/events: 3, n=38
Mathew 1981 ¹⁷⁴	No intervention/TAU Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 9, n=49
Mathew 1981 ¹⁷⁴	Propranolol Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 3, n=48
Mathew 1981 ¹⁷⁴	Amitriptyline Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 3, n=44
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback	Change from baseline: 6 month(s) Responders/events: 1, n=52

Reference	Intervention Group and Outcome	Results
	Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 2, n=47
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 3, n=43
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 4, n=46
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Adverse events: Withdrawal due to adverse events; Subgroup: Mix headache (migraine TH)	Change from baseline: 6 month(s) Responders/events: 4, n=46
Mathew 1981 ¹⁷⁴	No intervention/TAU Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 37.0 \pm 2.3
Mathew 1981 ¹⁷⁴	Propranolol Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 36.2 \pm 2.5
Mathew 1981 ¹⁷⁴	Amitriptyline Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 39.7 \pm 3.1
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 41.2 \pm 2.9
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 43.0 \pm 1.8
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 38.4 \pm 2.1
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 36.3 \pm 1.7
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 40.5 \pm 3.2

Reference	Intervention Group and Outcome	Results
Mathew 1981 ¹⁷⁴	No intervention/TAU Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 52.2 \pm 2.9
Mathew 1981 ¹⁷⁴	Propranolol Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 55.3 \pm 4.7
Mathew 1981 ¹⁷⁴	Amitriptyline Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 50.3 \pm 4.2
Mathew 1981 ¹⁷⁴	Relaxation training+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 51.2 \pm 3.1
Mathew 1981 ¹⁷⁴	Propranolol+Amitriptyline Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 47.8 \pm 3.6
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 52.6 \pm 2.1
Mathew 1981 ¹⁷⁴	Relaxation training+Amitriptyline+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 48.1 \pm 3.7
Mathew 1981 ¹⁷⁴	Relaxation training+Propranolol+Amitriptyline+Biofeedback Other headache: Other: depression score	Zung Self-Rating Depression Scale (SDS), average score 54.0 + 3.5
Minen 2020a ¹⁷⁵	PMR Functional status: MIDAS	Baseline Mean: 46, SD: 42, n=23
Minen 2020a ¹⁷⁵	No intervention/TAU Functional status: MIDAS	Baseline Mean: 35, SD: 46, n=21
Minen 2020b ¹⁷⁶	PMR Functional status: MIDAS	Baseline Mean: 35.9, SD: 41.2, n=NR
Minen 2020b ¹⁷⁶	No intervention/TAU Functional status: MIDAS	Baseline Mean: 27.2, SD: 27.9, n=NR
Minen 2020b ¹⁷⁶	PMR Functional status: MIDAS	Change from baseline: 3 month(s) Mean: -22.8, SD: 33.3, n=NR
Minen 2020b ¹⁷⁶	No intervention/TAU Functional status: MIDAS	Change from baseline: 3 month(s) Mean: -8.7, SD: 41.4, n=NR

Reference	Intervention Group and Outcome	Results
Minen 2020a ¹⁷⁵	No intervention/TAU	Change from baseline: 6 month(s)
	Functional status: MIDAS	Mean: -19.5, SD: 50, n=21
Minen 2020a ¹⁷⁵	PMR	Change from baseline: 6 month(s)
	Functional status: MIDAS	Mean: -4, SD: 49, n=23
Minen 2020b ¹⁷⁶	PMR	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 10.5, SD: 8.7, n=77
Minen 2020b ¹⁷⁶	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 10.1, SD: 10.1, n=61
Minen 2020b ¹⁷⁶	PMR	2023 total headache days; 1811 total headache-free days; 1.12 ratio headache days/headache-free days. Table 3
	Migraine frequency: Other: Headache days	
Minen 2020b ¹⁷⁶	No intervention/TAU	1779 total headache days; 2125 total headache-free days; 0.84 ratio headache days/headache-free days. Table 3
	Migraine frequency: Other: Headache days	
Minen 2021 ¹⁷⁸	HRV biofeedback	Baseline
	Anxiety, depression, or sleep: GAD-7	Mean: 8.5, SD: 5, n=26
Minen 2021 ¹⁷⁸	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: GAD-7	Mean: 5.5, SD: 3.9, n=26
Minen 2021 ¹⁷⁸	HRV biofeedback	Mean (SD): 13.3 (6.3)
	Anxiety, depression, or sleep: Other: Insomnia Sleep Index (ISI)	
Minen 2021 ¹⁷⁸	No intervention/TAU	Mean (SD): 12 (7.5)
	Anxiety, depression, or sleep: Other: Insomnia Sleep Index (ISI)	
Minen 2021 ¹⁷⁸	HRV biofeedback	Baseline
	Anxiety, depression, or sleep: PHQ-9	Mean: 7.8, SD: 5.7, n=26
Minen 2021 ¹⁷⁸	No intervention/TAU	Baseline
	Anxiety, depression, or sleep: PHQ-9	Mean: 6.3, SD: 5.3, n=26
Minen 2021 ¹⁷⁸	HRV biofeedback	MIDAS at baseline, n(%): Severe disability: 16 (61.6) Not severe: 10 (38.5)
	Functional status: Other: MIDAS severity	

Reference	Intervention Group and Outcome	Results
Minen 2021 ¹⁷⁸	No intervention/TAU Functional status: Other: MIDAS severity	MIDAS at baseline, n(%): Severe disability: 15 (57.7) Not severe: 11 (42.3)
Minen 2021 ¹⁷⁸	HRV biofeedback Migraine QOL: MSQoL v2.1	Change from baseline: 60 day(s) Mean: 1.3, Precision NR, n=26
Minen 2021 ¹⁷⁸	No intervention/TAU Migraine QOL: MSQoL v2.1	Change from baseline: 60 day(s) Mean: 1.6, Precision NR, n=26
Minen 2021 ¹⁷⁸	HRV biofeedback Migraine QOL: Other: Baseline MSQL subscales	Mean (SD), N=26 MSQL Role Function - Restrictive: 48.9 (15.2) MSQL Role Function - Preventive: 62.5 (17.7) MSQL Emotional Function - 44.2 (13.9)
Minen 2021 ¹⁷⁸	No intervention/TAU Migraine QOL: Other: Baseline MSQL subscales	Mean (SD), N=26 MSQL Role Function - Restrictive: 55.9 (14.2) MSQL Role Function - Preventive: 63.5 (15.4) MSQL Emotional Function - 43.3 (10.6)
Mérelle 2008 ¹⁷⁹	Autogenic training+Education Functional status: MIDAS	Baseline Mean: 23.2, SD: 16.9, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU Functional status: MIDAS	Baseline Mean: 23.9, SD: 13.5, n=57
Mérelle 2008 ¹⁷⁹	Autogenic training+Education Functional status: MIDAS; Subgroup: Completed protocol	Follow-up: 10 week(s) Mean: 21.3, SD: 16.6, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU Functional status: MIDAS; Subgroup: Completed protocol	Follow-up: 10 week(s) Mean: 20.9, SD: 14, n=57
Mérelle 2008 ¹⁷⁹	Autogenic training+Education Migraine QOL: MSQoL v2.1	Baseline Mean: 57.1, SD: 8.74, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU Migraine QOL: MSQoL v2.1	Baseline Mean: 56.6, SD: 8.76, n=57
Mérelle 2008 ¹⁷⁹	Autogenic training+Education Migraine QOL: MSQoL v2.1; Subgroup: Completed protocol	Follow-up: 10 week(s) Mean: 58.2, SD: 7.24, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU Migraine QOL: MSQoL v2.1; Subgroup: Completed protocol	Follow-up: 10 week(s) Mean: 56.8, SD: 8.94, n=57

Reference	Intervention Group and Outcome	Results
Mérelle 2008 ¹⁷⁹	Autogenic training+Education	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week-4	Mean: 3.08, SD: 1.61, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week-4	Mean: 3.09, SD: 1.67, n=57
Mérelle 2008 ¹⁷⁹	Autogenic training+Education	Follow-up: 10 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week-4; Subgroup: Completed protocol	Mean: 2.43, SD: 1.73, n=51
Mérelle 2008 ¹⁷⁹	No intervention/TAU	Follow-up: 10 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week-4; Subgroup: Completed protocol	Mean: 2.89, SD: 1.71, n=57
Odawara 2015 ¹⁸²	Thermal biofeedback+PMR+EMG biofeedback	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.2, SD: 3.3, n=17
Odawara 2015 ¹⁸²	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 5.8, SD: 3.7, n=11
Odawara 2015 ¹⁸²	Thermal biofeedback+PMR+EMG biofeedback	Follow-up: 14 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 4.3, SD: 2.9, n=17
Odawara 2015 ¹⁸²	No intervention/TAU	Follow-up: 14 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.5, SD: 4.4, n=11
Pickering 2012 ¹⁸³	Relaxation training	8 at 2 months f/u10 at 4 moths f/u
	Adverse events: Other: drop out	
Pickering 2012 ¹⁸³	No intervention/TAU	8 at 2 months f/u12 at 4 moths f/u
	Adverse events: Other: drop out	
Pickering 2012 ¹⁸³	Relaxation training	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9, SD: 3.19, n=21
Pickering 2012 ¹⁸³	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 8.57, SD: 2.38, n=21
Pickering 2012 ¹⁸³	Relaxation training	Follow-up: 2 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.1, SD: 2.98, n=21

Reference	Intervention Group and Outcome	Results
Pickering 2012 ¹⁸³	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 2 month(s) Mean: 7.71, SD: 3.13, n=21
Pickering 2012 ¹⁸³	Relaxation training Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 4 month(s) Mean: 6.47, SD: 3.24, n=17
Pickering 2012 ¹⁸³	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 4 month(s) Mean: 7.11, SD: 4.31, n=17
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Adverse events: Other: Various adverse events from amitriptyline	"There were a total of 199 adverse events of all grades reported during the trial(90intheCBTplusamitriptylinegroupvs109 in headache education plus amitriptyline group).The headache education group reported more regular level adverse events for central nervous system and respiratory categories than the CBT group. A total of 23 upper level events were reported. There were no differences between the CBT and headache education groups for upper level events. The majority of central nervous system adverse events involved status migrainosis or worsening of migraine, and others included expected adverse events of amitriptyline (fatigue or drowsiness and dizziness). Respiratory adverse events included influenza, pneumonia, seasonal allergies, and upper respiratory infections." All adverse events presented in Table2 .
Powers 2013 ¹⁸⁴	Amitriptyline+Education Adverse events: Other: Various adverse events from amitriptyline	"There were a total of 199 adverse events of all grades reported during the trial(90intheCBTplusamitriptylinegroupvs109 in headache education plus amitriptyline group).The headache education group reported more regular level adverse events for central nervous system and respiratory categories than the CBT group. A total of 23 upper level events were reported. There were no differences between the CBT and headache education groups for upper level events. The majority of central nervous system adverse events involved status migrainosis or worsening of migraine, and others included expected adverse events of amitriptyline (fatigue or drowsiness and dizziness). Respiratory adverse events included influenza, pneumonia, seasonal allergies, and upper respiratory infections." All adverse events presented in Table2 .
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Functional status: PedMIDAS	Baseline Mean: 68.2, SD: 31.7, n=64
Powers 2013 ¹⁸⁴	Amitriptyline+Education Functional status: PedMIDAS	Baseline Mean: 68.2, SD: 31.7, n=71

Reference	Intervention Group and Outcome	Results
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Functional status: PedMIDAS	Follow-up: 20 week(s) Mean: 15.5, SD: 17.4, n=57
Powers 2013 ¹⁸⁴	Amitriptyline+Education Functional status: PedMIDAS	Follow-up: 20 week(s) Mean: 29.6, SD: 42.2, n=70
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Functional status: PedMIDAS	Follow-up: 72 week(s) Mean: 7.8, 95% CI: 3.8 to 11.59, n=57
Powers 2013 ¹⁸⁴	Amitriptyline+Education Functional status: PedMIDAS	Follow-up: 72 week(s) Mean: 19, 95% CI: 11.6 to 26.5, n=70
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 20 week(s) Percent responders/events: 66, n=59
Powers 2013 ¹⁸⁴	Amitriptyline+Education Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 20 week(s) Percent responders/events: 36, n=69
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 72 week(s) Percent responders/events: 86, n=59
Powers 2013 ¹⁸⁴	Amitriptyline+Education Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 72 week(s) Percent responders/events: 68, n=67
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Migraine frequency: Count: Headache(s)-Days-days-28	Baseline Mean: 21.3, SD: 5.2, n=64
Powers 2013 ¹⁸⁴	Amitriptyline+Education Migraine frequency: Count: Headache(s)-Days-days-28	Baseline Mean: 21.3, SD: 5.2, n=71
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Migraine frequency: Count: Headache(s)-Days-days-28	Follow-up: 20 week(s) Mean: 9.8, SD: 9.8, n=59

Reference	Intervention Group and Outcome	Results
Powers 2013 ¹⁸⁴	Amitriptyline+Education Migraine frequency: Count: Headache(s)-Days-days-28	Follow-up: 20 week(s) Mean: 14.5, SD: 9.8, n=69
Powers 2013 ¹⁸⁴	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback Migraine frequency: Count: Headache(s)-Days-days-28	Follow-up: 72 week(s) Mean: 5.9, 95% CI: 3.8 to 7.9, n=57
Powers 2013 ¹⁸⁴	Amitriptyline+Education Migraine frequency: Count: Headache(s)-Days-days-28	Follow-up: 72 week(s) Mean: 8.6, 95% CI: 6.3 to 11.1, n=67
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Functional status: PedMIDAS	Baseline Mean: 13.26, SD: 9.69, n=18
Rapoff 2014 ¹⁸⁸	Education control Functional status: PedMIDAS	Baseline Mean: 15.53, SD: 10.08, n=17
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Functional status: PedMIDAS	Follow-up: 18 week(s) Mean: 0.91, SD: 1.45, n=11
Rapoff 2014 ¹⁸⁸	Education control Functional status: PedMIDAS	Follow-up: 18 week(s) Mean: 3.5, SD: 4.86, n=11
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Functional status: PedMIDAS	Follow-up: 4 week(s) Mean: 7.82, SD: 10.59, n=18
Rapoff 2014 ¹⁸⁸	Education control Functional status: PedMIDAS	Follow-up: 4 week(s) Mean: 12.29, SD: 12.94, n=17
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education General QOL: PedsQL	Baseline Mean: 82.1, SD: 12.18, n=18
Rapoff 2014 ¹⁸⁸	Education control General QOL: PedsQL	Baseline Mean: 79.35, SD: 11.55, n=17
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education General QOL: PedsQL	Follow-up: 18 week(s) Mean: 84.88, SD: 18.22, n=11

Reference	Intervention Group and Outcome	Results
Rapoff 2014 ¹⁸⁸	Education control General QOL: PedsQL	Follow-up: 18 week(s) Mean: 85.67, SD: 14.32, n=11
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education General QOL: PedsQL	Follow-up: 4 week(s) Mean: 83.7, SD: 12.07, n=18
Rapoff 2014 ¹⁸⁸	Education control General QOL: PedsQL	Follow-up: 4 week(s) Mean: 80.69, SD: 14.36, n=17
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Migraine frequency: Other: As reported by child: Percentage of days with headache	N=18 for this group for baseline and 4 weeks. N=11 at 18 weeks. At baseline, mean 41.09% SD 35.71%. At 4 weeks after start of intervention, mean 31.28% SD 28.24%. At 18 weeks after start of intervention, mean 21.43% SD 23.47%.
Rapoff 2014 ¹⁸⁸	Education control Migraine frequency: Other: As reported by child: Percentage of days with headache	N=17 for this group for baseline and 4 weeks. N=11 at 18 weeks. At baseline, mean 40.67% SD 28.79%. At 4 weeks after start of intervention, mean 32.14% SD 22.23%. At 18 weeks after start of intervention, mean 18.18% SD 17.6%.
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Other headache: VAS	Baseline Mean: 5.06, SD: 1.84, n=18
Rapoff 2014 ¹⁸⁸	Education control Other headache: VAS	Baseline Mean: 6, SD: 1.52, n=17
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Other headache: VAS	Follow-up: 18 week(s) Mean: 4.46, SD: 1.88, n=11
Rapoff 2014 ¹⁸⁸	Education control Other headache: VAS	Follow-up: 18 week(s) Mean: 3.68, SD: 2.04, n=11
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+Pain management education Other headache: VAS	Follow-up: 4 week(s) Mean: 5.06, SD: 1.5, n=18
Rapoff 2014 ¹⁸⁸	Education control Other headache: VAS	Follow-up: 4 week(s) Mean: 6.25, SD: 1.92, n=17
Rausa 2016 ¹⁸⁹	EMG biofeedback Migraine frequency: Count: Headache(s)-Days-month	Baseline Mean: 19.93, 95% CI: 17.5 to 22.4, n=15

Reference	Intervention Group and Outcome	Results
Rausa 2016 ¹⁸⁹	Attention control	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 22.1, 95% CI: 19.4 to 24.8, n=12
Rausa 2016 ¹⁸⁹	EMG biofeedback	Follow-up: 25 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 13, 95% CI: 9.6 to 16.4, n=15
Rausa 2016 ¹⁸⁹	Attention control	Follow-up: 25 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 22.3, 95% CI: 18.6 to 26.1, n=12
Rausa 2016 ¹⁸⁹	EMG biofeedback	Follow-up: 9 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 13.9, 95% CI: 10.5 to 17.3, n=21
Rausa 2016 ¹⁸⁹	Attention control	Follow-up: 9 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 24.3, 95% CI: 20.4 to 28.1, n=16
Rausa 2016 ¹⁸⁹	EMG biofeedback	Baseline
	Other headache: Number of acute headache medications used	Mean: 21.3, 95% CI: 13.7 to 28.9, n=15
Rausa 2016 ¹⁸⁹	Attention control	Baseline
	Other headache: Number of acute headache medications used	Mean: 26.6, 95% CI: 18.1 to 35.1, n=12
Rausa 2016 ¹⁸⁹	EMG biofeedback	Follow-up: 25 week(s)
	Other headache: Number of acute headache medications used	Mean: 12.4, 95% CI: 2.8 to 22, n=15
Rausa 2016 ¹⁸⁹	Attention control	Follow-up: 25 week(s)
	Other headache: Number of acute headache medications used	Mean: 21.2, 95% CI: 16.5 to 37.9, n=12
Rausa 2016 ¹⁸⁹	EMG biofeedback	Follow-up: 9 week(s)
	Other headache: Number of acute headache medications used	Mean: 11.9, 95% CI: 4.3 to 19.5, n=21
Rausa 2016 ¹⁸⁹	Attention control	Follow-up: 9 week(s)
	Other headache: Number of acute headache medications used	Mean: 26.6, 95% CI: 18.1 to 35.1, n=16
Reich 1989 ¹⁹⁰	Thermal biofeedback	Baseline
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 26, Precision NR, n=100

Reference	Intervention Group and Outcome	Results
Reich 1989 ¹⁹⁰	Relaxation training	Baseline
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 25, Precision NR, n=95
Reich 1989 ¹⁹⁰	Preference-based/tailored	Baseline
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 25, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 1, Precision NR, n=100
Reich 1989 ¹⁹⁰	Relaxation training	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 9.5, Precision NR, n=95
Reich 1989 ¹⁹⁰	Preference-based/tailored	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 3.3, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 25 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 1.3, Precision NR, n=100
Reich 1989 ¹⁹⁰	Preference-based/tailored	Follow-up: 25 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 4.5, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 37 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 1.8, Precision NR, n=100
Reich 1989 ¹⁹⁰	Preference-based/tailored	Follow-up: 37 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 4.8, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 9 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 1.3, Precision NR, n=100
Reich 1989 ¹⁹⁰	Preference-based/tailored	Follow-up: 9 month(s)
	Migraine frequency: Count: Headache(s)-Hours-week	Mean: 3.8, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback	Mean for those who attended $\hat{a}\% \neq 15$ sessions1 month: 1.3
	Migraine frequency: Other: headache hours per week	
Reich 1989 ¹⁹⁰	Thermal biofeedback	Mean for those who attended >15 sessions1 month: 0.75
	Migraine frequency: Other: headache hours per week	
Reich 1989 ¹⁹⁰	Relaxation training	Mean for those who attended $\hat{a}\% \neq 15$ sessions1 month: 4.6
	Migraine frequency: Other: headache hours per week	

Reference	Intervention Group and Outcome	Results
Reich 1989 ¹⁹⁰	Thermal biofeedback Migraine frequency: Other: headache hours per week	Mean for those who attended >15 sessions 1 month: 11.1
Reich 1989 ¹⁹⁰	Thermal biofeedback Other headache: VAS	Follow-up: 1 month(s) Mean: 1.4, Precision NR, n=100
Reich 1989 ¹⁹⁰	Relaxation training Other headache: VAS	Follow-up: 1 month(s) Mean: 2.7, Precision NR, n=95
Reich 1989 ¹⁹⁰	Preference-based/tailored Other headache: VAS	Follow-up: 1 month(s) Mean: 2, Precision NR, n=110
Reich 1989 ¹⁹⁰	Thermal biofeedback Other headache: VAS	Follow-up: 25 month(s) Mean: 1.4, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Preference-based/tailored Other headache: VAS	Follow-up: 25 month(s) Mean: 2, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training Other headache: VAS	Follow-up: 25 month(s) Mean: 3, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Thermal biofeedback Other headache: VAS	Follow-up: 37 month(s) Mean: 1.8, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training Other headache: VAS	Follow-up: 37 month(s) Mean: 3, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Preference-based/tailored Other headache: VAS	Follow-up: 37 month(s) Mean: 2.2, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Thermal biofeedback Other headache: VAS	Follow-up: 9 month(s) Mean: 1.4, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training Other headache: VAS	Follow-up: 9 month(s) Mean: 2.8, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Preference-based/tailored Other headache: VAS	Follow-up: 9 month(s) Mean: 2, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training Other headache: VAS; Subgroup: >15 sessions attended	Follow-up: 1 month(s) Mean: 2.4, Precision NR, n=NR

Reference	Intervention Group and Outcome	Results
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 1 month(s)
	Other headache: VAS; Subgroup: >15 sessions attended	Mean: 1.5, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 37 month(s)
	Other headache: VAS; Subgroup: >15 sessions attended	Mean: 1.5, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training	Follow-up: 37 month(s)
	Other headache: VAS; Subgroup: >15 sessions attended	Mean: 2.5, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training	Follow-up: 1 month(s)
	Other headache: VAS; Subgroup: ≤15 sessions attended	Mean: 2.8, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 1 month(s)
	Other headache: VAS; Subgroup: ≤15 sessions attended	Mean: 1.5, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Thermal biofeedback	Follow-up: 37 month(s)
	Other headache: VAS; Subgroup: ≤15 sessions attended	Mean: 2.4, Precision NR, n=NR
Reich 1989 ¹⁹⁰	Relaxation training	Follow-up: 37 month(s)
	Other headache: VAS; Subgroup: ≤15 sessions attended	Mean: 3.3, Precision NR, n=NR
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format	2/19 dropped out from treatment. A smaller n of pts completed followup (Ns not reported by group)
	Adverse events: Other: drop out	
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered	1/16 dropped out from treatment. A smaller n of pts completed followup (Ns not reported by group)
	Adverse events: Other: drop out	
Richardson 1989 ¹⁹¹	No intervention/TAU	0/15
	Adverse events: Other: drop out	
Richardson 1989 ¹⁹¹	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-NR-NR	Mean: 15.53, SD: 8.25, n=17
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered	Baseline
	Migraine frequency: Count: Headache(s)-NR-NR	Mean: 14.54, SD: 8.09, n=15
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format	Baseline
	Migraine frequency: Count: Headache(s)-NR-NR	Mean: 15.47, SD: 6.19, n=15
Richardson 1989 ¹⁹¹	No intervention/TAU	Follow-up: 2 month(s)
	Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: Less severe	Mean: 11.13, SD: 8.646, n=8

Reference	Intervention Group and Outcome	Results
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: Less severe	Follow-up: 2 month(s) Mean: 5.38, SD: 4.24, n=8
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: Less severe	Follow-up: 2 month(s) Mean: 5, SD: 3.38, n=8
Richardson 1989 ¹⁹¹	No intervention/TAU Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: More severe	Follow-up: 2 month(s) Mean: 18.67, SD: 8.65, n=9
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: More severe	Follow-up: 2 month(s) Mean: 16.29, SD: 7.65, n=7
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format Migraine frequency: Count: Headache(s)-NR-NR; Subgroup: More severe	Follow-up: 2 month(s) Mean: 12.14, SD: 4.95, n=7
Richardson 1989 ¹⁹¹	No intervention/TAU Other headache: VAS; Subgroup: Less severe	Follow-up: 2 month(s) Mean: 3.16, SD: 0.37, n=8
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered Other headache: VAS; Subgroup: Less severe	Follow-up: 2 month(s) Mean: 2.3, SD: 1.38, n=8
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format Other headache: VAS; Subgroup: Less severe	Follow-up: 2 month(s) Mean: 2.75, SD: 1.23, n=8
Richardson 1989 ¹⁹¹	No intervention/TAU Other headache: VAS; Subgroup: More severe	Follow-up: 2 month(s) Mean: 4.09, SD: 0.61, n=9
Richardson 1989 ¹⁹¹	CBT+PMR-Self-administered Other headache: VAS; Subgroup: More severe	Follow-up: 2 month(s) Mean: 3.36, SD: 0.75, n=7
Richardson 1989 ¹⁹¹	CBT+PMR-Clinic format Other headache: VAS; Subgroup: More severe	Follow-up: 2 month(s) Mean: 3.49, SD: 0.63, n=7
Richter 1986 ¹⁹²	CBT Migraine frequency: Count: Headache(s)-Days-week	Baseline Mean: 8.14, SD: 7.82, n=15

Reference	Intervention Group and Outcome	Results
Richter 1986 ¹⁹²	Attention control	Baseline
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 7.26, SD: 6.12, n=12
Richter 1986 ¹⁹²	PMR+Deep breathing	Baseline
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 9.03, SD: 8.05, n=15
Richter 1986 ¹⁹²	PMR+Deep breathing	Follow-up: 10 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 5.17, SD: 5.16, n=15
Richter 1986 ¹⁹²	CBT	Follow-up: 10 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 4.5, SD: 5.29, n=15
Richter 1986 ¹⁹²	Attention control	Follow-up: 10 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 6.45, SD: 6.09, n=12
Richter 1986 ¹⁹²	PMR+Deep breathing	Follow-up: 14 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.91, SD: 3.4, n=15
Richter 1986 ¹⁹²	CBT	Follow-up: 14 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 2.52, SD: 2.94, n=15
Richter 1986 ¹⁹²	Attention control	Follow-up: 14 week(s)
	Migraine frequency: Count: Headache(s)-Days-week	Mean: 4.68, SD: 5.83, n=12
Richter 1986 ¹⁹²	PMR+Deep breathing	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 2.52, SD: 1.19, n=15
Richter 1986 ¹⁹²	CBT	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 2.52, SD: 1.14, n=15
Richter 1986 ¹⁹²	Attention control	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 2.39, SD: 1.33, n=12
Richter 1986 ¹⁹²	PMR+Deep breathing	Follow-up: 14 week(s)
	Other headache: VAS	Mean: 2.08, SD: 1.73, n=15
Richter 1986 ¹⁹²	CBT	Follow-up: 14 week(s)
	Other headache: VAS	Mean: 1.96, SD: 1.23, n=15
Richter 1986 ¹⁹²	Attention control	Follow-up: 14 week(s)
	Other headache: VAS	Mean: 2.02, SD: 1.39, n=12

Reference	Intervention Group and Outcome	Results
Rothrock 2006 ¹⁹³	Education	Baseline
	Functional status: MIDAS	Mean: 38.75, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education control	Baseline
	Functional status: MIDAS	Mean: 68, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education	Change from baseline: 6 month(s)
	Functional status: MIDAS	Mean: -24, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education control	Change from baseline: 6 month(s)
	Functional status: MIDAS	Mean: -14, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 14, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education control	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 23, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education	Change from baseline: 6 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: -6, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education control	Change from baseline: 6 month(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 0, Precision NR, n=50
Rothrock 2006 ¹⁹³	Education	At 6 months after starting intervention: 0
	Other headache: Other: Analgesic overuse	“Analgesic overuse” was defined as self-administration of any given prescription or nonprescription analgesic (or different members from the same class of analgesic) more than 3 days per week for at least 4 consecutive weeks, with a minimum of 2 doses per day.
Rothrock 2006 ¹⁹³	Education control	At 6 months after starting intervention: 18 (35%)
	Other headache: Other: Analgesic overuse	“Analgesic overuse” was defined as self-administration of any given prescription or nonprescription analgesic (or different members from the same class of analgesic) more than 3 days per week for at least 4 consecutive weeks, with a minimum of 2 doses per day.
Rothrock 2006 ¹⁹³	Education	At 6 months after starting intervention: Mean 5.25 days per month of acute medication use
	Other headache: Other: Days per month of acute medication use	

Reference	Intervention Group and Outcome	Results
Rothrock 2006 ¹⁹³	Education control	At 6 months after intervention start: 15.75 mean days of acute medication use/month
	Other headache: Other: Monthly days acute medication use	
Rothrock 2006 ¹⁹³	Education	At 6 months after starting intervention: 25
	Other headache: Other: Unscheduled outpatient visits	
Rothrock 2006 ¹⁹³	Education control	At 6 months after starting intervention: 50
	Other headache: Other: Unscheduled visits	
Sargent 1986 ¹⁹⁴	No intervention/TAU	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.97, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 6.03, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 6.28, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Baseline
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 6.51, Precision NR, n=34
Sargent 1986 ¹⁹⁴	No intervention/TAU	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.53, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.5, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 4.87, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Follow-up: 12 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.08, Precision NR, n=34
Sargent 1986 ¹⁹⁴	No intervention/TAU	Follow-up: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.43, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Follow-up: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.11, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Follow-up: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.05, Precision NR, n=34

Reference	Intervention Group and Outcome	Results
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Follow-up: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Total-week	Mean: 5.05, Precision NR, n=34
Sargent 1986 ¹⁹⁴	No intervention/TAU	Baseline
	Other headache: VAS	Mean: 6.22, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Baseline
	Other headache: VAS	Mean: 6.79, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Baseline
	Other headache: VAS	Mean: 7.1, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Baseline
	Other headache: VAS	Mean: 7.56, Precision NR, n=34
Sargent 1986 ¹⁹⁴	No intervention/TAU	Follow-up: 12 week(s)
	Other headache: VAS	Mean: 5.94, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Follow-up: 12 week(s)
	Other headache: VAS	Mean: 6.01, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Follow-up: 12 week(s)
	Other headache: VAS	Mean: 5.38, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Follow-up: 12 week(s)
	Other headache: VAS	Mean: 5.78, Precision NR, n=34
Sargent 1986 ¹⁹⁴	No intervention/TAU	Follow-up: 32 week(s)
	Other headache: VAS	Mean: 5.8, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training	Follow-up: 32 week(s)
	Other headache: VAS	Mean: 5.64, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Relaxation training+EMG biofeedback	Follow-up: 32 week(s)
	Other headache: VAS	Mean: 5.21, Precision NR, n=34
Sargent 1986 ¹⁹⁴	Thermal biofeedback+Relaxation training	Follow-up: 32 week(s)
	Other headache: VAS	Mean: 5.82, Precision NR, n=34
Sartory 1998 ¹⁹⁶	PMR+SMT	Baseline
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.75, SD: 1.44, n=11

Reference	Intervention Group and Outcome	Results
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse	Baseline
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.73, SD: 1.25, n=10
Sartory 1998 ¹⁹⁶	Metoprolol	Baseline
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.46, SD: 0.9, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT	Follow-up: 12 month(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.14, SD: 1.19, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse	Follow-up: 12 month(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.05, SD: 0.72, n=10
Sartory 1998 ¹⁹⁶	Metoprolol	Follow-up: 12 month(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.25, SD: 0.82, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT	Follow-up: 14 week(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 0.82, SD: 1.15, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse	Follow-up: 14 week(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 0.8, SD: 0.95, n=10
Sartory 1998 ¹⁹⁶	Metoprolol	Follow-up: 18 week(s)
	Migraine frequency: Count: Migraine(s)-Days-week	Mean: 1.03, SD: 0.78, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT	Baseline
	Other headache: Number of acute headache medications used	Mean: 0.34, SD: 0.37, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse	Baseline
	Other headache: Number of acute headache medications used	Mean: 0.22, SD: 0.24, n=10
Sartory 1998 ¹⁹⁶	Metoprolol	Baseline
	Other headache: Number of acute headache medications used	Mean: 0.41, SD: 0.34, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT	Follow-up: 12 month(s)
	Other headache: Number of acute headache medications used	Mean: 0.09, SD: 0.2, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse	Follow-up: 12 month(s)
		Mean: 0.18, SD: 0.33, n=10

Reference	Intervention Group and Outcome	Results
	Other headache: Number of acute headache medications used	
Sartory 1998 ¹⁹⁶	Metoprolol Other headache: Number of acute headache medications used	Follow-up: 12 month(s) Mean: 0.15, SD: 0.34, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT Other headache: Number of acute headache medications used	Follow-up: 14 week(s) Mean: 0.13, SD: 0.31, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse Other headache: Number of acute headache medications used	Follow-up: 14 week(s) Mean: 0.02, SD: 0.05, n=10
Sartory 1998 ¹⁹⁶	Metoprolol Other headache: Number of acute headache medications used	Follow-up: 18 week(s) Mean: 0.42, SD: 0.38, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT Other headache: VAS	Baseline Mean: 5.24, SD: 1.18, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse Other headache: VAS	Baseline Mean: 4.65, SD: 2.57, n=10
Sartory 1998 ¹⁹⁶	Metoprolol Other headache: VAS	Baseline Mean: 4.63, SD: 2.28, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT Other headache: VAS	Follow-up: 12 month(s) Mean: 2.98, SD: 2.65, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse Other headache: VAS	Follow-up: 12 month(s) Mean: 3.09, SD: 1.67, n=10
Sartory 1998 ¹⁹⁶	Metoprolol Other headache: VAS	Follow-up: 12 month(s) Mean: 4.19, SD: 2.42, n=6
Sartory 1998 ¹⁹⁶	PMR+SMT Other headache: VAS	Follow-up: 14 week(s) Mean: 3.37, SD: 2.68, n=11
Sartory 1998 ¹⁹⁶	SMT+Blood volume pulse Other headache: VAS	Follow-up: 14 week(s) Mean: 2.51, SD: 2.37, n=10

Reference	Intervention Group and Outcome	Results
Sartory 1998 ¹⁹⁶	Metoprolol	Follow-up: 18 week(s)
	Other headache: VAS	Mean: 5.02, SD: 2.22, n=6
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT	Baseline
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 11.35, SE: 0.84, n=13
Scharff 2002 ¹⁹⁷	Sham	Baseline
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 9.48, SE: 1.35, n=11
Scharff 2002 ¹⁹⁷	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 12.04, SE: 0.92, n=12
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT	Follow-up: 3.5 month(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 6.94, SE: 1.79, n=13
Scharff 2002 ¹⁹⁷	Sham	Follow-up: 3.5 month(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 6.05, SE: 1.87, n=11
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT	Follow-up: 6.5 month(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 3.43, SE: 1.67, n=13
Scharff 2002 ¹⁹⁷	Sham	Follow-up: 6.5 month(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 6.77, SE: 2.22, n=11
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 7.14, SE: 1.12, n=13
Scharff 2002 ¹⁹⁷	Sham	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 7.89, SE: 1.73, n=11
Scharff 2002 ¹⁹⁷	No intervention/TAU	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Total-week-2	Mean: 12.13, SE: 0.89, n=12
Scharff 2002 ¹⁹⁷	Thermal biofeedback+Relaxation training+CBT	A headache index (HI) was calculated as the mean headache intensity value for a 2-week period. Headache indices were calculated before and after treatment. It is widely accepted that a clinically significant degree of change in headache is a 50% or greater reduction in HI. Seven in the HWB group (53.8%) achieved a clinically significant degree of improvement by the end of the monitoring period.
	Other headache: Other: Headache index (mean intensity)	
Scharff 2002 ¹⁹⁷	Sham	A headache index (HI) was calculated as the mean headache intensity value for a 2-week period. Headache indices were calculated before and after treatment. It is widely accepted that a
	Other headache: Other: Headache index (mean intensity)	

Reference	Intervention Group and Outcome	Results
		clinically significant degree of change in headache is a 50% or greater reduction in HI. One child in the HCB group (10%) achieved a clinically significant degree of improvement by the end of the monitoring period.
Scharff 2002 ¹⁹⁷	No intervention/TAU Other headache: Other: Headache index (mean intensity)	A headache index (HI) was calculated as the mean headache intensity value for a 2-week period. Headache indices were calculated before and after treatment. It is widely accepted that a clinically significant degree of change in headache is a 50% or greater reduction in HI. None of the 11 children and adolescents in the WLC group had demonstrated significant improvement by the end of the monitoring period.
Seminowicz 2020 ¹⁹⁸	Education+MBSR Anxiety, depression, or sleep: GAD-7	Baseline Median: 1, Range: 0 to 16, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT Anxiety, depression, or sleep: GAD-7	Baseline Median: 1.5, Range: 0 to 16, n=48
Seminowicz 2020 ¹⁹⁸	Education+MBSR Anxiety, depression, or sleep: Other: PSQI	Data from secondary publication. Pittsburgh Sleep Quality Index. Baseline median 3.5 (range 0-11.67). Group difference at as -0.42 (95% CI -1.39 to 0.55) (combined across 8 weeks and 18 weeks).
Seminowicz 2020 ¹⁹⁸	Education+SMT Anxiety, depression, or sleep: Other: PSQI	Data from secondary publication. Pittsburgh Sleep Quality Index. Baseline median 4.67 (range 0-14).
Seminowicz 2020 ¹⁹⁸	Education+MBSR Anxiety, depression, or sleep: PHQ-9	Baseline Median: 2, Range: 0 to 13, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT Anxiety, depression, or sleep: PHQ-9	Baseline Median: 3, Range: 0 to 7, n=48
Seminowicz 2020 ¹⁹⁸	Education+MBSR Functional status: HIT-6	Baseline Mean: 59.6, 95% CI: 57.9 to 61.3, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT Functional status: HIT-6	Baseline Mean: 59.6, 95% CI: 57.7 to 61.5, n=48
Seminowicz 2020 ¹⁹⁸	Education+MBSR Functional status: HIT-6	Follow-up: 18 week(s) Mean: 54.6, 95% CI: 52.9 to 56.4, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT Functional status: HIT-6	Follow-up: 18 week(s) Mean: 57.5, 95% CI: 55.5 to 59.4, n=46

Reference	Intervention Group and Outcome	Results
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 48 week(s)
	Functional status: HIT-6	Mean: 56.2, 95% CI: 54.4 to 58.1, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 48 week(s)
	Functional status: HIT-6	Mean: 58.4, 95% CI: 56.4 to 60.4, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 8 week(s)
	Functional status: HIT-6	Mean: 56.3, 95% CI: 54.5 to 58.1, n=48
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 8 week(s)
	Functional status: HIT-6	Mean: 58.5, 95% CI: 56.5 to 60.4, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.8, 95% CI: 6.9 to 8.8, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 7.7, 95% CI: 6.7 to 8.7, n=48
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 18 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 4.6, 95% CI: 3.7 to 5.6, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 18 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6, 95% CI: 4.9 to 7, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 50 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 4.6, 95% CI: 3.7 to 5.6, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 50 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 5.6, 95% CI: 4.6 to 6.7, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 5.5, 95% CI: 4.6 to 6.5, n=48
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.9, 95% CI: 5.9 to 7.9, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 3.3, 95% CI: 2.5 to 4.2, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 3.2, 95% CI: 2.2 to 4.2, n=48

Reference	Intervention Group and Outcome	Results
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 18 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 2, 95% CI: 1.1 to 2.9, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 18 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 3.7, 95% CI: 2.7 to 4.7, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 50 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 2.1, 95% CI: 1.2 to 3, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 50 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 3.1, 95% CI: 2.1 to 4, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 8 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 1.9, 95% CI: 1 to 2.8, n=48
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 8 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 4, 95% CI: 3 to 5, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Baseline
	Other headache: VAS	Mean: 4.7, 95% CI: 4.2 to 5.2, n=50
Seminowicz 2020 ¹⁹⁸	Education+SMT	Baseline
	Other headache: VAS	Mean: 4.3, 95% CI: 3.8 to 4.8, n=48
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 18 week(s)
	Other headache: VAS	Mean: 4.4, 95% CI: 4 to 4.9, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 18 week(s)
	Other headache: VAS	Mean: 4.4, 95% CI: 3.9 to 5, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 48 week(s)
	Other headache: VAS	Mean: 4.5, 95% CI: 4.1 to 5, n=49
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 48 week(s)
	Other headache: VAS	Mean: 4.7, 95% CI: 4.2 to 5.3, n=46
Seminowicz 2020 ¹⁹⁸	Education+MBSR	Follow-up: 8 week(s)
	Other headache: VAS	Mean: 4.4, 95% CI: 4 to 4.9, n=48
Seminowicz 2020 ¹⁹⁸	Education+SMT	Follow-up: 8 week(s)
	Other headache: VAS	Mean: 4.4, 95% CI: 3.9 to 4.9, n=46

Reference	Intervention Group and Outcome	Results
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Baseline
	Functional status: HDI	Mean: 52.5, SD: 21.2, n=31
Seng 2019 ²⁰¹	No intervention/TAU	Baseline
	Functional status: HDI	Mean: 50.2, SD: 16.2, n=29
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Follow-up: 1 month(s)
	Functional status: HDI	Mean: 41.9, 95% CI: 35.2 to 48.7, n=29
Seng 2019 ²⁰¹	No intervention/TAU	Follow-up: 1 month(s)
	Functional status: HDI	Mean: 47.9, 95% CI: 42 to 53.8, n=26
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Follow-up: 3 month(s)
	Functional status: HDI	Mean: 36.4, 95% CI: 29.6 to 43.2, n=29
Seng 2019 ²⁰¹	No intervention/TAU	Follow-up: 3 month(s)
	Functional status: HDI	Mean: 49.3, 95% CI: 43.3 to 55.4, n=26
Seng 2019 ²⁰¹	No intervention/TAU	Baseline
	Functional status: HDI; Subgroup: Chronic	Mean: 54, 95% CI: 50.3 to 57.7, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Baseline
	Functional status: HDI; Subgroup: Chronic	Mean: 56.6, 95% CI: 52.2 to 60.9, n=15
Seng 2019 ²⁰¹	No intervention/TAU	Follow-up: 1 month(s)
	Functional status: HDI; Subgroup: Chronic	Mean: 51.5, 95% CI: 47.9 to 55.1, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Follow-up: 1 month(s)
	Functional status: HDI; Subgroup: Chronic	Mean: 45.7, 95% CI: 41.5 to 50, n=15
Seng 2019 ²⁰¹	No intervention/TAU	Follow-up: 3 month(s)
	Functional status: HDI; Subgroup: Chronic	Mean: 54.3, 95% CI: 50.6 to 57.9, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Follow-up: 3 month(s)
	Functional status: HDI; Subgroup: Chronic	Mean: 46, 95% CI: 41.7 to 50.2, n=15
Seng 2019 ²⁰¹	No intervention/TAU	Baseline
	Functional status: HDI; Subgroup: Episodic	Mean: 43.7, 95% CI: 35 to 52.3, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Baseline
	Functional status: HDI; Subgroup: Episodic	Mean: 43.9, 95% CI: 34.7 to 53.2, n=14

Reference	Intervention Group and Outcome	Results
Seng 2019 ²⁰¹	No intervention/TAU Functional status: HDI; Subgroup: Episodic	Follow-up: 1 month(s) Mean: 43.3, 95% CI: 34.7 to 52, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: HDI; Subgroup: Episodic	Follow-up: 1 month(s) Mean: 38.9, 95% CI: 29.6 to 48.3, n=14
Seng 2019 ²⁰¹	No intervention/TAU Functional status: HDI; Subgroup: Episodic	Follow-up: 3 month(s) Mean: 43.2, 95% CI: 33.9 to 52.4, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: HDI; Subgroup: Episodic	Follow-up: 3 month(s) Mean: 29.4, 95% CI: 20.2 to 38.6, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: MIDI	The MIDI is a 4-item scale designed to assess the extent to which the headache attack interfered with family/home, recreation, social, and occupational functioning on each headache attack day 45, with response options for each domain ranging from 0, "not at all," to 10, "totally." Responses to the four items are averaged to obtain a day-level score. Baseline mean 2.81 (95% CI 2.43 to 3.19) and 3 month mean 2.22 (95% CI 1.83 to 2.61). Data estimated using web digitizer
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: MIDI	The MIDI is a 4-item scale designed to assess the extent to which the headache attack interfered with family/home, recreation, social, and occupational functioning on each headache attack day 45, with response options for each domain ranging from 0, "not at all," to 10, "totally." Responses to the four items are averaged to obtain a day-level score. Baseline mean 3.40 (95% CI 2.79 to 4.02) and 3 month mean 3.77 (95% CI 3.16 to 4.39). Data estimated using web digitizer
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: MIDI (Migraine Disability Index)	EPISODIC ONLY. Estimated from figure 4 from a secondary article. Author error that episodic/chronic were switched. Baseline mean 3.6 (95% CI 2.9 to 4.3). 3 month mean 3.8 (95% CI 3.2 to 4.5).
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: MIDI (Migraine Disability Index)	EPISODIC ONLY. Estimated from figure 4 from a secondary article. Author error that episodic/chronic were switched. Baseline mean 2.7 (95% CI 2.1 to 3.2). 3 month mean 1.9 (95% CI 1.4 to 2.5).
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: MIDI (Migraine Disability Index)	CHRONIC ONLY. Estimated from figure 4 from a secondary article. Author error that episodic/chronic were switched. Baseline mean 3.1 (95% CI 1.8 to 4.3). 3 month mean 3.5 (95% CI 2.2 to 4.8).
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: MIDI (Migraine Disability Index)	CHRONIC ONLY. Estimated from figure 4 from a secondary article. Author error that episodic/chronic were switched. Baseline mean 2.8 (95% CI 2.1 to 3.5). 3 month mean 2.5 (95% CI 1.8 to 3.2).
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: Percent with MIDAS >=21 (severe)	EPISODIC MIGRANE PATIENTS ONLY. Data estimated from Fig 3 of a secondary publication. Author error that some CI's went above 100%. Author error that Figure 3 switched episodic/chronic.

Reference	Intervention Group and Outcome	Results
		Baseline mean 86% (95% CI 65% to 108%). 1 month mean 71% (95% CI 36% to 100%). 3 month mean 73% (95% CI 45% to 100%). Statistically significant interaction such that the between group difference was only significant for episodic migraine
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: Percent with MIDAS ≥ 21 (severe)	CHRONIC MIGRAINE PATIENTS ONLY. Data estimated from Fig 3 of a secondary publication. Author error that some CI's went above 100%. Author error that Figure 3 switched episodic/chronic. Baseline mean 82% (95% CI 60% to 104%). 1 month mean 69% (95% CI 40% to 99%). 3 month mean 77% (95% CI 50% to 104%). Statistically significant interaction such that the between group difference was only significant for episodic migraine
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: Percent with MIDAS ≥ 21 (severe)	EPISODIC MIGRAINE PATIENTS ONLY. Data estimated from Fig 3 of a secondary publication. Author error that some CI's went above 100%. Author error that Figure 3 switched episodic/chronic. Baseline mean 75% (95% CI 49% to 101%). 1 month mean 40% (95% CI 11% to 69%). 3 month mean 34% (95% CI 7% to 62%).
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: Percent with MIDAS ≥ 21 (severe)	CHRONIC MIGRAINE PATIENTS ONLY. Data estimated from Fig 3 of a secondary publication. Author error that some CI's went above 100%. Author error that Figure 3 switched episodic/chronic. Baseline mean 82% (95% CI 60% to 104%). 1 month mean 72% (95% CI 44% to 100%). 3 month mean 91% (95% CI 68% to 114%).
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Functional status: Other: Proportion with MIDAS ≥ 21	The proportion of subjects with severe MIDAS score (≥ 21) was 77.4% at baseline, 59% (95% CI 41% to 78%) at 1 month after the start of treatment, and also 59% (95% CI 41% to 78%) at 3 months after the start of treatment. Post baseline data estimated from web digitizer. For comparisons to the other group, authors stated: "For the MIDAS Severe Disability (Scores ≥ 21), the group*month interaction was not significant when accounting for the divided alpha, $F(3, 213) = 3.12, p = .027$ (group*month 0 vs. 4 B = 1.6, 95% CI = -0.7, 3.9; Figure 3b). Sensitivity analyses found the results did not differ when evaluated adjusting for age [group*month $F(3, 212) = 3.10, p = .028$; group*month 0 vs 4 B = 1.6, 95% CI = -.1, 4.0]. In completers, the group*month interaction was significant, $F(3, 200) = 3.42, p = .018$; however the group*month 0 vs. 4 contrast was not significant (B = 1.9, 95% CI = -0.6, 4.5). When evaluated without the interaction in the model, the month effect was significant $F(3, 216) = 12.4, p < .001$; among participants in both groups, the estimated proportion of participants falling in the "Severe Disability" category fell from 88.3% at month 0 to 66.7% at month 4, (B = -2.4, 95% CI = -3.3, -1.4). Sensitivity analyses found the results did not differ when evaluated adjusting for age [month $F(3, 215) = 12.58, p < .001$; month 0 vs 4 B = -2.4, 95% CI = -3.4, -1.4] or only in

Reference	Intervention Group and Outcome	Results
		completers [month F(3, 203) = 12.77, p < .001; month 0 vs. 4 B = -2.7, 95% CI = -3.7, -1.6]."
Seng 2019 ²⁰¹	No intervention/TAU Functional status: Other: Proportion with MIDAS >=21	The proportion of subjects with severe MIDAS score (>=21) was 75% at baseline, and 74% (95% CI 56% to 91%) at 1 month after the start of treatment , and 77% (95% CI 60% to 94%) at 3 months after the start of treatment. Post baseline data estimated from web digitizer.
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month	Baseline Mean: 16.7, 95% CI: 14.7 to 18.6, n=31
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Baseline Mean: 15.5, 95% CI: 13.5 to 17.6, n=29
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 3 month(s) Mean: 14.9, 95% CI: 12.9 to 16.8, n=29
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 3 month(s) Mean: 14.3, 95% CI: 12.3 to 16.3, n=26
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Chronic	Baseline Mean: 20.1, 95% CI: 18.5 to 21.7, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Chronic	Baseline Mean: 20.7, 95% CI: 19.1 to 22.3, n=15
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Chronic	Follow-up: 3 month(s) Mean: 19.9, 95% CI: 15.7 to 24.1, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Chronic	Follow-up: 3 month(s) Mean: 20.4, 95% CI: 15.6 to 25.3, n=15
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Episodic	Baseline Mean: 10.6, 95% CI: 8.8 to 12.4, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Episodic	Baseline Mean: 12.4, 95% CI: 9.8 to 15.1, n=14

Reference	Intervention Group and Outcome	Results
Seng 2019 ²⁰¹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Episodic	Follow-up: 3 month(s) Mean: 8.7, 95% CI: 4.6 to 12.8, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Migraine frequency: Count: Headache(s)-Days-month; Subgroup: Episodic	Follow-up: 3 month(s) Mean: 9.7, 95% CI: 6.5 to 13, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Other headache: VAS	Baseline Mean: 1.67, 95% CI: 1.58 to 1.77, n=31
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS	Baseline Mean: 1.78, 95% CI: 1.68 to 1.87, n=29
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Other headache: VAS	Follow-up: 3 month(s) Mean: 1.66, 95% CI: 1.57 to 1.76, n=29
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS	Follow-up: 3 month(s) Mean: 1.74, 95% CI: 1.65 to 1.83, n=26
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS; Subgroup: Chronic	Baseline Mean: 1.8, 95% CI: 1.61 to 1.98, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Other headache: VAS; Subgroup: Chronic	Baseline Mean: 1.71, 95% CI: 1.51 to 1.9, n=15
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS; Subgroup: Chronic	Follow-up: 3 month(s) Mean: 1.74, 95% CI: 1.49 to 2, n=14
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Other headache: VAS; Subgroup: Chronic	Follow-up: 3 month(s) Mean: 1.7, 95% CI: 1.37 to 2.02, n=15
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS; Subgroup: Episodic	Baseline Mean: 1.72, 95% CI: 1.53 to 1.92, n=12
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR Other headache: VAS; Subgroup: Episodic	Baseline Mean: 1.61, 95% CI: 1.42 to 1.79, n=14
Seng 2019 ²⁰¹	No intervention/TAU Other headache: VAS; Subgroup: Episodic	Follow-up: 3 month(s) Mean: 1.63, 95% CI: 1.38 to 1.88, n=12

Reference	Intervention Group and Outcome	Results
Seng 2019 ²⁰¹	Education+Cognitive therapy+MBSR	Follow-up: 3 month(s)
	Other headache: VAS; Subgroup: Episodic	Mean: 1.56, 95% CI: 1.36 to 1.77, n=14
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	dissatisfaction with treatment: 3/27
	Adverse events: Other: Drop out	Other diseases: 2/27
		time constraints: 1/27
		Unspecified: 1/27
		Overall 7/27
Simshäuser 2022 ²⁰³	No intervention/TAU	dissatisfaction with treatment: 0/27
	Adverse events: Other: Drop out	Other diseases: 0/27
		time constraints: 4/27
		Alleviation of migraine: 2/27
		Length of waiting period: 1/27
		Overall 7/27
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 5.99, SE: 0.42, n=27
Simshäuser 2022 ²⁰³	No intervention/TAU	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 7.33, SE: 0.42, n=27
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 4.14, SE: 0.41, n=27
Simshäuser 2022 ²⁰³	No intervention/TAU	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: HADS	Mean: 4.86, SE: 0.41, n=27
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	Follow-up: 8 week(s)
	Functional status: PDI	Mean: 4.03, SE: 0.31, n=24
Simshäuser 2022 ²⁰³	No intervention/TAU	Follow-up: 8 week(s)
	Functional status: PDI	Mean: 4.41, SE: 0.31, n=24
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.04, SD: 3.04, n=27
Simshäuser 2022 ²⁰³	No intervention/TAU	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 5.3, SD: 2.61, n=27
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 6.07, SE: 0.87, n=24
Simshäuser 2022 ²⁰³	No intervention/TAU	Follow-up: 8 week(s)
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 8.27, SE: 0.87, n=24

Reference	Intervention Group and Outcome	Results
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR Other headache: Number of acute headache medications used	Follow-up: 8 week(s) Mean: 4.32, SE: 0.26, n=24
Simshäuser 2022 ²⁰³	No intervention/TAU Other headache: Number of acute headache medications used	Follow-up: 8 week(s) Mean: 4.21, SE: 0.26, n=24
Simshäuser 2022 ²⁰³	Cognitive therapy+MBSR Other headache: Other: Days with medication per month	group x time adjM(SEM) at 8 weeks f/u (post-intervention) 4.07 (0.46)
Simshäuser 2022 ²⁰³	No intervention/TAU Other headache: Other: Days with medication per month	group x time adjM(SEM) at 8 weeks f/u (post-intervention) 4.01 (0.46)
Smitherman 2016 ²⁰⁴	NA Adverse events: Other: Any dropout after treatment start	2 of 16 dropped out after treatment start
Smitherman 2016 ²⁰⁴	NA Adverse events: Other: Any dropout after treatment start	4 of 15 dropped out after treatment start
Smitherman 2016 ²⁰⁴	NA Anxiety, depression, or sleep: GAD-7	Baseline Mean: 10.6, SD: 6.4, n=16
Smitherman 2016 ²⁰⁴	Sham Anxiety, depression, or sleep: GAD-7	Baseline Mean: 9.8, SD: 5.3, n=15
Smitherman 2016 ²⁰⁴	NA Anxiety, depression, or sleep: GAD-7	Follow-up: 10 week(s) Mean: 6.3, SD: 4.8, n=16
Smitherman 2016 ²⁰⁴	Sham Anxiety, depression, or sleep: GAD-7	Follow-up: 10 week(s) Mean: 6.9, SD: 4.9, n=15
Smitherman 2016 ²⁰⁴	NA Anxiety, depression, or sleep: GAD-7	Follow-up: 4 week(s) Mean: 6.6, SD: 5.2, n=16
Smitherman 2016 ²⁰⁴	Sham Anxiety, depression, or sleep: GAD-7	Follow-up: 4 week(s) Mean: 7, SD: 4.6, n=15
Smitherman 2016 ²⁰⁴	NA Anxiety, depression, or sleep: PHQ-9	Baseline Mean: 12.1, SD: 5.8, n=16

Reference	Intervention Group and Outcome	Results
Smitherman 2016 ²⁰⁴	Sham	Baseline
	Anxiety, depression, or sleep: PHQ-9	Mean: 10.5, SD: 4.5, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 10 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 6.3, SD: 4.6, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 10 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 8.6, SD: 4.7, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 4 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 6.9, SD: 4.8, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 4 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 8.4, SD: 4.7, n=15
Smitherman 2016 ²⁰⁴	NA	Baseline
	Functional status: HIT-6	Mean: 66.9, SD: 3.8, n=16
Smitherman 2016 ²⁰⁴	Sham	Baseline
	Functional status: HIT-6	Mean: 64.8, SD: 3.9, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 10 week(s)
	Functional status: HIT-6	Mean: 59.9, SD: 5.5, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 10 week(s)
	Functional status: HIT-6	Mean: 59.6, SD: 7.2, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 4 week(s)
	Functional status: HIT-6	Mean: 62.6, SD: 5.3, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 4 week(s)
	Functional status: HIT-6	Mean: 61.4, SD: 3.9, n=15
Smitherman 2016 ²⁰⁴	NA	Baseline
	Functional status: MIDAS	Mean: 59.9, SD: 39, n=16
Smitherman 2016 ²⁰⁴	Sham	Baseline
	Functional status: MIDAS	Mean: 54.5, SD: 51, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 10 week(s)
	Functional status: MIDAS	Mean: 31.9, SD: 33.2, n=16

Reference	Intervention Group and Outcome	Results
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 10 week(s)
	Functional status: MIDAS	Mean: 34.7, SD: 34.5, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 4 week(s)
	Functional status: MIDAS	Mean: 44.2, SD: 43.1, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 4 week(s)
	Functional status: MIDAS	Mean: 41, SD: 46.2, n=15
Smitherman 2016 ²⁰⁴	NA	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 22.7, Precision NR, n=16
Smitherman 2016 ²⁰⁴	Sham	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 20.5, Precision NR, n=16
Smitherman 2016 ²⁰⁴	NA	Baseline
	Other headache: VAS	Mean: 5.2, SD: 0.95, n=16
Smitherman 2016 ²⁰⁴	Sham	Baseline
	Other headache: VAS	Mean: 5.4, SD: 1.6, n=15
Smitherman 2016 ²⁰⁴	NA	Follow-up: 10 week(s)
	Other headache: VAS	Mean: 4.5, SD: 1.5, n=16
Smitherman 2016 ²⁰⁴	NA	Follow-up: 4 week(s)
	Other headache: VAS	Mean: 5.1, SD: 1.4, n=16
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 4 week(s)
	Other headache: VAS	Mean: 5.2, SD: 2.1, n=15
Smitherman 2016 ²⁰⁴	Sham	Follow-up: 4 week(s)
	Other headache: VAS	Mean: 5.1, SD: 1.9, n=15
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Baseline
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: 0.27, Precision NR, n=11
Sorbi 1984 ²⁰⁶	CBT+PMR	Baseline
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: 0.2, Precision NR, n=10
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Percent CfB: 14 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: -22, Precision NR, n=11

Reference	Intervention Group and Outcome	Results
Sorbi 1984 ²⁰⁶	CBT+PMR	Percent CfB: 14 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: -47, Precision NR, n=10
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Percent CfB: 48 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: -58, Precision NR, n=11
Sorbi 1984 ²⁰⁶	CBT+PMR	Percent CfB: 48 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: -59, Precision NR, n=10
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Percent CfB: 5 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: 8, Precision NR, n=11
Sorbi 1984 ²⁰⁶	CBT+PMR	Percent CfB: 5 week(s)
	Migraine frequency: Count: Headache(s)-Total-days-1	Mean: -9, Precision NR, n=10
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	1-5 scale where 1 is low intensity and 5 is very high. See other row for baseline. At 5 weeks the % reduction was -2% (dispersion NR) and at 14 weeks it was -14% (dispersion NR) and at 48 weeks it was +4% (dispersion NR). F test comparing groups was F=0.527 at 5 weeks, 0.24 at 14 weeks, and 0.343 at 48 weeks. N=total21 for all timepoints. Note that these are F values not p values
	Other headache: Other: % change in intensity from baseline	
Sorbi 1984 ²⁰⁶	CBT+PMR	1-5 scale where 1 is low intensity and 5 is very high. See other row for baseline. At 5 weeks the % reduction was -10% (dispersion NR) and at 14 weeks it was -23% (dispersion NR) and at 48 weeks it was -3% (dispersion NR). See other group for F values for comparing groups.
	Other headache: Other: % change in intensity from baseline	
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Medication use index. average meds per day was multiplied by a potency factor ranging from 2 for aspirin to 5 for 2 mg ergotamine tartrate. Baseline mean 0.49 (dispersion NR). 5 weeks % reduction from baseline was +36% (dispersion NR). 14 weeks % reduction from baseline was -28% (dispersion NR). 48 weeks % reduction from baseline was -50% (dispersion NR). F values comparing groups were 1.125 for 5 weeks, 0.046 for 14 weeks, and 0.655 for 48 weeks
	Other headache: Other: Medication use index (see below)	
Sorbi 1984 ²⁰⁶	CBT+PMR	Medication use index. average meds per day was multiplied by a potency factor ranging from 2 for aspirin to 5 for 2 mg ergotamine tartrate. Baseline mean 0.52 (dispersion NR). 5 weeks % reduction from baseline was -12% (dispersion NR). 14 weeks % reduction from baseline was -19% (dispersion NR). 48 weeks % reduction from baseline was -32% (dispersion NR). See other group for F values
	Other headache: Other: Medication use index (see below)	

Reference	Intervention Group and Outcome	Results
Sorbi 1984 ²⁰⁶	Thermal biofeedback+CBT+PMR	Baseline
	Other headache: VAS	Mean: 3.09, Precision NR, n=11
Sorbi 1984 ²⁰⁶	CBT+PMR	Baseline
	Other headache: VAS	Mean: 3.72, Precision NR, n=10
Sorbi 1986 ²⁰⁷	Autogenic training+Education	Baseline
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 0.19, SD: 0.1, n=13
Sorbi 1986 ²⁰⁷	Education+SMT	Baseline
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 0.12, SD: 0.1, n=16
Sorbi 1986 ²⁰⁷	Education+SMT	Percent CfB: 13 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 31, SD: 56.7, n=16
Sorbi 1986 ²⁰⁷	Autogenic training+Education	Percent CfB: 16 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 40, SD: 38.7, n=13
Sorbi 1986 ²⁰⁷	Autogenic training+Education	Percent CfB: 20 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 27, SD: 56.6, n=13
Sorbi 1986 ²⁰⁷	Education+SMT	Percent CfB: 20 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 36, SD: 64.3, n=16
Sorbi 1986 ²⁰⁷	Autogenic training+Education	Percent CfB: 48 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 38, Precision NR, n=10
Sorbi 1986 ²⁰⁷	Education+SMT	Percent CfB: 48 week(s)
	Migraine frequency: Count: Migraine(s)-Total-days-1	Mean: 36, Precision NR, n=16
Sorbi 1986 ²⁰⁷	Autogenic training+Education	N=11 for analgesic medications. Baseline 0.68 meds/day (SD 0.4). at 16 weeks it had reduced by 44% (SD 55.4%) and at 20 weeks it had reduced by 40% (SD 60..9%). Neither reduction was statistically significantly different from the other group. 48 week data not extracted due to N<10
	Other headache: Other: Number of analgesic medications per day	
Sorbi 1986 ²⁰⁷	Education+SMT	N=14 for analgesic medications. Baseline 0.32 meds/day (SD 0.4). at 16 weeks it had reduced by 28% (SD 67.4%) and at 20 weeks it had reduced by 39% (SD 87.6.9%). Neither reduction was statistically significantly different from the other group. 48 week data not extracted due to N<10
	Other headache: Other: Number of analgesic medications per day	
Sorbi 1986 ²⁰⁷	Autogenic training+Education	N=13. Baseline 3.5 (SD 0.4). At 16 weeks it had reduced by 3% (SD 33%) and at 20 weeks it had reduced by 16% (SD 41.1%). Neither reduction was statistically significantly different from the other group.

Reference	Intervention Group and Outcome	Results
	Other headache: Other: Pain intensity 1-5 scale (higher's worse)	At 48 weeks (N=10), the reduction was 19%, still not statistically significantly different from the other group
Sorbi 1986 ²⁰⁷	Education+SMT Other headache: Other: Pain intensity 1-5 scale (higher's worse)	N=16. Baseline 3.5 (SD 0.4). At 16 weeks it had reduced by 22% (SD 47.4%) and at 20 weeks it had reduced by 32% (SD 55.1%). Neither reduction was statistically significantly different from the other group. At 48 weeks (N=14), the reduction was 15%, still not statistically significant from the other group
Underwood 2022 ²⁰⁹	Minimal intervention Adverse events: Other: Number and severity	N=351 Number of AE's reported: 1 Number of serious AE's reported: 1 (death)
Underwood 2022 ²⁰⁹	Education Adverse events: Other: Number and severity	N=351 Number of AE's reported: 6 Number of serious AE's reported: 0
Underwood 2022 ²⁰⁹	Minimal intervention Functional status: HIT-6	Baseline Mean: 64.6, SD: 5.5, n=350
Underwood 2022 ²⁰⁹	Education Functional status: HIT-6	Baseline Mean: 64.4, SD: 5.4, n=374
Underwood 2022 ²⁰⁹	Minimal intervention Functional status: HIT-6	Follow-up: 12 month(s) Mean: 60.7, SD: 7, n=282
Underwood 2022 ²⁰⁹	Education Functional status: HIT-6	Follow-up: 12 month(s) Mean: 60.1, SD: 6.9, n=282
Underwood 2022 ²⁰⁹	Minimal intervention Functional status: HIT-6	Follow-up: 4 month(s) Mean: 62.3, SD: 7.1, n=275
Underwood 2022 ²⁰⁹	Education Functional status: HIT-6	Follow-up: 4 month(s) Mean: 61, SD: 7, n=276
Underwood 2022 ²⁰⁹	Minimal intervention Functional status: HIT-6	Follow-up: 8 month(s) Mean: 61.1, SD: 7.2, n=263
Underwood 2022 ²⁰⁹	Education Functional status: HIT-6	Follow-up: 8 month(s) Mean: 60.8, SD: 6.4, n=283
Underwood 2022 ²⁰⁹	Minimal intervention Functional status: HIT-6; Subgroup: Chronic	Follow-up: 12 month(s) Mean: 62.7, SD: 6.1, n=149
Underwood 2022 ²⁰⁹	Education Functional status: HIT-6; Subgroup: Chronic	Follow-up: 12 month(s) Mean: 61.4, SD: 6.8, n=159

Reference	Intervention Group and Outcome	Results
Underwood 2022 ²⁰⁹	Minimal intervention	Baseline
	General QOL: EQ-5D	Mean: 0.62, SD: 0.25, n=346
Underwood 2022 ²⁰⁹	Education	Baseline
	General QOL: EQ-5D	Mean: 0.64, SD: 0.26, n=372
Underwood 2022 ²⁰⁹	Minimal intervention	Follow-up: 12 month(s)
	General QOL: EQ-5D	Mean: 0.67, SD: 0.26, n=282
Underwood 2022 ²⁰⁹	Education	Follow-up: 12 month(s)
	General QOL: EQ-5D	Mean: 0.69, SD: 0.25, n=301
Underwood 2022 ²⁰⁹	Minimal intervention	Follow-up: 4 month(s)
	General QOL: EQ-5D	Mean: 0.63, SD: 0.28, n=275
Underwood 2022 ²⁰⁹	Education	Follow-up: 4 month(s)
	General QOL: EQ-5D	Mean: 0.68, SD: 0.26, n=274
Underwood 2022 ²⁰⁹	Minimal intervention	Follow-up: 8 month(s)
	General QOL: EQ-5D	Mean: 0.65, SD: 0.27, n=261
Underwood 2022 ²⁰⁹	Education	Follow-up: 8 month(s)
	General QOL: EQ-5D	Mean: 0.7, SD: 0.24, n=280
Underwood 2022 ²⁰⁹	Minimal intervention	Baseline Mean (SD), N=350: 62.2 (19.6) 4 months follow-up Mean (SD), N=241: 65.0 (20.7) 8 months follow-up Mean (SD), N=224: 66.1 (21.3) 12 months follow-up Mean (SD), N=227: 65.3 (22.5)
	General QOL: Other: EQ-5D VAS	
Underwood 2022 ²⁰⁹	Education	Baseline Mean (SD), N=371: 62.9 (20.5) 4 months follow-up Mean (SD), N=250: 67.1 (20.6) 8 months follow-up Mean (SD), N=253: 69.0 (20.1) 12 months follow-up Mean (SD), N=264: 69.7 (20.7)
	General QOL: Other: EQ-5D VAS	
Underwood 2022 ²⁰⁹	Minimal intervention	Baseline Mean (SD) HADS Anxiety, N=349:10.9 (2.7) HADS Depression, N=349:8.9 (2.0) 4 months follow-up Mean (SD) HADS Anxiety, N=244:10.5 (2.7) HADS Depression, N=244:9.1 (1.8) 8 months follow-up Mean (SD) HADS Anxiety, N=226:10.5 (2.7) HADS Depression, N=226: 9.1 (1.9) 12 months follow-up Mean (SD)
	General QOL: Other: HADS	

Reference	Intervention Group and Outcome	Results
		HADS Anxiety, N=234:10.3 (2.8) HADS Depression, N=234:9.1 (1.8)
Underwood 2022 ²⁰⁹	Education General QOL: Other: HADS	Baseline Mean (SD) HADS Anxiety, N=373:10.5 (2.7) HADS Depression, N=373:9.2 (1.8) 4 months follow-up Mean (SD) HADS Anxiety, N=251:10.3 (2.7) HADS Depression, N=251:9.0 (1.7) 8 months follow-up Mean (SD) HADS Anxiety, N=252:10.0 (2.7) HADS Depression, N=252:9.0 (1.6) 12 months follow-up Mean (SD) HADS Anxiety, N=266:10.2 (2.7) HADS Depression, N=266:9.1 (1.7)
Underwood 2022 ²⁰⁹	Minimal intervention General QOL: Other: HeiQ	Baseline Mean(SD), N=348: 2.8 (0.6) 4 months follow-up Mean(SD), N=244: 2.9 (0.70) 8 months follow-up Mean(SD), N=224: 2.9 (0.7) 12 months follow-up Mean(SD), N=233: 2.9 (0.70)
Underwood 2022 ²⁰⁹	Education General QOL: Other: HeiQ	Baseline Mean(SD), N=373: 2.8 (0.7) 4 months follow-up Mean(SD), N=251: 3.0 (0.70) 8 months follow-up Mean(SD), N=253: 3.0 (0.69) 12 months follow-up Mean(SD), N=267: 3.0 (0.7)
Underwood 2022 ²⁰⁹	Minimal intervention General QOL: Other: PSEQ	Baseline Mean(SD), N=348: 32.9 (13.3) 4 months follow-up Mean(SD), N=244: 35.4 (14.2) 8 months follow-up Mean(SD), N=226: 37.0 (14.8) 12 months follow-up Mean(SD), N=234: 37.1 (14.6)
Underwood 2022 ²⁰⁹	Education General QOL: Other: PSEQ	Baseline Mean(SD), N=371: 32.5 (13.8) 4 months follow-up Mean(SD), N=250: 37.8 (13.5) 8 months follow-up Mean(SD), N=253: 38.7 (13.2) 12 months follow-up Mean(SD), N=267: 39.4 (13.6)
Underwood 2022 ²⁰⁹	Minimal intervention General QOL: Other: SF-12	Baseline Mean (SD) SF-12 Physical, N=347:43.7 (10.9) SF-12 Mental, N=348: 39.6 (10.3) 4 months follow-up Mean (SD) SF-12 Physical, N=242:46.1 (10.7) SF-12 Mental, N=243: 41.2 (10.8) 8 months follow-up Mean (SD) SF-12 Physical, N=226:46.8 (10.7) SF-12 Mental, N=226: 41.5 (10.1) 12 months follow-up Mean (SD) SF-12 Physical, N=234:46.0 (10.8) SF-12 Mental, N=234: 42.2 (10.9)

Reference	Intervention Group and Outcome	Results
Underwood 2022 ²⁰⁹	Education General QOL: Other: SF-12	Baseline Mean (SD) SF-12 Physical, N=370:44.9 (10.0) SF-12 Mental, N=370: 39.8 (10.6) 4 months follow-up Mean (SD) SF-12 Physical, N=251:46.3 (10.0) SF-12 Mental, N=251: 42.8 (10.2) 8 months follow-up Mean (SD) SF-12 Physical, N=253:47.3 (9.9) SF-12 Mental, N=253: 42.9 (10.4) 12 months follow-up Mean (SD) SF-12 Physical, N=265:46.9 (9.4) SF-12 Mental, N=267: 43.9 (10.5)
Underwood 2022 ²⁰⁹	Minimal intervention Migraine QOL: Other: CH-QLQ	Baseline, Mean (SD) CH-QLQ role restrictive, N=351: 54.5 (17.3) CH-QLQ role preventive, N=351: 69.4 (21.2) CH-QLQ emotional function, N=351: 57.2 (22.3) 4 months follow-up, Mean (SD) CH-QLQ role restrictive, N=244: 61.6 (18.3) CH-QLQ role preventive, N=244:75.9 (20.5) CH-QLQ emotional function, N=244: 64.8 (23.4) 8 months follow-up, Mean (SD) CH-QLQ role restrictive, N=228: 65.3 (19.6) CH-QLQ role preventive, N=228:77.2 (22.1) CH-QLQ emotional function, N=228: 69.2 (23.3) 12 months follow-up, Mean (SD) CH-QLQ role restrictive, N=235: 66.0 (19.0) CH-QLQ role preventive, N=235:77.5 (20.3) CH-QLQ emotional function, N=351: 68.7 (23.3)
Underwood 2022 ²⁰⁹	Education Migraine QOL: Other: CH-QLQ	Baseline, Mean (SD) CH-QLQ role restrictive, N=374: 54.4 (16.9) CH-QLQ role preventive, N=374: 69.4 (20.5) CH-QLQ emotional function, N=373: 57.0 (22.4) 4 months follow-up, Mean (SD) CH-QLQ role restrictive, N=251: 64.1 (17.6) CH-QLQ role preventive, N=251: 78.6 (18.7) CH-QLQ emotional function, N=251: 66.5 (23.0) 8 months follow-up, Mean (SD) CH-QLQ role restrictive, N=254: 66.3 (17.8) CH-QLQ role preventive, N=254: 79.2 (19.2) CH-QLQ emotional function, N=253: 69.3 (22.6) 12 months follow-up, Mean (SD) CH-QLQ role restrictive, N=268: 66.9 (18.1)

Reference	Intervention Group and Outcome	Results
		CH-QLQ role preventive, N=268: 80.0 (18.4) CH-QLQ emotional function, N=268: 70.5 (22.1)
Underwood 2022 ²⁰⁹	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-month	Baseline Median: 16, IQR: 10 to 20, n=349
Underwood 2022 ²⁰⁹	Education Migraine frequency: Count: Migraine(s)-Days-month	Baseline Median: 16, IQR: 12 to 20, n=372
Underwood 2022 ²⁰⁹	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 12 month(s) Mean: 11.4, SD: 7.8, n=233
Underwood 2022 ²⁰⁹	Education Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 12 month(s) Mean: 11.8, SD: 7.8, n=268
Underwood 2022 ²⁰⁹	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 4 month(s) Mean: 12.3, SD: 7.5, n=239
Underwood 2022 ²⁰⁹	Education Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 4 month(s) Mean: 13.4, SD: 7.6, n=248
Underwood 2022 ²⁰⁹	Minimal intervention Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 8 month(s) Mean: 11.8, SD: 8.1, n=226
Underwood 2022 ²⁰⁹	Education Migraine frequency: Count: Migraine(s)-Days-month	Follow-up: 8 month(s) Mean: 11.8, SD: 7.4, n=252
Underwood 2022 ²⁰⁹	Minimal intervention Other headache: Other: Acute medication use	Baseline median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=346: 12 (8, 16) 4 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=241: 8 (4, 12) 8 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=226: 8 (3, 14) 12 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=233: 8 (3, 12)
Underwood 2022 ²⁰⁹	Education Other headache: Other: Acute medication use	Baseline median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=371: 12 (6, 17) 4 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine

Reference	Intervention Group and Outcome	Results
		<p>over the last 4 weeks, N=249: 8 (4, 13)</p> <p>8 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=252: 7.5 (3.5, 12)</p> <p>12 months follow-up median (IQR) number of days pain killers or triptans were used as acute medications for headache/migraine over the last 4 weeks, N=266: 8 (3, 14)</p>
Underwood 2022 ²⁰⁹	<p>Minimal intervention</p> <p>Other headache: Other: Headache duration</p>	<p>Baseline median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=236: 7(14,15)</p> <p>4 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=223: 6 (4, 12)</p> <p>8 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=223: 6 (3, 10)</p> <p>12 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=230: 6 (4, 12)</p>
Underwood 2022 ²⁰⁹	<p>Education</p> <p>Other headache: Other: Headache duration</p>	<p>Baseline median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=255: 8(4,14)</p> <p>4 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=220: 6 (4, 12)</p> <p>8 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=246:7 (4, 12)</p> <p>12 months follow-up median (IQR) headache duration (number of hours the headache/migraine lasted on the days they had it), N=265: 7 (4, 12)</p>
Underwood 2022 ²⁰⁹	<p>Minimal intervention</p> <p>Other headache: Other: Headache severity</p>	<p>Baseline Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=242: 7(6,8)</p> <p>4 months follow-up Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=224: 6 (5, 8)</p> <p>8 months follow-up Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=222: 6 (5, 7)</p> <p>12 months follow-up Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=234:6 (5, 7)</p>
Underwood 2022 ²⁰⁹	<p>Education</p> <p>Other headache: Other: Headache severity</p>	<p>Baseline Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=264: 7(6,8)</p> <p>4 months follow-up Median (IQR) average severity (0-10; No pain to</p>

Reference	Intervention Group and Outcome	Results
		Extremely severe pain) on the headache/migraine Days, N=222 :6 (5, 7) 8 months follow-up Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=246: 6 (5, 7) 12 months follow-up Median (IQR) average severity (0-10; No pain to Extremely severe pain) on the headache/migraine Days, N=267:6 (5, 7)
Varkey 2011 ²¹²	Topiramate Adverse events: Other	AEs were documented by eight participants in the topiramate group (33%). The safety population (i.e. the patients who took at least one dose of medicine) consisted of 24 individuals. Three of them (12.5%) reported AEs as the cause of their withdrawal from the study. The most common AEs reported were paresthesia (n = 5), fatigue (n = 3), a depressed mood (n = 3), vertigo (n = 2), and infrequent bowel movements (n = 2). Headaches, tremors, muscle twitching, mood swings, dysgeusia, nausea, dry eyes, epistaxis, a dry mouth, urinary incontinence, amnesia, cognitive disorders, diarrhoea, and musculoskeletal chest pain were each reported by one patient. The same patients often reported several symptoms. No serious AEs were reported.
Varkey 2011 ²¹²	Relaxation training Migraine QOL: MSQoL v2.1	Baseline Median: 58, IQR: 51 to 67, n=30
Varkey 2011 ²¹²	Topiramate Migraine QOL: MSQoL v2.1	Baseline Median: 60, IQR: 48 to 73, n=31
Varkey 2011 ²¹²	Relaxation training Migraine QOL: MSQoL v2.1	Change from baseline: 14 month(s) Mean: 4, SE: 2.2, n=30
Varkey 2011 ²¹²	Topiramate Migraine QOL: MSQoL v2.1	Change from baseline: 14 month(s) Mean: 2.5, SE: 2.2, n=31
Varkey 2011 ²¹²	Relaxation training Migraine QOL: MSQoL v2.1	Change from baseline: 3 month(s) Mean: 3.4, SE: 1.9, n=30
Varkey 2011 ²¹²	Topiramate Migraine QOL: MSQoL v2.1	Change from baseline: 3 month(s) Mean: 1.9, SE: 1.9, n=31
Varkey 2011 ²¹²	Relaxation training Migraine QOL: MSQoL v2.1	Change from baseline: 7 month(s) Mean: 3.1, SE: 2.4, n=30

Reference	Intervention Group and Outcome	Results
Varkey 2011 ²¹²	Topiramate Migraine QOL: MSQoL v2.1	Change from baseline: 7 month(s) Mean: 2.4, SE: 2.3, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: 50% responder rate: Migraine(s)-Total-month	NR: 14 month(s) Responders/events: 7, n=30
Varkey 2011 ²¹²	Topiramate Migraine frequency: 50% responder rate: Migraine(s)-Total-month	NR: 14 month(s) Responders/events: 8, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 7.6, SD: 3.8, n=30
Varkey 2011 ²¹²	Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 7.5, SD: 3.9, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 14 month(s) Mean: -1.83, SE: 0.52, n=30
Varkey 2011 ²¹²	Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 14 month(s) Mean: -1.98, SE: 0.51, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 3 month(s) Mean: -1.32, SE: 0.55, n=30
Varkey 2011 ²¹²	Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 3 month(s) Mean: -2.13, SE: 0.54, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 7 month(s) Mean: -1.47, SE: 0.55, n=30
Varkey 2011 ²¹²	Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Change from baseline: 7 month(s) Mean: -2.08, SE: 0.54, n=31
Varkey 2011 ²¹²	Relaxation training Migraine frequency: Other: Attack frequency	Attacks per month; Baseline mean (SD): 4.2(1.6); change from baseline to last month of treatment least square means \pm SE: -0.83 \pm 0.31; change from baseline at 7months least square means \pm SE: -0.94 \pm 0.28; change from baseline at 14 months least square means \pm SE: -0.95 \pm 0.27; ITT population
Varkey 2011 ²¹²	Topiramate Migraine frequency: Other: Attack frequency	Attacks per month; Baseline mean (SD): 3.6(1.6); change from baseline to last month of treatment least square means \pm SE: -0.97 \pm 0.31; change from baseline at 7months least square means

Reference	Intervention Group and Outcome	Results
		\pm SE: -0.68 \pm 0.28; change from baseline at 14 months least square means \pm SE: -0.73 \pm 0.27; ITT population
Varkey 2011 ²¹²	Relaxation training Other headache: Other: Frequency of headache medication (doses)	Frequency of headache medication used (doses) Baseline mean (SD): 4.2(1.6); change from baseline to last month of treatment least square mean \pm SE: -1.56 \pm 0.65; change from baseline at 7month follow-up least square mean \pm SE: -2.84 \pm 0.54; change from baseline at 14month follow-up least square mean \pm SE: -2.91 \pm 0.52; ITT population
Varkey 2011 ²¹²	Topiramate Other headache: Other: Frequency of headache medication (doses)	Frequency of headache medication used (doses) Baseline mean (SD): 7.1(5.3); change from baseline to last month of treatment least square mean \pm SE: -2.15 \pm 0.65; change from baseline at 7month follow-up least square mean \pm SE: -2.71 \pm 0.54; change from baseline at 14month follow-up least square mean \pm SE: -3.64 \pm 0.52; ITT population
Varkey 2011 ²¹²	Relaxation training Other headache: VAS	Baseline Median: 39, IQR: 26 to 55, n=30
Varkey 2011 ²¹²	Topiramate Other headache: VAS	Baseline Median: 40, IQR: 29 to 58, n=31
Varkey 2011 ²¹²	Relaxation training Other headache: VAS	Change from baseline: 14 month(s) Mean: -4.6, SE: 3.6, n=30
Varkey 2011 ²¹²	Topiramate Other headache: VAS	Change from baseline: 14 month(s) Mean: -11.3, SE: 3.5, n=31
Varkey 2011 ²¹²	Relaxation training Other headache: VAS	Change from baseline: 3 month(s) Mean: -6.2, SE: 3.2, n=30
Varkey 2011 ²¹²	Topiramate Other headache: VAS	Change from baseline: 3 month(s) Mean: -14.5, SE: 3.2, n=31
Varkey 2011 ²¹²	Relaxation training Other headache: VAS	Change from baseline: 7 month(s) Mean: -5.1, SE: 3.5, n=30
Varkey 2011 ²¹²	Topiramate Other headache: VAS	Change from baseline: 7 month(s) Mean: -13.7, SE: 3.4, n=31
Vasiliou 2021 ²¹³	ACT Functional status: HDI	Baseline Mean: 51.4, SD: 21.3, n=47

Reference	Intervention Group and Outcome	Results
Vasiliou 2021 ²¹³	No intervention/TAU Functional status: HDI	Baseline Mean: 57.2, SD: 23.1, n=47
Vasiliou 2021 ²¹³	ACT Functional status: HDI	Follow-up: 20 week(s) Mean: 31.3, SD: 21.3, n=31
Vasiliou 2021 ²¹³	No intervention/TAU Functional status: HDI	Follow-up: 20 week(s) Mean: 49.9, SD: 27, n=31
Vasiliou 2021 ²¹³	ACT Functional status: HDI	Follow-up: 8 week(s) Mean: 34.1, SD: 21, n=31
Vasiliou 2021 ²¹³	No intervention/TAU Functional status: HDI	Follow-up: 8 week(s) Mean: 51.2, SD: 29, n=30
Vasiliou 2021 ²¹³	ACT Migraine QOL: Other: Restrictive, preventive, emotional	Subscales: Role restrictive: (mean, SD) Baseline: 57.14 (sd 17.3); 8 weeks: 74.6 (SD 16.7); 20 weeks: 77.5 (SD 15) Role preventive: Baseline: 73.2 (SD 19.5); 8 weeks: 86 (SD 16.9); 20 weeks: 89 (SD 13.3) Role emotional: Baseline: 71.8 (SD 20.2); 8 weeks: 83 (SD 18.6); 20 weeks: 86.5 (SD 15.8)
Vasiliou 2021 ²¹³	No intervention/TAU Migraine QOL: Other: Restrictive, preventive, emotional	Subscales: Role restrictive: (mean, SD) Baseline: 49.9 (SD 19.1), 8 weeks: 56.6 (SD 23.3), 20 weeks: 58.2 (SD 20.6) Role preventive: Baseline: 66.1 (SD 21.1); 8 weeks: 69 (SD 23.5); 20 weeks: 69.5 (SD 26) Role emotional: Baseline: 63 (SD 24.2); 8 weeks: 67.5 (SD 25.7); 20 weeks: 67.5 (SD 30)

Reference	Intervention Group and Outcome	Results
Vasiliou 2021 ²¹³	ACT Other headache: Other: HADS subscales	HADS- Anxiety subscale Mean (SD) Baseline: 7.1 (3.9); 8 weeks: 6.2 (3.5); 20 weeks: 6.5 (3.6) HADS Depression subscale Baseline: 5.4 (3.2); 8 weeks 4.7 (3.1); 20 weeks 2.5 (1.5)
Vasiliou 2021 ²¹³	No intervention/TAU Other headache: Other: HADS subscales	HADS- Anxiety subscale Mean (SD) Baseline: 9.8 (3.8); 8 weeks: 9.3 (3.8); 20 weeks: 9.2 (3.6) HADS Depression subscale Baseline: 7.4 (3.7); 8 weeks 6.8 (3.7); 20 weeks 3.2 (1.5)
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Anxiety, depression, or sleep: CES-D	Baseline Mean: 35.9, SD: 10.7, n=25
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Anxiety, depression, or sleep: CES-D	Baseline Mean: 37.6, SD: 9.8, n=22
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation Anxiety, depression, or sleep: CES-D	Baseline Mean: 34.6, SD: 8.3, n=23
Wachholtz 2008 ²¹⁵	PMR Anxiety, depression, or sleep: CES-D	Baseline Mean: 37.2, SD: 7.3, n=22
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Anxiety, depression, or sleep: CES-D	Follow-up: 1 month(s) Mean: 31, SD: 7.5, n=22
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Anxiety, depression, or sleep: CES-D	Follow-up: 1 month(s) Mean: 34.2, SD: 9.9, n=21
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation Anxiety, depression, or sleep: CES-D	Follow-up: 1 month(s) Mean: 29.3, SD: 4.8, n=20
Wachholtz 2008 ²¹⁵	PMR Anxiety, depression, or sleep: CES-D	Follow-up: 1 month(s) Mean: 29.4, SD: 7.1, n=20
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Anxiety, depression, or sleep: Other: State Trait Anxiety Inventory	Baseline: 41.2 (SD 10.7) 1 month: 32 (SD 6.9)

Reference	Intervention Group and Outcome	Results
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Anxiety, depression, or sleep: Other: State Trait Anxiety Inventory	Baseline: 43.6 (SD 10.2) 1 month: 37.4 (SD 9.9)
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation Anxiety, depression, or sleep: Other: State Trait Anxiety Inventory	Baseline: 40.7 (SD 6.9) 1 month: 37.6 (SD 6.2)
Wachholtz 2008 ²¹⁵	PMR Anxiety, depression, or sleep: Other: State Trait Anxiety Inventory	Baseline: 43.7 (SD 7.9) 1 month: 34.5 (SD 6.6)
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Migraine QOL: MSQoL	Baseline Mean: 77.3, SD: 10.2, n=25
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Migraine QOL: MSQoL	Baseline Mean: 75.8, SD: 12.8, n=22
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation Migraine QOL: MSQoL	Baseline Mean: 76.7, SD: 8.5, n=23
Wachholtz 2008 ²¹⁵	PMR Migraine QOL: MSQoL	Baseline Mean: 76.7, SD: 10.7, n=22
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Migraine QOL: MSQoL	Follow-up: 1 month(s) Mean: 82, SD: 11.8, n=22
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Migraine QOL: MSQoL	Follow-up: 1 month(s) Mean: 79, SD: 8.7, n=21
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation Migraine QOL: MSQoL	Follow-up: 1 month(s) Mean: 77.1, SD: 10.8, n=20
Wachholtz 2008 ²¹⁵	PMR Migraine QOL: MSQoL	Follow-up: 1 month(s) Mean: 76.4, SD: 12.7, n=20
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation Migraine frequency: Count: Headache(s)-Total-month	Baseline Mean: 13.7, SD: 6.36, n=22
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation Migraine frequency: Count: Headache(s)-Total-month	Baseline Mean: 12.8, SD: 5.1, n=21

Reference	Intervention Group and Outcome	Results
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation	Baseline
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 11.1, SD: 5.24, n=20
Wachholtz 2008 ²¹⁵	PMR	Baseline
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 11.4, SD: 6.25, n=20
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 8.7, SD: 5.19, n=22
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 9.7, SD: 5.23, n=21
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 10.4, SD: 6.3, n=20
Wachholtz 2008 ²¹⁵	PMR	Follow-up: 1 month(s)
	Migraine frequency: Count: Headache(s)-Total-month	Mean: 10.1, SD: 5.72, n=20
Wachholtz 2008 ²¹⁵	Meditation-Spiritual Meditation	Follow-up: 1 month(s)
	Other headache: VAS	Mean: 3.9, SD: 0.77, n=22
Wachholtz 2008 ²¹⁵	Meditation-Internal secular meditation	Follow-up: 1 month(s)
	Other headache: VAS	Mean: 3.9, SD: 0.92, n=21
Wachholtz 2008 ²¹⁵	Meditation-External secular meditation	Follow-up: 1 month(s)
	Other headache: VAS	Mean: 4.1, SD: 1.19, n=20
Wachholtz 2008 ²¹⁵	PMR	Follow-up: 1 month(s)
	Other headache: VAS	Mean: 4, SD: 1.03, n=20
Wells 2021 ²¹⁸	MBSR	16/45
	Adverse events: Other: Drop out (any reason)	
Wells 2021 ²¹⁸	Education	15/44
	Adverse events: Other: Drop out (any reason)	
Wells 2021 ²¹⁸	MBSR	Follow-up: 20 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 10.8, 95% CI: 9.8 to 11.8, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 20 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 12, 95% CI: 11 to 13, n=44

Reference	Intervention Group and Outcome	Results
Wells 2021 ²¹⁸	MBSR	Follow-up: 32 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 10.9, 95% CI: 9.85 to 11.9, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 32 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 12.1, 95% CI: 11.06 to 13, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 11, 95% CI: 10 to 12, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: GAD-7	Mean: 12.2, 95% CI: 11.2 to 13.1, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 20 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 4, 95% CI: 3 to 4.9, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 20 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 5.6, 95% CI: 4.6 to 6.5, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 32 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 3.6, 95% CI: 2.6 to 4.5, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 32 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 5.1, 95% CI: 4.2 to 6.1, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 3.9, 95% CI: 3 to 4.9, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 8 week(s)
	Anxiety, depression, or sleep: PHQ-9	Mean: 5.5, 95% CI: 4.6 to 6.4, n=44
Wells 2021 ²¹⁸	MBSR	Baseline
	Functional status: HIT-6	Mean: 63, 95% CI: 60.8 to 65.2, n=45
Wells 2021 ²¹⁸	Education	Baseline
	Functional status: HIT-6	Mean: 63, 95% CI: 61.8 to 64.3, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 20 week(s)
	Functional status: HIT-6	Mean: 57.9, 95% CI: 55.8 to 59.9, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 20 week(s)
	Functional status: HIT-6	Mean: 58.7, 95% CI: 56.8 to 60.7, n=44

Reference	Intervention Group and Outcome	Results
Wells 2021 ²¹⁸	MBSR	Follow-up: 32 week(s)
	Functional status: HIT-6	Mean: 56.6, 95% CI: 54.6 to 58.6, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 32 week(s)
	Functional status: HIT-6	Mean: 58.5, 95% CI: 56.5 to 60.4, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 8 week(s)
	Functional status: HIT-6	Mean: 56.3, 95% CI: 54.4 to 58.2, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 8 week(s)
	Functional status: HIT-6	Mean: 61.6, 95% CI: 59.8 to 63.4, n=44
Wells 2021 ²¹⁸	MBSR	Baseline
	Functional status: MIDAS	Mean: 16.9, 95% CI: 12.3 to 21.5, n=45
Wells 2021 ²¹⁸	Education	Baseline
	Functional status: MIDAS	Mean: 11.8, 95% CI: 9.5 to 14.4, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 20 week(s)
	Functional status: MIDAS	Mean: 6.4, 95% CI: 3.8 to 9.1, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 20 week(s)
	Functional status: MIDAS	Mean: 12.4, 95% CI: 9.8 to 15, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 32 week(s)
	Functional status: MIDAS	Mean: 5.2, 95% CI: 2.6 to 7.8, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 32 week(s)
	Functional status: MIDAS	Mean: 11.1, 95% CI: 8.5 to 13.7, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 8 week(s)
	Functional status: MIDAS	Mean: 6.7, 95% CI: 4.1 to 9.2, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 8 week(s)
	Functional status: MIDAS	Mean: 12.6, 95% CI: 10.1 to 15.1, n=44
Wells 2021 ²¹⁸	MBSR	Baseline
	Migraine QOL: MSQoL v2.1	Mean: 44.9, 95% CI: 40 to 49.7, n=45
Wells 2021 ²¹⁸	Education	Baseline
	Migraine QOL: MSQoL v2.1	Mean: 43.5, 95% CI: 40 to 47.1, n=44

Reference	Intervention Group and Outcome	Results
Wells 2021 ²¹⁸	MBSR	Follow-up: 20 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 29.9, 95% CI: 26.7 to 33.1, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 20 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 35, 95% CI: 31.9 to 38.1, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 32 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 29.6, 95% CI: 26.5 to 32.8, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 32 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 34.7, 95% CI: 31.6 to 37.8, n=44
Wells 2021 ²¹⁸	MBSR	Follow-up: 8 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 33.6, 95% CI: 30.5 to 36.6, n=45
Wells 2021 ²¹⁸	Education	Follow-up: 8 week(s)
	Migraine QOL: MSQoL v2.1	Mean: 38.6, 95% CI: 35.6 to 41.6, n=44
Wells 2021 ²¹⁸	MBSR	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.5, SD: 3.4, n=45
Wells 2021 ²¹⁸	Education	Baseline
	Migraine frequency: Count: Headache(s)-Days-month	Mean: 9.8, SD: 3.6, n=44
Wells 2021 ²¹⁸	MBSR	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 7.2, SD: 2.5, n=45
Wells 2021 ²¹⁸	Education	Baseline
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: 7.4, SD: 3, n=44
Wells 2021 ²¹⁸	MBSR	Change from baseline: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: -2.2, 95% CI: -1.2 to -3.2, n=45
Wells 2021 ²¹⁸	Education	Change from baseline: 32 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: -2.7, 95% CI: -1.7 to -3.8, n=44
Wells 2021 ²¹⁸	MBSR	Change from baseline: 8 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: -1.6, 95% CI: -0.7 to -2.5, n=45
Wells 2021 ²¹⁸	Education	Change from baseline: 8 week(s)
	Migraine frequency: Count: Migraine(s)-Days-month	Mean: -2, 95% CI: -1.1 to -2.9, n=44

Reference	Intervention Group and Outcome	Results
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Functional status: Other: # days/week with severe impairment	N=10 in this group. The mean number of weekly days with severe performance impairments was 2.4 (SD 3.2) at baseline and 1.7 (SD 1.8) at three months. The study did not report a between-groups statistical comparison
Wittchen 1983 ²¹⁹	No intervention/TAU Functional status: Other: # days/week with severe impairment	N=10 in this group. The mean number of weekly days with severe performance impairments was 3.5 (SD 5) at baseline and 3 (SD 3.7) at three months. The study did not report a between-groups statistical comparison
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Migraine frequency: Count: Headache(s)-Days-month	Baseline Mean: 12.5, SD: 3.8, n=10
Wittchen 1983 ²¹⁹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Baseline Mean: 11.6, SD: 4, n=10
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 3 month(s) Mean: 7, SD: 3.7, n=10
Wittchen 1983 ²¹⁹	No intervention/TAU Migraine frequency: Count: Headache(s)-Days-month	Follow-up: 3 month(s) Mean: 10.4, SD: 4.7, n=10
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Other headache: Other: weighted medication use	N=10 in this group. The weighted amount of medication use (weights 3 for ergotamine combination, 2 for ergotamine alone, 1 for others) was 14.4 (SD 7.8) at baseline and 1.7 (SD 1) at three months. The study did not report a between-groups statistical comparison
Wittchen 1983 ²¹⁹	No intervention/TAU Other headache: Other: weighted medication use	N=10 in this group. The weighted amount of medication use (weights 3 for ergotamine combination, 2 for ergotamine alone, 1 for others) was 10.8 (SD 5.7) at baseline and 10 (SD 5.8) at three months. The study did not report a between-groups statistical comparison
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Other headache: VAS	Baseline Mean: 4.6, SD: 2.7, n=10
Wittchen 1983 ²¹⁹	No intervention/TAU Other headache: VAS	Baseline Mean: 4.3, SD: 2.6, n=10
Wittchen 1983 ²¹⁹	Relaxation training+CBT+Education Other headache: VAS	Follow-up: 3 month(s) Mean: 2.4, SD: 1.3, n=10
Wittchen 1983 ²¹⁹	No intervention/TAU Other headache: VAS	Follow-up: 3 month(s) Mean: 4.2, SD: 3.4, n=10

Reference	Intervention Group and Outcome	Results
de Tommaso 2017 ²²⁰	Biofeedback Adverse events: Withdrawal due to adverse events	Follow-up: 3 month(s) Responders/events: 0, n=11
de Tommaso 2017 ²²⁰	Biofeedback+Topiramate Adverse events: Withdrawal due to adverse events	Follow-up: 3 month(s) Responders/events: 0, n=11
de Tommaso 2017 ²²⁰	Topiramate Adverse events: Withdrawal due to adverse events	Follow-up: 3 month(s) Responders/events: 1, n=11
de Tommaso 2017 ²²⁰	Biofeedback Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 3 month(s) Responders/events: 10, n=11
de Tommaso 2017 ²²⁰	Biofeedback+Topiramate Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 3 month(s) Responders/events: 9, n=11
de Tommaso 2017 ²²⁰	Topiramate Migraine frequency: 50% responder rate: Headache(s)-Days-month	Follow-up: 3 month(s) Responders/events: 8, n=10
de Tommaso 2017 ²²⁰	Biofeedback Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 11.9, SD: 5.15, n=11
de Tommaso 2017 ²²⁰	Biofeedback+Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 12.9, SD: 8.1, n=11
de Tommaso 2017 ²²⁰	Topiramate Migraine frequency: Count: Migraine(s)-Days-month	Baseline Mean: 13.1, SD: 8.2, n=11

Abbreviations: ACT=acceptance and commitment therapy; BDI=Beck Depression Inventory; CBT=cognitive behavioral therapy; CfB=change from baseline; CI=confidence interval; DASS=Depression Anxiety Stress Scales; EMG=electromyography; EQ-5D=EuroQol-5D; GAD-7=General Anxiety Disorder-7; HADS=Hamilton Anxiety and Depression Scale; HDI=Headache Disability Index; HDRS=Hamilton Depression Rating Scale; HIT-6=Headache Impact Test; IQR=interquartile range; MADRS= Montgomery-Åsberg Depression Rating Scale; MANOVA=multivariate analysis of variance; MBSR=mindfulness-based stress reduction; MIDAS=Migraine Disability Assessment Test; MSQl-A=Migraine-Specific Quality of Life-Adolescent; MSQoL=Migraine-Specific Quality of Life; NR=not reported; PDI=Pain Disability Index; PedMIDAS=Pediatric Migraine-Specific Disability Assessment; PHQ-9=Patient Health Questionnaire; PMR=progressive muscle relaxation; QOL=quality of life; SD=standard deviation; SE=standard error; SF-12=12-Item Short Form Survey; SF-36=36-Item Short Form Survey; SMT=stress management therapy; TAU=treatment-as-usual; VAS=visual analogue scale

Table C-4. Risk of bias

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
Aguirrezabal 2019 ¹²⁸ Included for: KQ1	Neuroscience education therapy	No intervention/TAU	All	Some concerns	Low	Low	High	-	High
Albers 2015 ¹²⁹ Included for: KQ1	Relaxation training+CBT+Education	No intervention/TAU	Migraine frequency / headache cessation	Some concerns	Low	High	High	Some concerns	High
Allen 1998 ¹³⁰ Included for: KQ3	Thermal biofeedback+Education	Thermal biofeedback	All up to and including 3 months	Some concerns	Low	Low	High	-	High
Allen 1998 ¹³⁰ Included for: KQ3	Thermal biofeedback+Education	Thermal biofeedback	All at one year	Some concerns	Low	High	Some concerns	-	Some concerns
Blanchard 1978 ¹³¹ Included for: KQ1, KQ2	Thermal biofeedback+Autogenic training; PMR	No intervention/TAU	All	Some concerns	Some concerns	Low	High	-	High
Blanchard 1978 ¹³¹ Included for: KQ1, KQ2	Thermal biofeedback+Autogenic training	PMR	All	Some concerns	Some concerns	Low	High	-	High
Bromberg 2012 ¹³³ Included for: KQ1, KQ1a	Relaxation training+Biofeedback+CBT+Education	No intervention/TAU	All 4 weeks	Some concerns	Low	Low	High	-	High
Bromberg 2012 ¹³³ Included for: KQ1, KQ1a	Relaxation training+Biofeedback+CBT+Education	No intervention/TAU	All timepoints after 4 weeks	Some concerns	Low	High	High	-	High
Brown 1984 ¹³⁴ Included for: KQ1, KQ2	Guided imagery-1 hr/week for 4 weeks, using relaxing statements; Guided imagery-5 hours over 4 weeks,	Guided imagery-5 hours over 4 weeks, imaging details of the scene; Guided imagery-1 hr/week for 4	All	Some concerns	Low	Low	Some concerns	-	Some concerns

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
	imaging details of the scene	weeks, using relaxing statements; Sham							
Calhoun 2007 ¹³⁵ Included for: KQ4	Sleep counseling	Sham	All	Some concerns	Low	Low	Low	-	Some concerns
Connelly 2006 ¹³⁶ Included for: KQ1, KQ1a	Relaxation training+CBT +Education	No intervention/ TAU	All	Some concerns	Low	Low	High	-	High
Cottrell 2007 ¹³⁷ Included for: KQ1, KQ1a	Thermal biofeedback+ Education+P MR+SMT+A ctivity pacing	Attention control and education	All	Some concerns	Low	Some concerns	High	-	High
Cousins 2015 ¹³⁸ Included for: KQ1	CBT+PMR+ Deep breathing	No intervention/ TAU	All	Low	Low	Some concerns	High	-	High
Cuneo 2023 ¹³⁹ Included for: KQ1, KQ1a	Biofeedback	No intervention/ TAU	All	Some concerns	Low	High	High	-	High
D'Souza 2008 ¹⁴⁰ Included for: KQ1, KQ1a	Relaxation training	Attention control	All	High	Low	Low	Some concerns	-	High
Day 2014 ¹⁴¹ Included for: KQ1	MBCT	No intervention/ TAU	Headache frequency	High	Low	High	High	-	High
Dindo 2020 ¹⁴⁵ Included for: KQ2	Education+A CT	Relaxation training+Edu cation	All	Some concerns	Low	High	Low	-	High
Dittrich 2008 ¹⁴⁶ Included for: KQ1	PMR+Exerci se	No intervention/ TAU	Migraine frequency	Some concerns	Low	Low	High	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
Dittrich 2008 ¹⁴⁶ Included for: KQ1	PMR+Exercise	No intervention/TAU	All except migraine frequency	Some concerns	Low	Low	High	-	High
Fichtel 2001 ¹⁴⁷ Included for: KQ1	PMR	No intervention/TAU	All	High	Low	Some concerns	High	-	High
Flynn 2019 ¹⁴⁸ Included for: KQ1, KQ1a	Hypnotherapy	No intervention/TAU	Headache Disability Index	Low	Low	High	Low	-	High
Fritsche 2010 ¹⁴⁹ Included for: KQ3	CBT+Education+PMR	Education+PMR	All but long term follow-up	Low	Low	Low	High	-	High
Fritsche 2010 ¹⁴⁹ Included for: KQ3	CBT+Education+PMR	Education+PMR	Long term follow-up time point 3	Low	Low	High	High	-	High
Gerber 2010 ¹⁵⁰ Included for: KQ2	CBT+Education+PMR	Thermal biofeedback+Relaxation training+Education+EMG biofeedback	All	High	Low	High	Low	-	High
Grazzi 2021 ¹⁵¹ Included for: KQ1	ACT	No intervention/TAU	All	Low	Low	Low	Some concerns	-	High
Hedborg 2011 ¹⁵⁴ Included for: KQ1, KQ1a, KQ5	Relaxation training+Healthy lifestyle counseling+Sleep counseling+Stress management+Massage therapy; Relaxation training+Healthy lifestyle	Minimal intervention	All	Low	Low	Low	High	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
	counseling+ Sleep counseling+ Stress management								
Holroyd 1988 ¹⁵⁶ Included for: KQ1, KQ1a	Thermal biofeedback+ Relaxation training	Attention control and education	All	Some concerns	Low	Low	Some concerns	-	Some concerns
Holroyd 2010 ¹⁵⁸ Included for: KQ1, KQ2	Propranolol+ CBT+PMR+ Preference- based/tailore d; CBT+PMR+ Preference- based/tailore d	CBT+PMR+ Preference- based/tailore d; Propranolol+ CBT+PMR+ Preference- based/tailore d; Propranolol; Placebo	All	Low	Low	Some concerns	Some concerns	-	Some concerns
Janssen 1986 ¹⁶¹ Included for: KQ2	PMR	Autogenic training	All	Some concerns	Low	Low	Some concerns	-	Some concerns
Kewman 1980 ¹⁶² Included for: KQ1	Thermal biofeedback	Sham	Headache frequency per week	Some concerns	Low	Low	Low	-	Some concerns
Klan 2022 ¹⁶³ Included for: KQ1, KQ2	PMR	No intervention/ TAU	All	Low	Low	Some concerns	High	-	High
Klan 2022 ¹⁶³ Included for: KQ1, KQ2	Relaxation training+CBT +Education	PMR	All	Low	Low	Low	Low	-	Low
Kleiboer 2014 ¹⁶⁵ Included for: KQ1, KQ1a	Relaxation training+CBT +Education	No intervention/ TAU	Headache frequency, migraine frequency, MSQOL, MIDAS	Low	Low	High	High	-	High
Kohlenberg 1981 ¹⁶⁸	Thermal biofeedback+	Attention control	Migraine frequency	High	Low	High	Low	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
Included for: KQ1	Relaxation training+CBT +Meditation								
Kropp 1997 ¹⁶⁹ Included for: KQ2	Relaxation training+CBT	Biofeedback	All	Some concerns	Low	Low	Some concerns	-	Some concerns
Labbe 1984 ¹⁷⁰ Included for: KQ1	Thermal biofeedback+ Autogenic training	No intervention/ TAU	Headache frequency	Some concerns	Some concerns	Low	High	-	High
Labbe 1995 ¹⁷¹ Included for: KQ1, KQ3	Thermal biofeedback+ Autogenic training	Autogenic training	Headache frequency	Some concerns	Some concerns	High	Some concerns	-	Some concerns
Labbe 1995 ¹⁷¹ Included for: KQ1, KQ3	Thermal biofeedback+ Autogenic training; Autogenic training	No intervention/ TAU	Headache frequency	Some concerns	Some concerns	High	High	-	High
Lemstra 2002 ¹⁷² Included for: KQ1	Relaxation training+CBT +Education+ Exercise+Ma ssage therapy+Phy sical therapy	No intervention/ TAU	Pain Disability Index	Low	Low	Low	High	-	High
Matchar 2008 ¹⁷³ Included for: KQ1	Relaxation training+Edu cation	No intervention/ TAU	MIDAS	Some concerns	Some concerns	Low	High	-	High
Mathew 1981 ¹⁷⁴ Included for: KQ1, KQ2	Relaxation training+Prop ranolol+Amitr iptyline+Biof edback; Relaxation training+Prop ranolol+Biof edback; Relaxation	No intervention/ TAU; Propranolol; Amitriptyline	Adverse events	Some concerns	Some concerns	High	High	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
	training+Amitriptyline+Biofeedback; Relaxation training+Biofeedback								
Minen 2020a ¹⁷⁵ Included for: KQ1, KQ1a	PMR	No intervention/TAU	All	Some concerns	Low	High	Some concerns	-	High
Minen 2020b ¹⁷⁶ Included for: KQ1, KQ1a	PMR	No intervention/TAU	MIDAS	Some concerns	Low	Some concerns	High	-	High
Minen 2021 ¹⁷⁸ Included for: KQ1, KQ1a	HRV biofeedback	No intervention/TAU	All	Some concerns	Low	Low	High	-	High
Mérelle 2008 ¹⁷⁹ Included for: KQ1	Autogenic training+Education	No intervention/TAU	Frequency; Functional status; Migraine-specific quality of life	Low	Some concerns	Low	High	-	High
Odawara 2015 ¹⁸² Included for: KQ1	Thermal biofeedback+PMR+EMG biofeedback	No intervention/TAU	All	Low	Low	Some concerns	High	-	High
Pickering 2012 ¹⁸³ Included for: KQ1	Relaxation training	No intervention/TAU	Migraine frequency	Low	Low	High	Some concerns	-	High
Powers 2013 ¹⁸⁴ Included for: KQ2	Thermal biofeedback+Relaxation training+Amitriptyline+CBT+EMG biofeedback	Amitriptyline+Education	Headache days/month, PEDMIDAS, 50% reduction	Some concerns	Low	Low	Some concerns	-	Low
Rapoff 2014 ¹⁸⁸	Relaxation training+CBT+Education+	Education control	All	Some concerns	Low	Some concerns	Low	-	Some concerns

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
Included for: KQ1, KQ1a	Pain management education								
Rapoff 2014 ¹⁸⁸ Included for: KQ1, KQ1a	Relaxation training+CBT +Education+ Pain management education	Education control	All	Some concerns	Low	High	Low	-	Some concerns
Rausa 2016 ¹⁸⁹ Included for: KQ1	EMG Biofeedback	Attention control	Headache frequency	Low	Low	High	Some concerns	-	High
Reich 1989 ¹⁹⁰ Included for: KQ2	Relaxation training	Thermal biofeedback	All	Some concerns	Low	High	Low	-	High
Reich 1989 ¹⁹⁰ Included for: KQ2	Preference-based/tailored	Relaxation training; Thermal biofeedback	All	Some concerns	Low	High	High	-	High
Richardson 1989 ¹⁹¹ Included for: KQ1, KQ5	CBT+PMR-Clinic format; CBT+PMR-Self-administered	No intervention/TAU	Migraine frequency	High	Some concerns	High	High	-	High
Richter 1986 ¹⁹² Included for: KQ1, KQ2	PMR+Deep breathing; CBT	CBT; PMR+Deep breathing; Attention control	All	Some concerns	Low	Some concerns	Low	-	Some concerns
Rothrock 2006 ¹⁹³ Included for: KQ1	Education	Education control	MIDAS	High	Low	Low	Low	-	Some concerns
Sargent 1986 ¹⁹⁴ Included for: KQ1, KQ2, KQ3	Relaxation training+EMG biofeedback; Thermal biofeedback+ Relaxation	No intervention/TAU	All	Some concerns	Low	High	Some concerns	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
	training; Relaxation training; Relaxation training								
Sartory 1998 ¹⁹⁶ Included for: KQ2	SMT+Blood volume pulse; PMR+SMT	Metoprolol	Headache freq.	Some concerns	Low	High	Low	-	High
Scharff 2002 ¹⁹⁷ Included for: KQ1	Thermal biofeedback+ Relaxation training+CBT	Sham; No intervention/ TAU	All	Some concerns	Low	Low	Some concerns	-	High
Seminowicz 2020 ¹⁹⁸ Included for: KQ2	Education+M BSR	Education+S MT	All	Low	Low	Low	Low	-	Low
Seng 2019 ²⁰¹ Included for: KQ1, KQ5	Education+C ognitive therapy+MB SR	No intervention/ TAU	All except 1 month headache/migr aine frequenc	Some concerns	Low	Low	High	-	High
Seng 2019 ²⁰¹ Included for: KQ1, KQ5	Education+C ognitive therapy+MB SR	No intervention/ TAU	1 month headache/migr aine frequency	Some concerns	Low	Low	High	-	High
Simshäuser 2022 ²⁰³ Included for: KQ1	Cognitive therapy+MB SR	No intervention/ TAU	PDI, Headache days/week at 8 weeks	Low	Low	Low	High	-	High
Smitherman 2016 ²⁰⁴ Included for: KQ4	Non- headache CBT	Shm	All	Low	Low	Low	Low	-	Low
Sorbi 1984 ²⁰⁶ Included for: KQ3	Thermal biofeedback+ CBT+PMR	CBT+PMR	All	Some concerns	Low	Low	Low	-	Some concerns
Sorbi 1986 ²⁰⁷ Included for: KQ2	Autogenic training+Edu cation	Education+S MT	All	Some concerns	Low	Some concerns	Low	-	Some concerns
Underwood 2022 ²⁰⁹ Included for:	Education	Minimal intervention	All	Low	Low	Some concerns	High	-	High

Reference	Intervention	Comparator	Outcome/ Result	Domain 1	Domain 2	Domain 3	Domain 4	Domain S	Overall
KQ1, KQ1a, KQ5									
Varkey 2011 ²¹² Included for: KQ2	Relaxation training	Topiramate	Headache frequency	Low	Low	High	High	-	High
Vasiliou 2021 ²¹³ Included for: KQ1	ACT	No intervention/ TAU	Disability/Functional status	Low	Low	Low	High	-	High
Vasiliou 2021 ²¹³ Included for: KQ1	ACT	No intervention/ TAU	Disability/Functional status	Low	Low	Low	High	-	High
Wachholtz 2008 ²¹⁵ Included for: KQ2	Meditation-External secular meditation; Meditation-Internal secular meditation; Meditation-Spiritual Meditation	PMR	Headache count	Some concerns	Low	Low	Some concerns	-	High
Wells 2021 ²¹⁸ Included for: KQ2	MBSR	Education	Frequency, Functional status, Migraine QOL	Low	Low	Low	Low	-	Low
Wittchen 1983 ²¹⁹ Included for: KQ1	Relaxation training+CBT +Education	No intervention/ TAU	All	Some concerns	Low	Low	High	-	High
de Tommaso 2017 ²²⁰ Included for: KQ2	Biofeedback +Topiramate	Biofeedback; Topiramate	All	Some concerns	Low	Low	High	-	High

Domain 1: Risk of bias arising from the randomization process

Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)

Domain 3: Risk of bias due to missing outcome data

Domain 4: Risk of bias in measurement of the outcome

Domain 5: Risk of bias arising from the timing of identification or recruitment of participants in a cluster-randomized trial

Abbreviations: ACT=acceptance and commitment therapy; CBT=cognitive behavioral therapy; EMG=electromyography; MBSR=mindfulness-based stress reduction; PMR=progressive muscle relaxation; TAU=treatment-as-usual

Appendix D. Appendix References

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Appendix E. Patient-Centered Outcomes Research Institute (PCORI) Methodology Standards

Contract No.	AHRQ 75Q80120D00002				
Task Order No.	AHRQ 75Q80122F32006				
EPC	ECRI-Penn				
Project Title	Behavioral Interventions for Migraine Prevention				
Standard Category	Abbrev.	Standard	Is this standard applicable to this SR?	List sections and pages of the SR report where you address this standard	If applicable, describe how and why the SR deviated from this standard?
Cross-Cutting Standards for PCOR					
Standards for Formulating Research Questions	RQ-1	Identify gaps in evidence.	Yes	1	
	RQ-2	Develop a formal study protocol.	Yes	3	

	RQ-3	Identify specific populations and health decision(s) affected by the research.	Yes	1	
	RQ-4	Identify and assess participant subgroups.	Yes	92-93	
	RQ-5	Select appropriate interventions and comparators.	Yes	6-7	
	RQ-6	Measure outcomes that people representing the population of interest notice and care about.	Yes	8-9	

Standards Associated with Patient-Centeredness	PC-1	Engage people representing the population of interest and other relevant stakeholders in ways that are appropriate and necessary in a given research context.	Yes	3, 101-102	
	PC-2	Identify, select, recruit, and retain study participants representative of the spectrum of the population of interest and ensure that data are collected thoroughly and systematically from all study participants.	No	NA	This is a review not a primary study

	PC-3	Use patient-reported outcomes when patients or people at risk of a condition are the best source of information for outcomes of interest.	Yes	8-9	
	PC-4	Support dissemination and implementation of study results.	Yes	iv	
Standards for Data Integrity and Rigorous Analyses	IR-1	A priori, specify plans for quantitative data analysis that correspond to major aims.	Yes	11-13	
	IR-2	Assess data source adequacy.	Yes	10	
	IR-3	Describe data linkage plans, if applicable.	No	NA	The appendices have the data

	IR-4	Document validated scales and tests.	No	NA	This is a review not a primary study
	IR-5	Provide sufficient information in reports to allow for assessments of the study's internal and external validity.	Yes	3-14	
	IR-6	Masking should be used when feasible.	No	NA	This is a review not a primary study

	IR-7	In the study protocol, specify a data management plan that addresses, at a minimum, the following elements: collecting data, organizing data, handling data, describing data, preserving data, and sharing data.	Yes	9-10	
Standards for Preventing and Handling Missing Data	MD-1	Describe methods to prevent and monitor missing data.	No	NA	This is a review not a primary study
	MD-2	Use valid statistical methods to deal with missing data that properly account for statistical uncertainty due to missingness.	No	NA	This is a review not a primary study

	MD-3	Record and report all reasons for dropout and missing data, and account for all patients in reports.	No	NA	This is a review not a primary study
	MD-4	Examine sensitivity of inferences to missing data methods and assumptions, and incorporate into interpretation.	No	NA	This is a review not a primary study
Standards for Heterogeneity of Treatment Effect (HTE)	HT-1	State the goals of HTE analyses, including hypotheses and the supporting evidence base.	No	NA	This is a review not a primary study

	HT-2	For all HTE analyses, provide an analysis plan, including the use of appropriate statistical methods.	No	NA	This is a review not a primary study
	HT-3	Report all prespecified HTE analyses and, at minimum, the number of post-hoc HTE analyses, including all subgroups and outcomes analyzed.	No	NA	This is a review not a primary study
Standards for Specific Study Designs and Methods					
Standards for Data Registries	DR-1	Requirements for the design of registries.	No	NA	This is a review not a primary study

	DR-2	Documentation and reporting requirements of registry materials, characteristics, and bias.	No	NA	This is a review not a primary study
	DR-3	Adapting established registries for PCOR.	No	NA	This is a review not a primary study
	DR-4	Documentation requirements when using registry data.	No	NA	This is a review not a primary study
Standards for Data Networks as Research-Facilitating Structures	DN-1	Requirements for the design and features of data networks.	No	NA	This is a review not a primary study
	DN-2	Selection and use of data networks.	No	NA	This is a review not a primary study

Causal Inference Standards	CI-1	Specify the causal model underlying the research question (cross-cutting standard, applies to all PCOR/CER studies).	No	NA	This is a review not a primary study
	CI-2	Define and appropriately characterize the analysis population used to generate effect estimates.	No	NA	This is a review not a primary study
	CI-3	Define with the appropriate precision the timing of the outcome assessment relative to the initiation and duration of exposure.	No	NA	This is a review not a primary study

	CI-4	Measure potential confounders before start of exposure and report data on potential confounders with study results.	No	NA	This is a review not a primary study
	CI-5	Report the assumptions underlying the construction of propensity scores and the comparability of the resulting groups in terms of the balance of covariates and overlap.	No	NA	This is a review not a primary study

	CI-6	Assess the validity of the instrumental variable (i.e., how the assumptions are met) and report the balance of covariates in the groups created by the instrumental variable.	No	NA	This is a review not a primary study
Standards for Adaptive and Bayesian Trial Designs	AT-1	Specify planned adaptations, decisional thresholds, and statistical properties of those adaptations.	No	NA	No Bayesian analyses were conducted
	AT-2	Specify the structure and analysis plan for Bayesian adaptive randomized clinical trial designs.	No	NA	No Bayesian analyses were conducted

	AT-3	Ensure that clinical trial infrastructure is adequate to support planned adaptation(s) and independent interim analyses.	No	NA	No Bayesian analyses were conducted
	AT-4	When reporting adaptive randomized clinical trials, use the CONSORT statement, with modifications.	No	NA	No Bayesian analyses were conducted
Standards for Studies of Medical Tests	MT-1	Specify clinical context and key elements of the medical test.	No	NA	Not about medical tests
	MT-2	Assess the effect of factors known to affect performance and outcomes.	No	NA	Not about medical tests

	MT-3	Focus studies of medical tests on patient-centered outcomes, using rigorous study designs with a preference for randomized controlled trials.	No	NA	Not about medical tests
Standards for Systematic Reviews	SR-1	Adhere to National Academy of Medicine (NAM) standards for systematic reviews of comparative effectiveness research, as appropriate.	Yes	3-14	

Standards on Research Designs Using Clusters	RC-1	Specify whether the study objectives, the interventions, and the primary outcomes pertain to the cluster level or the individual level.	No	NA	Not about clusters
	RC-2	Justify the choice of cluster randomization.	No	NA	Not about clusters
	RC-3	Power and sample size estimates must use appropriate methods to account for the dependence of observations within clusters and the degrees of freedom available at the cluster level.	No	NA	Not about clusters

	RC-4	Data analyses must account for the dependence of observations within clusters regardless of its magnitude.	No	NA	Not about clusters
	RC-5	Stratified randomization should be used when feasible.	No	NA	Not about clusters
Standards for Studies of Complex Interventions	SCI-1	Fully describe the intervention and comparator and define their core functions.	No	NA	This is a review not a primary study
	SCI-2	Specify the hypothesized causal pathways and their theoretical basis.	No	NA	This is a review not a primary study

	SCI-3	Specify how adaptations to the form of the intervention and comparator will be allowed and recorded.	No	NA	This is a review not a primary study
	SCI-4	Plan and describe a process evaluation.	No	NA	This is a review not a primary study
	SCI-5	Select patient outcomes informed by the causal pathway.	No	NA	This is a review not a primary study
Standards for Qualitative Methods	QM-1	State the qualitative approach to research inquiry, design, and conduct.	No	NA	Not a qualitative study
	QM-2	Select and justify appropriate qualitative methods sampling strategy.	No	NA	Not a qualitative study

	QM-3	Link the qualitative data analysis, interpretations, and conclusions to the study question.	No	NA	Not a qualitative study
	QM-5	Establish trustworthiness and credibility of qualitative research.	No	NA	Not a qualitative study
Standards for Mixed Methods Research	MM-2	Specify how mixed methods are integrated across design, data sources, and/or data collection phases.	No	NA	Not a mixed methods review
	MM-2	Select and justify appropriate mixed methods sampling strategy.	No	NA	Not a mixed methods review
	MM-3	Integrate data analysis, data interpretation, and conclusions.	No	NA	Not a mixed methods review

Standards for Individual Participant-Level Data Meta-Analysis (IPD-MA)	IPD-1	Specify the research question(s) that will be addressed through the IPD-MA and describe the specific information it will provide that other approaches would not.	No	NA	Not an IPD meta-analysis
	IPD-2	Describe the proposed governance structure for the IPD-MA in the protocol and study reports.	No	NA	Not an IPD meta-analysis
	IPD-3	Use systematic, reproducible methods to identify studies for inclusion in the IPD-MA.	No	NA	Not an IPD meta-analysis

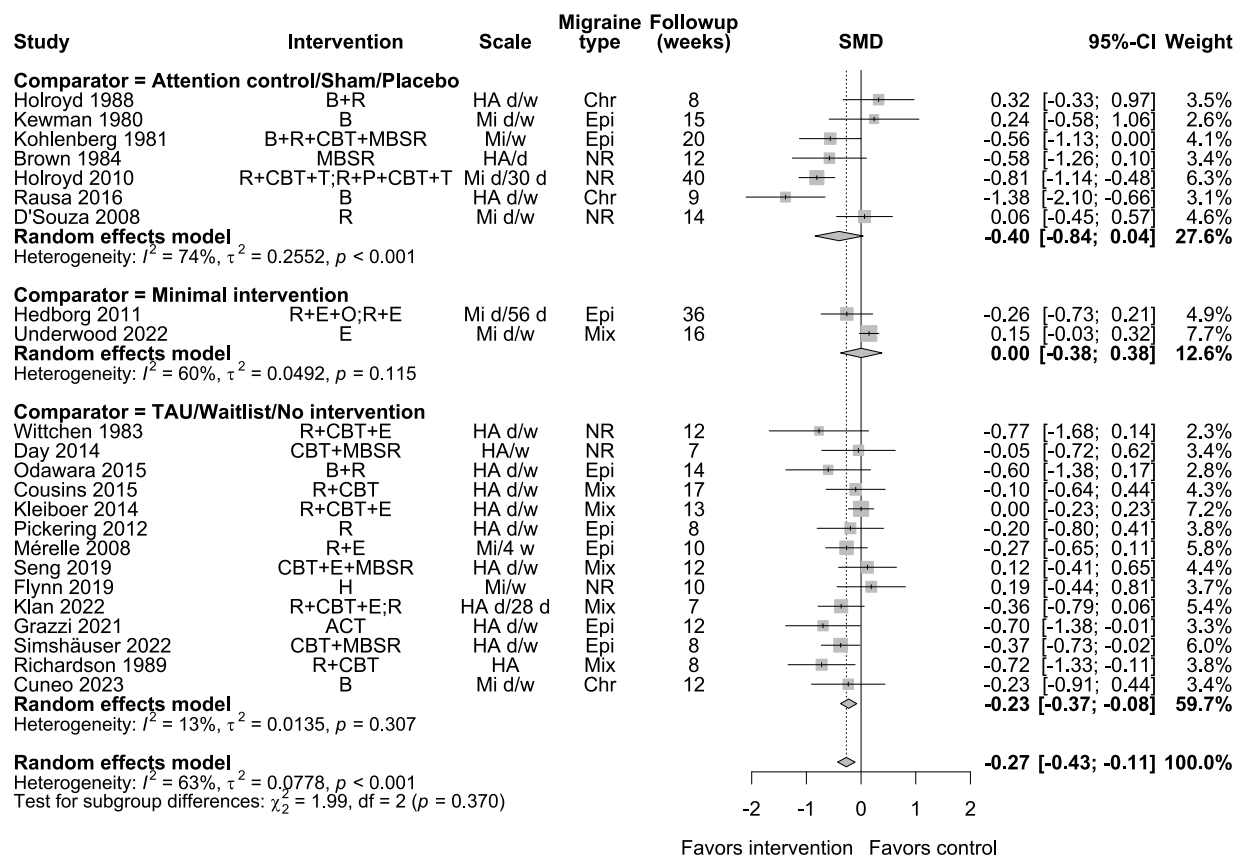
	IPD-4	Specify the design and planned analyses of the IPD-MA in a protocol, document any changes, and report significant amendments and modifications.	No	NA	Not an IPD meta-analysis
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Appendix F. Meta-Analyses of Any Behavioral Intervention for Key Question 1

Adults: Combined Analyses of All Behavioral Treatments

We also conducted analyses of *any behavioral treatment* compared to *any inactive treatment*. These analyses were intended to maximize statistical power and determine if an overall signal can be detected. We performed three standard meta-analyses: migraine/headache frequency (Figure F-1), migraine disability (Figure F-2), and migraine-specific quality of life (Figure F-3). All of these analyses combined timepoints, and if a study reported multiple timepoints, we chose the one closest to 12 weeks.

Figure F-1. Meta-analysis of any behavioral treatment, adults, migraine/headache frequency



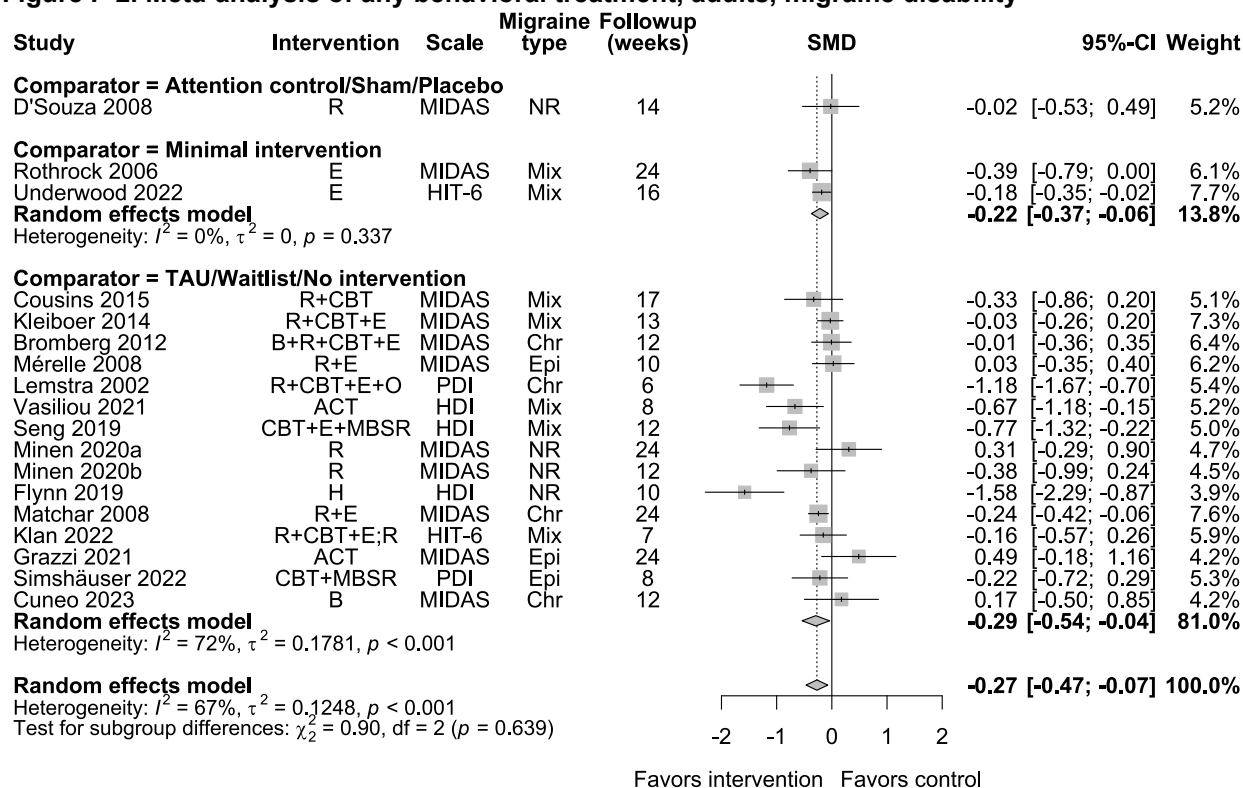
For Intervention: ACT – Acceptance and commitment therapy; B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; H – Hypnotherapy; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

For Scale: Mi d/w- Migraine days per week; Mi d/30 d – Migraine days per 30 day period; Mi/w –Migraine attacks per week; Mi /4w – Migraine attacks per 4 week period HA d/w –Headache days per week; HA d/28 d – Headache days per 28 day period; HA – Headaches (unreported timeframe); HA/d – Headaches per day; HA/w – Headaches per week; HA /2 w –Headaches per 2 week period

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

Figure F-2. Meta-analysis of any behavioral treatment, adults, migraine disability



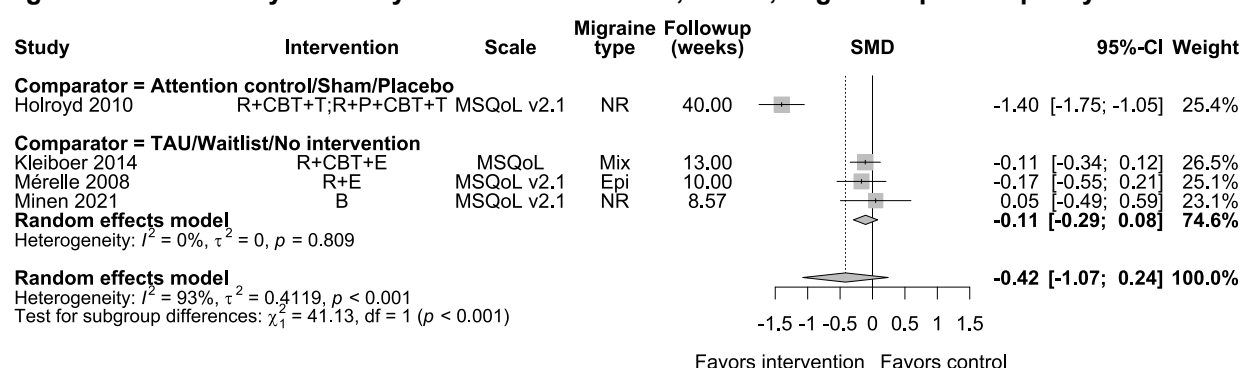
For Intervention: ACT – Acceptance and commitment therapy; B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; H – Hypnotherapy; MBSR – Mindfulness based stress reduction; O – Other (neither behavioral nor pharmacologic); P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: HDI – Headache Disability Inventory; HIT-6 – Headache Impact Test-6; MIDAS – Migraine Disability Assessment; PDI – Pain Disability Inventory

For Migraine Type: Chr – Only patients with chronic migraine; Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

Figure F-3. Meta-analysis of any behavioral treatment, adults, migraine-specific quality of life



For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; P – Pharmacologic; R – Relaxation training; T – Tailored treatment

For Scale: MSQoL – Migraine-Specific Quality of Life

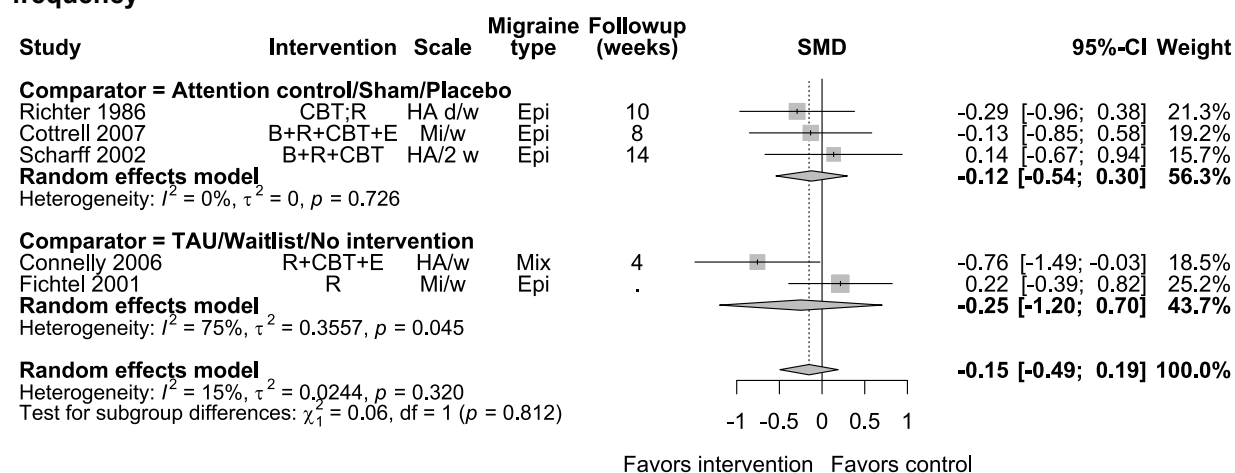
For Migraine Type: Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients; NR – Not reported

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

Children: Combined Analyses of All Behavioral Treatments

We also conducted analyses of *any behavioral treatment* compared to *any inactive treatment*. These analyses were intended to maximize statistical power and determine if an overall signal can be detected. Nevertheless, we performed two standard meta-analyses: migraine/headache frequency (Figure F-4), and migraine disability (Figure F-5). For migraine-specific quality of life, none of the studies reported effect-size calculated information. All of these analyses combined timepoints.

Figure F-4. Meta-analysis of any behavioral treatment, children/adolescents, migraine/headache frequency



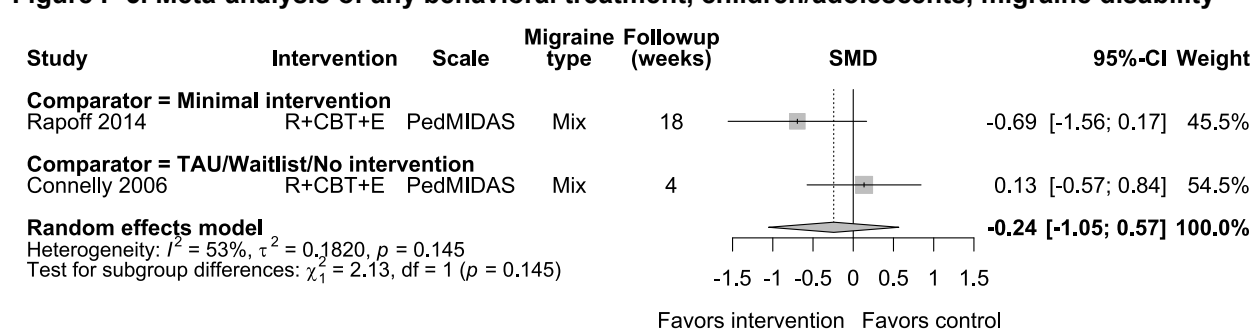
For Intervention: B – Biofeedback; CBT – Cognitive behavioral therapy; E – Education; R – Relaxation training

For Migraine Type: Epi – Only patients with episodic migraine; Mix – Both episodic and chronic patients

For Scale: Mi/w –Migraine attacks per week; HA d/w –Headache days per week; HA/d – Headaches per day; HA/w – Headaches per week

Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

Figure F-5. Meta-analysis of any behavioral treatment, children/adolescents, migraine disability



For Intervention: CBT – Cognitive behavioral therapy; E – Education; R – Relaxation training

For Scale: PedMIDAS – Pediatric Migraine Disability Assessment

For Migraine Type: Mix – Both episodic and chronic patients

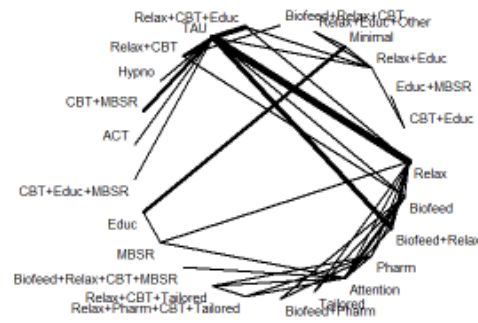
Other: CI – Confidence interval; SMD – Standardized mean difference; TAU – Treatment as usual

Appendix G. Network Meta-Analyses for Key Questions 1, 2, and 3

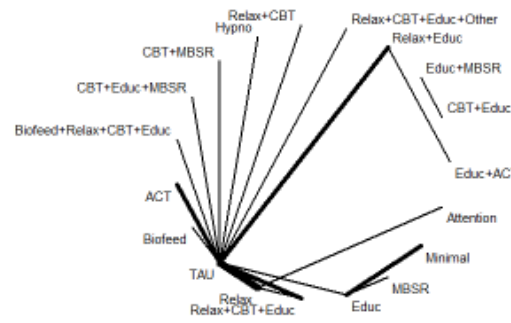
We considered (but ultimately rejected) the idea of applying network meta-analyses (NMAs) as an efficient way to simultaneously and efficiently addressing KQ1, KQ2, and KQ3. Below are visualizations of the networks we conducted and statistical results.

Figure G-1. Network structures of evidence base for each age group by key outcome

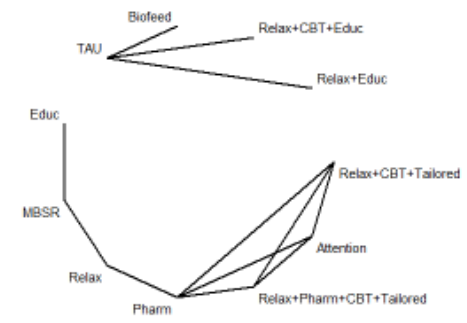
Adults, Migraine/headache frequency



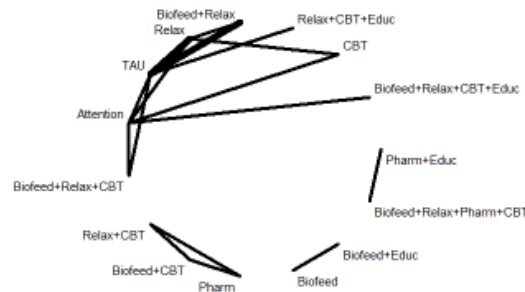
Adults, Migraine disability



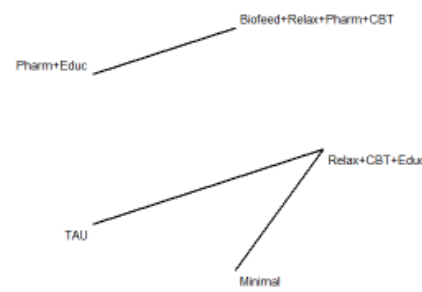
Adults, Migraine-specific quality of life



Children/adolescents, Migraine/headache frequency



Children/adolescents, Migraine disability



Children/adolescents, Migraine-specific quality of life



Each network represents a different population category and outcome. Within a network, edges represent direct comparisons between interventions; the width of the edge is based on the number of studies comparing the interventions. Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy; TAU=treatment-as-usual

Figure G-1 represents the entire evidence base of studies for each target population (adults vs. children/adolescents) and outcome (migraine/headache frequency vs. migraine disability vs. migraine-specific quality of life) considering any time point. Most of these networks were disconnected, meaning that there were interventions that could not be connected to the rest of the evidence base via direct or indirect evidence, creating different subnetworks. For each network, we decided to focus on the largest subnetwork for further consideration. We then considered the potential to evaluate incoherence (statistical disagreement between direct and indirect evidence), which requires at least one closed loop of evidence (where a set of interventions all have direct and indirect evidence) and the closed loops are not just made up of multi-arm studies. Based on these criteria, we excluded the network on migraine-specific quality of life in adults and all of children from further consideration. We used the R packages netmeta (v2.8-1) and viscomp (v1.0.0) to conduct these analyses.

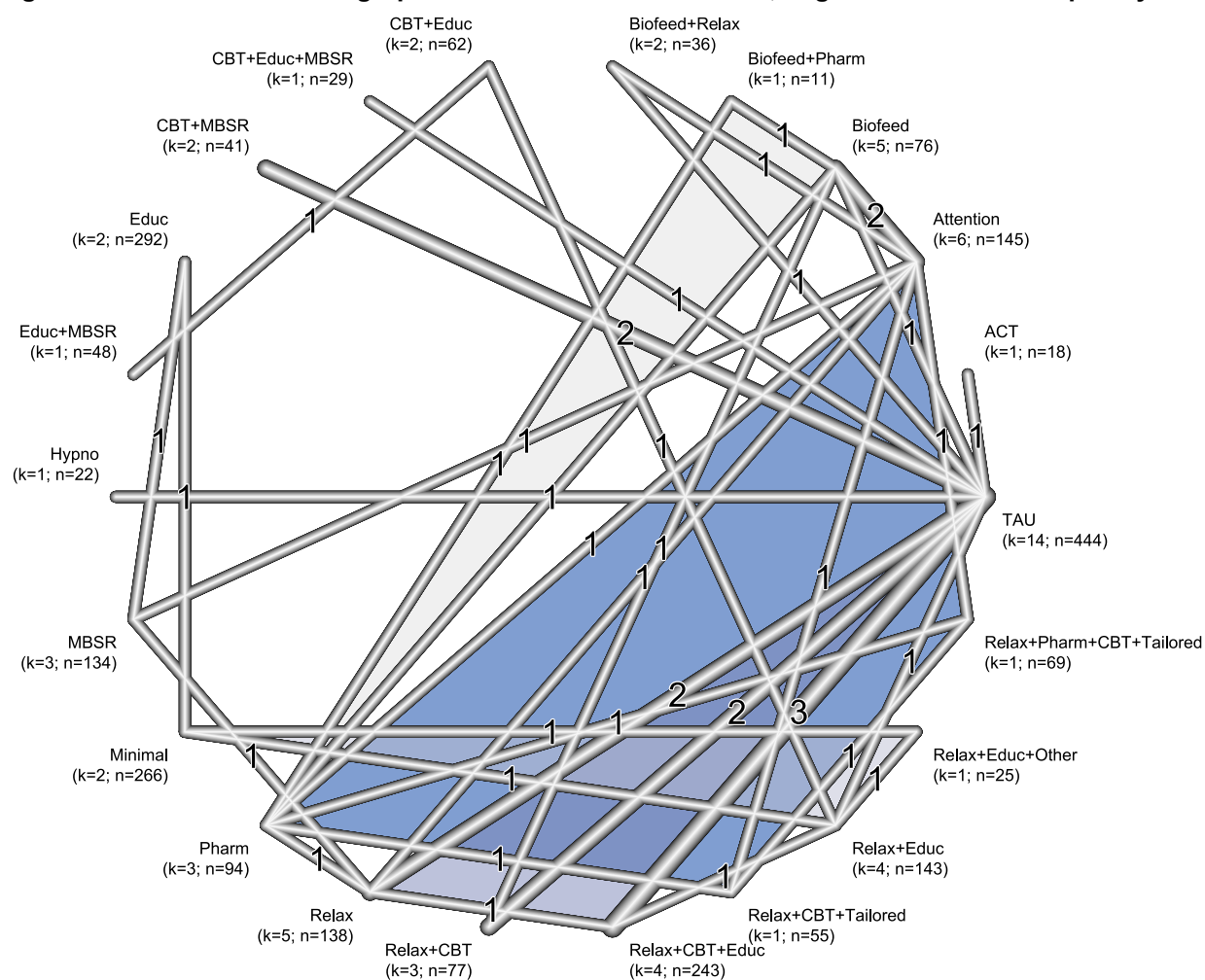
Network Meta-Analysis, Adults, Migraine/Headache Frequency

The network of studies evaluating behavioral interventions in adults for migraine frequency included 30 studies (2468 patients). There are 22 distinct interventions, of which 18 included at least one behavioral component, one was any pharmacological treatment alone, and three were controls (attention control, minimal intervention, or TAU) (Figure G-2). The most common comparator was TAU, which was used as the reference treatment for the analysis.

We first evaluated the effect of all interventions on migraine frequency using the standard NMA approach. Three behavioral interventions displayed statistically significant improvements compared to TAU: relaxation training + pharmacologic + education + tailored and biofeedback alone (Figure G-3, Table G-1). Note that “tailored” refers a component of the intervention where different types of behavioral components were available, and the specific intervention received was based on patient or provider preference (and not constant within the trial arm). Relaxation + pharmacologic + CBT + tailored also significantly improved frequency over all other interventions, except for education + MBSR. Neither education + MBSR nor biofeedback demonstrated statistically significant improvements over interventions beyond TAU.

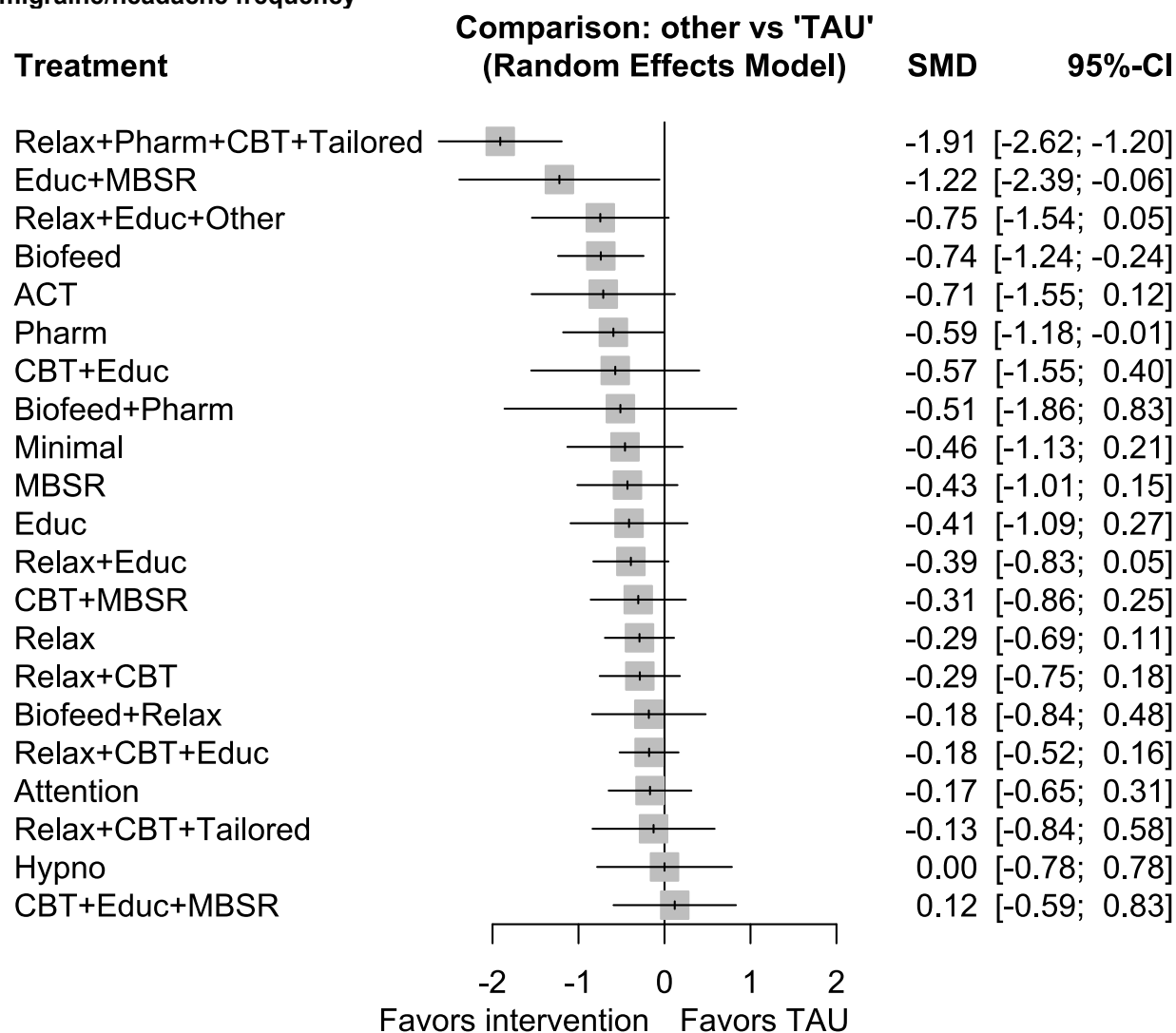
To assess incoherence, we used the node-splitting and design-by-treatment interaction approaches. Neither approach provided clear evidence of incoherence in the network (node-splitting: p-values ranged from 0.135 to 0.932 (Table G-1); design-by-treatment interaction: p-value = 0.992).

Figure G-2. Detailed network graph of evidence base for adults, migraine/headache frequency



Edges represent direct comparisons between interventions; the width of the edge is based on the number of studies comparing the interventions. k represents the number of studies evaluating an intervention for the outcome, and n represents the number of participants evaluated for that intervention and outcome. Shading indicates loops which include multi-arm trials. Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; k=number of studies; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; n=number of participants; Pharm=pharmacologic; Relax=relaxation therapy; TAU=treatment-as-usual

Figure G-3. Forest plot of network results for all interventions compared to TAU, adults, migraine/headache frequency



Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; CI=confidence interval; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy; SMD=standardized mean difference; TAU=treatment-as-usual

Table G-1. Direct, indirect, and network estimates for adults, migraine/headache frequency

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
ACT	Attention	0	.	.	.	-0.54 [-1.51; 0.42]	-0.54 [-1.51; 0.42]	.
ACT	Biofeed	0	.	.	.	0.03 [-0.94; 1.00]	0.03 [-0.94; 1.00]	.
ACT	Biofeed+Pharm	0	.	.	.	-0.20 [-1.78; 1.38]	-0.20 [-1.78; 1.38]	.
ACT	Biofeed+Relax	0	.	.	.	-0.53 [-1.59; 0.53]	-0.53 [-1.59; 0.53]	.
ACT	CBT+Educ	0	.	.	.	-0.14 [-1.42; 1.14]	-0.14 [-1.42; 1.14]	.
ACT	CBT+Educ+MBSR	0	.	.	.	-0.83 [-1.93; 0.26]	-0.83 [-1.93; 0.26]	.
ACT	CBT+MBSR	0	.	.	.	-0.41 [-1.41; 0.59]	-0.41 [-1.41; 0.59]	.
ACT	Educ	0	.	.	.	-0.30 [-1.38; 0.78]	-0.30 [-1.38; 0.78]	.
ACT	Educ+MBSR	0	.	.	.	0.51 [-0.92; 1.94]	0.51 [-0.92; 1.94]	.
ACT	Hypno	0	.	.	.	-0.71 [-1.86; 0.43]	-0.71 [-1.86; 0.43]	.
ACT	MBSR	0	.	.	.	-0.28 [-1.30; 0.74]	-0.28 [-1.30; 0.74]	.
ACT	Minimal	0	.	.	.	-0.25 [-1.32; 0.82]	-0.25 [-1.32; 0.82]	.
ACT	Pharm	0	.	.	.	-0.12 [-1.14; 0.90]	-0.12 [-1.14; 0.90]	.
ACT	Relax	0	.	.	.	-0.42 [-1.35; 0.50]	-0.42 [-1.35; 0.50]	.
ACT	Relax+CBT	0	.	.	.	-0.43 [-1.38; 0.53]	-0.43 [-1.38; 0.53]	.
ACT	Relax+CBT+Educ	0	.	.	.	-0.53 [-1.43; 0.37]	-0.53 [-1.43; 0.37]	.
ACT	Relax+CBT+Tailored	0	.	.	.	-0.59 [-1.68; 0.51]	-0.59 [-1.68; 0.51]	.
ACT	Relax+Educ	0	.	.	.	-0.32 [-1.26; 0.62]	-0.32 [-1.26; 0.62]	.
ACT	Relax+Educ+Other	0	.	.	.	0.03 [-1.12; 1.19]	0.03 [-1.12; 1.19]	.
ACT	Relax+Pharm+CBT+Tailored	0	.	.	.	1.20 [0.10; 2.30]	1.20 [0.10; 2.30]	.
ACT	TAU	1	35	.	-0.71 [-1.55; 0.12]	.	-0.71 [-1.55; 0.12]	.
Attention	Biofeed	2	60	88.6%	0.66 [0.02; 1.30]	0.45 [-0.33; 1.22]	0.57 [0.08; 1.07]	0.6849
Attention	Biofeed+Pharm	0	.	.	.	0.34 [-0.98; 1.66]	0.34 [-0.98; 1.66]	.
Attention	Biofeed+Relax	1	37	.	-0.33 [-1.13; 0.48]	0.60 [-0.45; 1.65]	0.01 [-0.62; 0.65]	0.1712
Attention	CBT+Educ	0	.	.	.	0.40 [-0.66; 1.47]	0.40 [-0.66; 1.47]	.
Attention	CBT+Educ+MBSR	0	.	.	.	-0.29 [-1.15; 0.57]	-0.29 [-1.15; 0.57]	.
Attention	CBT+MBSR	0	.	.	.	0.14 [-0.60; 0.87]	0.14 [-0.60; 0.87]	.
Attention	Educ	0	.	.	.	0.24 [-0.46; 0.95]	0.24 [-0.46; 0.95]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Attention	Educ+MBSR	0	.	.	.	1.05 [-0.18; 2.29]	1.05 [-0.18; 2.29]	.
Attention	Hypno	0	.	.	.	-0.17 [-1.09; 0.75]	-0.17 [-1.09; 0.75]	.
Attention	MBSR	1	39	.	0.59 [-0.24; 1.42]	-0.00 [-0.75; 0.74]	0.26 [-0.29; 0.82]	0.2966
Attention	Minimal	0	.	.	.	0.29 [-0.44; 1.02]	0.29 [-0.44; 1.02]	.
Attention	Pharm	1	108	.	0.51 [-0.10; 1.12]	0.29 [-0.48; 1.07]	0.43 [-0.05; 0.90]	0.6629
Attention	Relax	1	59	.	-0.06 [-0.76; 0.63]	0.24 [-0.31; 0.78]	0.12 [-0.31; 0.55]	0.5080
Attention	Relax+CBT	0	.	.	.	0.12 [-0.50; 0.73]	0.12 [-0.50; 0.73]	.
Attention	Relax+CBT+Educ	0	.	.	.	0.01 [-0.54; 0.56]	0.01 [-0.54; 0.56]	.
Attention	Relax+CBT+Tailored	1	110	.	0.00 [-0.60; 0.60]	-0.44 [-2.31; 1.44]	-0.04 [-0.62; 0.53]	0.6629
Attention	Relax+Educ	0	.	.	.	0.22 [-0.38; 0.83]	0.22 [-0.38; 0.83]	.
Attention	Relax+Educ+Other	0	.	.	.	0.58 [-0.29; 1.45]	0.58 [-0.29; 1.45]	.
Attention	Relax+Pharm+CBT+Tailored	1	124	.	1.78 [1.17; 2.40]	1.35 [-0.51; 3.21]	1.74 [1.16; 2.33]	0.6629
Attention	TAU	0	.	.	.	-0.17 [-0.65; 0.31]	-0.17 [-0.65; 0.31]	.
Biofeed	Biofeed+Pharm	1	22	.	-0.48 [-2.11; 1.14]	0.27 [-2.00; 2.55]	-0.23 [-1.55; 1.09]	0.5949
Biofeed	Biofeed+Relax	0	.	.	.	-0.56 [-1.30; 0.18]	-0.56 [-1.30; 0.18]	.
Biofeed	CBT+Educ	0	.	.	.	-0.17 [-1.25; 0.92]	-0.17 [-1.25; 0.92]	.
Biofeed	CBT+Educ+MBSR	0	.	.	.	-0.86 [-1.73; 0.01]	-0.86 [-1.73; 0.01]	.
Biofeed	CBT+MBSR	0	.	.	.	-0.44 [-1.18; 0.31]	-0.44 [-1.18; 0.31]	.
Biofeed	Educ	0	.	.	.	-0.33 [-1.11; 0.45]	-0.33 [-1.11; 0.45]	.
Biofeed	Educ+MBSR	0	.	.	.	0.48 [-0.77; 1.74]	0.48 [-0.77; 1.74]	.
Biofeed	Hypno	0	.	.	.	-0.74 [-1.67; 0.19]	-0.74 [-1.67; 0.19]	.
Biofeed	MBSR	0	.	.	.	-0.31 [-0.98; 0.36]	-0.31 [-0.98; 0.36]	.
Biofeed	Minimal	0	.	.	.	-0.28 [-1.07; 0.51]	-0.28 [-1.07; 0.51]	.
Biofeed	Pharm	1	21	.	-0.56 [-2.19; 1.08]	-0.08 [-0.75; 0.59]	-0.15 [-0.77; 0.47]	0.5949
Biofeed	Relax	0	.	.	.	-0.45 [-0.99; 0.09]	-0.45 [-0.99; 0.09]	.
Biofeed	Relax+CBT	1	38	.	-0.70 [-1.51; 0.11]	-0.22 [-1.00; 0.56]	-0.45 [-1.02; 0.11]	0.4024
Biofeed	Relax+CBT+Educ	0	.	.	.	-0.56 [-1.14; 0.02]	-0.56 [-1.14; 0.02]	.
Biofeed	Relax+CBT+Tailored	0	.	.	.	-0.61 [-1.34; 0.12]	-0.61 [-1.34; 0.12]	.
Biofeed	Relax+Educ	0	.	.	.	-0.35 [-0.99; 0.29]	-0.35 [-0.99; 0.29]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Biofeed	Relax+Educ+Other	0	.	.	.	0.01 [-0.90; 0.91]	0.01 [-0.90; 0.91]	.
Biofeed	Relax+Pharm+CBT+Tailored	0	.	.	.	1.17 [0.44; 1.90]	1.17 [0.44; 1.90]	.
Biofeed	TAU	1	36	.	-0.24 [-1.06; 0.58]	-1.03 [-1.65; -0.40]	-0.74 [-1.24; -0.24]	0.1347
Biofeed+Pharm	Biofeed+Relax	0	.	.	.	-0.33 [-1.77; 1.11]	-0.33 [-1.77; 1.11]	.
Biofeed+Pharm	CBT+Educ	0	.	.	.	0.06 [-1.59; 1.71]	0.06 [-1.59; 1.71]	.
Biofeed+Pharm	CBT+Educ+MBSR	0	.	.	.	-0.63 [-2.16; 0.89]	-0.63 [-2.16; 0.89]	.
Biofeed+Pharm	CBT+MBSR	0	.	.	.	-0.21 [-1.66; 1.25]	-0.21 [-1.66; 1.25]	.
Biofeed+Pharm	Educ	0	.	.	.	-0.10 [-1.56; 1.36]	-0.10 [-1.56; 1.36]	.
Biofeed+Pharm	Educ+MBSR	0	.	.	.	0.71 [-1.06; 2.48]	0.71 [-1.06; 2.48]	.
Biofeed+Pharm	Hypno	0	.	.	.	-0.51 [-2.07; 1.05]	-0.51 [-2.07; 1.05]	.
Biofeed+Pharm	MBSR	0	.	.	.	-0.08 [-1.48; 1.31]	-0.08 [-1.48; 1.31]	.
Biofeed+Pharm	Minimal	0	.	.	.	-0.05 [-1.52; 1.41]	-0.05 [-1.52; 1.41]	.
Biofeed+Pharm	Pharm	1	21	.	-0.07 [-1.48; 1.33]	0.88 [-2.32; 4.07]	0.08 [-1.20; 1.37]	0.5949
Biofeed+Pharm	Relax	0	.	.	.	-0.22 [-1.56; 1.11]	-0.22 [-1.56; 1.11]	.
Biofeed+Pharm	Relax+CBT	0	.	.	.	-0.23 [-1.62; 1.17]	-0.23 [-1.62; 1.17]	.
Biofeed+Pharm	Relax+CBT+Educ	0	.	.	.	-0.33 [-1.71; 1.04]	-0.33 [-1.71; 1.04]	.
Biofeed+Pharm	Relax+CBT+Tailored	0	.	.	.	-0.39 [-1.77; 1.00]	-0.39 [-1.77; 1.00]	.
Biofeed+Pharm	Relax+Educ	0	.	.	.	-0.12 [-1.52; 1.28]	-0.12 [-1.52; 1.28]	.
Biofeed+Pharm	Relax+Educ+Other	0	.	.	.	0.23 [-1.30; 1.77]	0.23 [-1.30; 1.77]	.
Biofeed+Pharm	Relax+Pharm+CBT+Tailored	0	.	.	.	1.40 [0.01; 2.78]	1.40 [0.01; 2.78]	.
Biofeed+Pharm	TAU	0	.	.	.	-0.51 [-1.86; 0.83]	-0.51 [-1.86; 0.83]	.
Biofeed+Relax	CBT+Educ	0	.	.	.	0.39 [-0.78; 1.56]	0.39 [-0.78; 1.56]	.
Biofeed+Relax	CBT+Educ+MBSR	0	.	.	.	-0.30 [-1.27; 0.67]	-0.30 [-1.27; 0.67]	.
Biofeed+Relax	CBT+MBSR	0	.	.	.	0.12 [-0.74; 0.98]	0.12 [-0.74; 0.98]	.
Biofeed+Relax	Educ	0	.	.	.	0.23 [-0.66; 1.12]	0.23 [-0.66; 1.12]	.
Biofeed+Relax	Educ+MBSR	0	.	.	.	1.04 [-0.29; 2.37]	1.04 [-0.29; 2.37]	.
Biofeed+Relax	Hypno	0	.	.	.	-0.18 [-1.21; 0.84]	-0.18 [-1.21; 0.84]	.
Biofeed+Relax	MBSR	0	.	.	.	0.25 [-0.54; 1.04]	0.25 [-0.54; 1.04]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Biofeed+Relax	Minimal	0	.	.	.	0.28 [-0.62; 1.17]	0.28 [-0.62; 1.17]	.
Biofeed+Relax	Pharm	0	.	.	.	0.41 [-0.35; 1.18]	0.41 [-0.35; 1.18]	.
Biofeed+Relax	Relax	0	.	.	.	0.11 [-0.58; 0.80]	0.11 [-0.58; 0.80]	.
Biofeed+Relax	Relax+CBT	0	.	.	.	0.10 [-0.68; 0.89]	0.10 [-0.68; 0.89]	.
Biofeed+Relax	Relax+CBT+Educ	0	.	.	.	-0.00 [-0.73; 0.72]	-0.00 [-0.73; 0.72]	.
Biofeed+Relax	Relax+CBT+Tailored	0	.	.	.	-0.06 [-0.90; 0.79]	-0.06 [-0.90; 0.79]	.
Biofeed+Relax	Relax+Educ	0	.	.	.	0.21 [-0.56; 0.98]	0.21 [-0.56; 0.98]	.
Biofeed+Relax	Relax+Educ+Other	0	.	.	.	0.56 [-0.44; 1.57]	0.56 [-0.44; 1.57]	.
Biofeed+Relax	Relax+Pharm+CBT+Tailored	0	.	.	.	1.73 [0.88; 2.58]	1.73 [0.88; 2.58]	.
Biofeed+Relax	TAU	1	28	.	-0.62 [-1.53; 0.29]	0.30 [-0.66; 1.26]	-0.18 [-0.84; 0.48]	0.1712
CBT+Educ	CBT+Educ+MBSR	0	.	.	.	-0.69 [-1.90; 0.52]	-0.69 [-1.90; 0.52]	.
CBT+Educ	CBT+MBSR	0	.	.	.	-0.27 [-1.39; 0.86]	-0.27 [-1.39; 0.86]	.
CBT+Educ	Educ	0	.	.	.	-0.16 [-1.26; 0.94]	-0.16 [-1.26; 0.94]	.
CBT+Educ	Educ+MBSR	1	94	.	0.65 [0.02; 1.28]	.	0.65 [0.02; 1.28]	.
CBT+Educ	Hypno	0	.	.	.	-0.57 [-1.83; 0.68]	-0.57 [-1.83; 0.68]	.
CBT+Educ	MBSR	0	.	.	.	-0.14 [-1.23; 0.94]	-0.14 [-1.23; 0.94]	.
CBT+Educ	Minimal	0	.	.	.	-0.11 [-1.18; 0.95]	-0.11 [-1.18; 0.95]	.
CBT+Educ	Pharm	0	.	.	.	0.02 [-1.09; 1.14]	0.02 [-1.09; 1.14]	.
CBT+Educ	Relax	0	.	.	.	-0.28 [-1.31; 0.75]	-0.28 [-1.31; 0.75]	.
CBT+Educ	Relax+CBT	0	.	.	.	-0.29 [-1.36; 0.79]	-0.29 [-1.36; 0.79]	.
CBT+Educ	Relax+CBT+Educ	0	.	.	.	-0.39 [-1.37; 0.59]	-0.39 [-1.37; 0.59]	.
CBT+Educ	Relax+CBT+Tailored	0	.	.	.	-0.45 [-1.63; 0.74]	-0.45 [-1.63; 0.74]	.
CBT+Educ	Relax+Educ	1	29	.	-0.18 [-1.06; 0.69]	.	-0.18 [-1.06; 0.69]	.
CBT+Educ	Relax+Educ+Other	0	.	.	.	0.17 [-0.95; 1.30]	0.17 [-0.95; 1.30]	.
CBT+Educ	Relax+Pharm+CBT+Tailored	0	.	.	.	1.34 [0.15; 2.52]	1.34 [0.15; 2.52]	.
CBT+Educ	TAU	0	.	.	.	-0.57 [-1.55; 0.40]	-0.57 [-1.55; 0.40]	.
CBT+Educ+MBSR	CBT+MBSR	0	.	.	.	0.42 [-0.48; 1.33]	0.42 [-0.48; 1.33]	.
CBT+Educ+MBSR	Educ	0	.	.	.	0.53 [-0.45; 1.52]	0.53 [-0.45; 1.52]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
CBT+Educ+MBSR	Educ+MBSR	0	.	.	.	1.34 [-0.02; 2.71]	1.34 [-0.02; 2.71]	.
CBT+Educ+MBSR	Hypno	0	.	.	.	0.12 [-0.94; 1.18]	0.12 [-0.94; 1.18]	.
CBT+Educ+MBSR	MBSR	0	.	.	.	0.55 [-0.37; 1.47]	0.55 [-0.37; 1.47]	.
CBT+Educ+MBSR	Minimal	0	.	.	.	0.58 [-0.40; 1.56]	0.58 [-0.40; 1.56]	.
CBT+Educ+MBSR	Pharm	0	.	.	.	0.71 [-0.21; 1.63]	0.71 [-0.21; 1.63]	.
CBT+Educ+MBSR	Relax	0	.	.	.	0.41 [-0.41; 1.23]	0.41 [-0.41; 1.23]	.
CBT+Educ+MBSR	Relax+CBT	0	.	.	.	0.41 [-0.45; 1.26]	0.41 [-0.45; 1.26]	.
CBT+Educ+MBSR	Relax+CBT+Educ	0	.	.	.	0.30 [-0.49; 1.09]	0.30 [-0.49; 1.09]	.
CBT+Educ+MBSR	Relax+CBT+Tailored	0	.	.	.	0.25 [-0.76; 1.25]	0.25 [-0.76; 1.25]	.
CBT+Educ+MBSR	Relax+Educ	0	.	.	.	0.51 [-0.33; 1.35]	0.51 [-0.33; 1.35]	.
CBT+Educ+MBSR	Relax+Educ+Other	0	.	.	.	0.87 [-0.20; 1.93]	0.87 [-0.20; 1.93]	.
CBT+Educ+MBSR	Relax+Pharm+CBT+Tailored	0	.	.	.	2.03 [1.02; 3.04]	2.03 [1.02; 3.04]	.
CBT+Educ+MBSR	TAU	1	55	.	0.12 [-0.59; 0.83]	.	0.12 [-0.59; 0.83]	.
CBT+MBSR	Educ	0	.	.	.	0.11 [-0.77; 0.98]	0.11 [-0.77; 0.98]	.
CBT+MBSR	Educ+MBSR	0	.	.	.	0.92 [-0.37; 2.21]	0.92 [-0.37; 2.21]	.
CBT+MBSR	Hypno	0	.	.	.	-0.31 [-1.26; 0.65]	-0.31 [-1.26; 0.65]	.
CBT+MBSR	MBSR	0	.	.	.	0.13 [-0.68; 0.93]	0.13 [-0.68; 0.93]	.
CBT+MBSR	Minimal	0	.	.	.	0.15 [-0.71; 1.02]	0.15 [-0.71; 1.02]	.
CBT+MBSR	Pharm	0	.	.	.	0.29 [-0.52; 1.09]	0.29 [-0.52; 1.09]	.
CBT+MBSR	Relax	0	.	.	.	-0.01 [-0.70; 0.67]	-0.01 [-0.70; 0.67]	.
CBT+MBSR	Relax+CBT	0	.	.	.	-0.02 [-0.74; 0.71]	-0.02 [-0.74; 0.71]	.
CBT+MBSR	Relax+CBT+Educ	0	.	.	.	-0.13 [-0.78; 0.52]	-0.13 [-0.78; 0.52]	.
CBT+MBSR	Relax+CBT+Tailored	0	.	.	.	-0.18 [-1.08; 0.72]	-0.18 [-1.08; 0.72]	.
CBT+MBSR	Relax+Educ	0	.	.	.	0.09 [-0.62; 0.79]	0.09 [-0.62; 0.79]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
CBT+MBSR	Relax+Educ+Other	0	.	.	.	0.44 [-0.53; 1.41]	0.44 [-0.53; 1.41]	.
CBT+MBSR	Relax+Pharm+CBT+Tailored	0	.	.	.	1.60 [0.70; 2.51]	1.60 [0.70; 2.51]	.
CBT+MBSR	TAU	2	82	6.8%	-0.31 [-0.86; 0.25]	.	-0.31 [-0.86; 0.25]	.
Educ	Educ+MBSR	0	.	.	.	0.81 [-0.46; 2.08]	0.81 [-0.46; 2.08]	.
Educ	Hypno	0	.	.	.	-0.41 [-1.45; 0.63]	-0.41 [-1.45; 0.63]	.
Educ	MBSR	1	89	.	-0.13 [-0.77; 0.50]	0.56 [-0.63; 1.75]	0.02 [-0.54; 0.58]	0.3124
Educ	Minimal	1	487	.	0.15 [-0.36; 0.65]	-0.55 [-1.79; 0.70]	0.05 [-0.42; 0.52]	0.3124
Educ	Pharm	0	.	.	.	0.18 [-0.61; 0.97]	0.18 [-0.61; 0.97]	.
Educ	Relax	0	.	.	.	-0.12 [-0.79; 0.55]	-0.12 [-0.79; 0.55]	.
Educ	Relax+CBT	0	.	.	.	-0.13 [-0.93; 0.68]	-0.13 [-0.93; 0.68]	.
Educ	Relax+CBT+Educ	0	.	.	.	-0.23 [-0.94; 0.47]	-0.23 [-0.94; 0.47]	.
Educ	Relax+CBT+Tailored	0	.	.	.	-0.29 [-1.17; 0.60]	-0.29 [-1.17; 0.60]	.
Educ	Relax+Educ	0	.	.	.	-0.02 [-0.69; 0.65]	-0.02 [-0.69; 0.65]	.
Educ	Relax+Educ+Other	0	.	.	.	0.33 [-0.46; 1.13]	0.33 [-0.46; 1.13]	.
Educ	Relax+Pharm+CBT+Tailored	0	.	.	.	1.50 [0.61; 2.38]	1.50 [0.61; 2.38]	.
Educ	TAU	0	.	.	.	-0.41 [-1.09; 0.27]	-0.41 [-1.09; 0.27]	.
Educ+MBSR	Hypno	0	.	.	.	-1.22 [-2.63; 0.18]	-1.22 [-2.63; 0.18]	.
Educ+MBSR	MBSR	0	.	.	.	-0.79 [-2.05; 0.46]	-0.79 [-2.05; 0.46]	.
Educ+MBSR	Minimal	0	.	.	.	-0.76 [-2.00; 0.48]	-0.76 [-2.00; 0.48]	.
Educ+MBSR	Pharm	0	.	.	.	-0.63 [-1.91; 0.65]	-0.63 [-1.91; 0.65]	.
Educ+MBSR	Relax	0	.	.	.	-0.93 [-2.14; 0.27]	-0.93 [-2.14; 0.27]	.
Educ+MBSR	Relax+CBT	0	.	.	.	-0.94 [-2.19; 0.31]	-0.94 [-2.19; 0.31]	.
Educ+MBSR	Relax+CBT+Educ	0	.	.	.	-1.04 [-2.21; 0.12]	-1.04 [-2.21; 0.12]	.
Educ+MBSR	Relax+CBT+Tailored	0	.	.	.	-1.10 [-2.44; 0.25]	-1.10 [-2.44; 0.25]	.
Educ+MBSR	Relax+Educ	0	.	.	.	-0.83 [-1.91; 0.25]	-0.83 [-1.91; 0.25]	.
Educ+MBSR	Relax+Educ+Other	0	.	.	.	-0.48 [-1.77; 0.81]	-0.48 [-1.77; 0.81]	.
Educ+MBSR	Relax+Pharm+CBT+Tailored	0	.	.	.	0.69 [-0.66; 2.03]	0.69 [-0.66; 2.03]	.
Educ+MBSR	TAU	0	.	.	.	-1.22 [-2.39; -0.06]	-1.22 [-2.39; -0.06]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Hypno	MBSR	0	.	.	.	0.43 [-0.55; 1.41]	0.43 [-0.55; 1.41]	.
Hypno	Minimal	0	.	.	.	0.46 [-0.57; 1.49]	0.46 [-0.57; 1.49]	.
Hypno	Pharm	0	.	.	.	0.59 [-0.38; 1.57]	0.59 [-0.38; 1.57]	.
Hypno	Relax	0	.	.	.	0.29 [-0.59; 1.17]	0.29 [-0.59; 1.17]	.
Hypno	Relax+CBT	0	.	.	.	0.29 [-0.62; 1.20]	0.29 [-0.62; 1.20]	.
Hypno	Relax+CBT+Educ	0	.	.	.	0.18 [-0.68; 1.03]	0.18 [-0.68; 1.03]	.
Hypno	Relax+CBT+Tailored	0	.	.	.	0.13 [-0.93; 1.18]	0.13 [-0.93; 1.18]	.
Hypno	Relax+Educ	0	.	.	.	0.39 [-0.51; 1.29]	0.39 [-0.51; 1.29]	.
Hypno	Relax+Educ+Other	0	.	.	.	0.75 [-0.37; 1.86]	0.75 [-0.37; 1.86]	.
Hypno	Relax+Pharm+CBT+Tailored	0	.	.	.	1.91 [0.85; 2.97]	1.91 [0.85; 2.97]	.
Hypno	TAU	1	40	.	0.00 [-0.78; 0.78]	.	0.00 [-0.78; 0.78]	.
MBSR	Minimal	0	.	.	.	0.03 [-0.62; 0.68]	0.03 [-0.62; 0.68]	.
MBSR	Pharm	0	.	.	.	0.16 [-0.50; 0.83]	0.16 [-0.50; 0.83]	.
MBSR	Relax	1	83	.	-0.09 [-0.79; 0.60]	-0.20 [-0.97; 0.58]	-0.14 [-0.66; 0.38]	0.8466
MBSR	Relax+CBT	0	.	.	.	-0.14 [-0.86; 0.57]	-0.14 [-0.86; 0.57]	.
MBSR	Relax+CBT+Educ	0	.	.	.	-0.25 [-0.87; 0.37]	-0.25 [-0.87; 0.37]	.
MBSR	Relax+CBT+Tailored	0	.	.	.	-0.30 [-1.07; 0.46]	-0.30 [-1.07; 0.46]	.
MBSR	Relax+Educ	0	.	.	.	-0.04 [-0.68; 0.60]	-0.04 [-0.68; 0.60]	.
MBSR	Relax+Educ+Other	0	.	.	.	0.32 [-0.53; 1.17]	0.32 [-0.53; 1.17]	.
MBSR	Relax+Pharm+CBT+Tailored	0	.	.	.	1.48 [0.71; 2.25]	1.48 [0.71; 2.25]	.
MBSR	TAU	0	.	.	.	-0.43 [-1.01; 0.15]	-0.43 [-1.01; 0.15]	.
Minimal	Pharm	0	.	.	.	0.14 [-0.67; 0.94]	0.14 [-0.67; 0.94]	.
Minimal	Relax	0	.	.	.	-0.17 [-0.86; 0.52]	-0.17 [-0.86; 0.52]	.
Minimal	Relax+CBT	0	.	.	.	-0.17 [-0.97; 0.63]	-0.17 [-0.97; 0.63]	.
Minimal	Relax+CBT+Educ	0	.	.	.	-0.28 [-0.97; 0.41]	-0.28 [-0.97; 0.41]	.
Minimal	Relax+CBT+Tailored	0	.	.	.	-0.33 [-1.23; 0.57]	-0.33 [-1.23; 0.57]	.
Minimal	Relax+Educ	1	51	.	0.13 [-0.59; 0.86]	-0.56 [-1.69; 0.57]	-0.07 [-0.68; 0.54]	0.3124
Minimal	Relax+Educ+Other	1	52	.	0.39 [-0.34; 1.11]	-1.04 [-3.70; 1.62]	0.29 [-0.41; 0.99]	0.3124

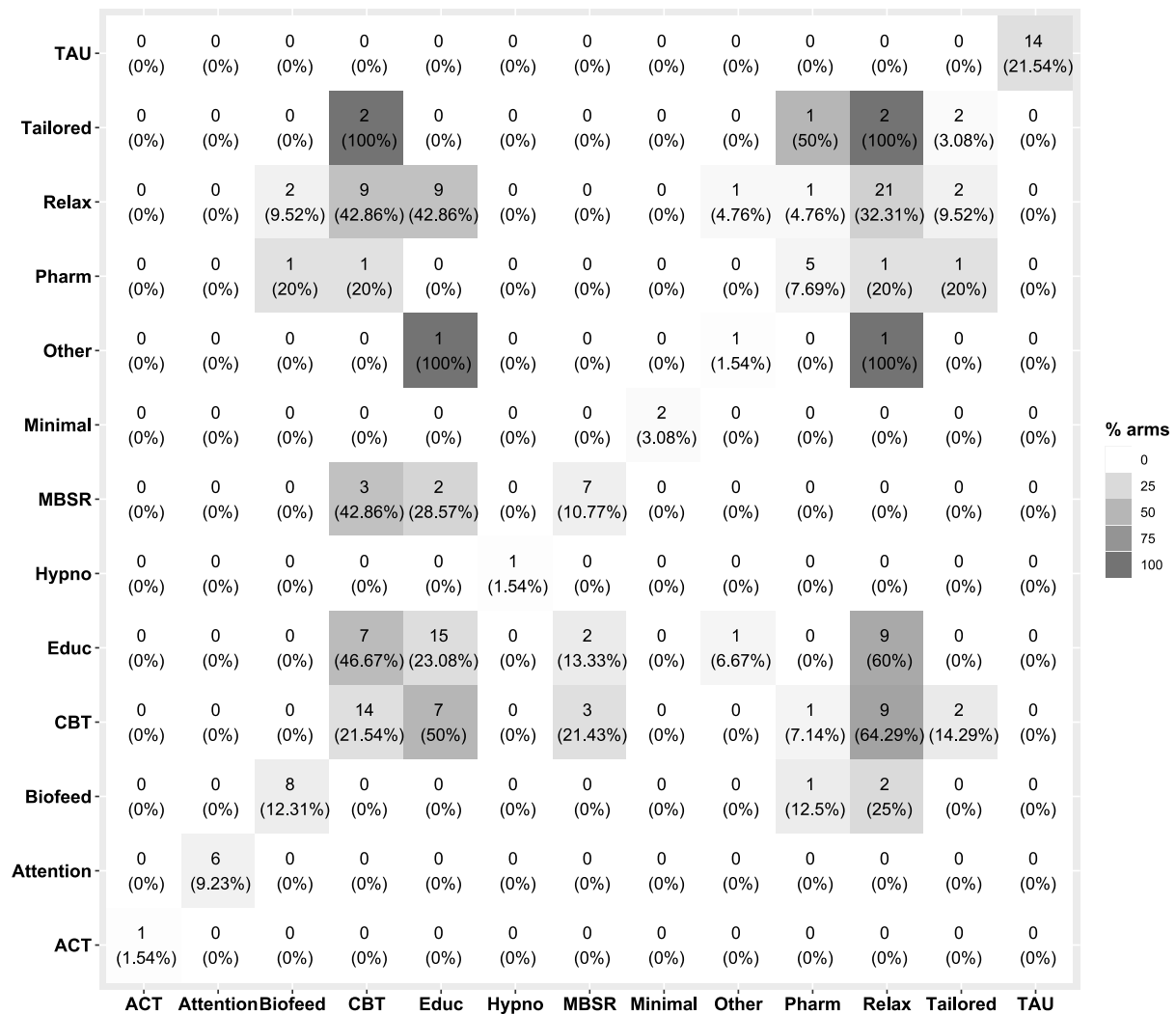
Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Minimal	Relax+Pharm+CBT+Tailored	0	.	.	.	1.45 [0.55; 2.35]	1.45 [0.55; 2.35]	.
Minimal	TAU	0	.	.	.	-0.46 [-1.13; 0.21]	-0.46 [-1.13; 0.21]	.
Pharm	Relax	1	61	.	-0.27 [-0.96; 0.42]	-0.34 [-1.08; 0.39]	-0.30 [-0.81; 0.20]	0.8867
Pharm	Relax+CBT	0	.	.	.	-0.31 [-1.01; 0.40]	-0.31 [-1.01; 0.40]	.
Pharm	Relax+CBT+Educ	0	.	.	.	-0.42 [-1.05; 0.22]	-0.42 [-1.05; 0.22]	.
Pharm	Relax+CBT+Tailored	1	108	.	-0.51 [-1.12; 0.10]	-0.08 [-1.93; 1.77]	-0.47 [-1.05; 0.11]	0.6629
Pharm	Relax+Educ	0	.	.	.	-0.20 [-0.89; 0.49]	-0.20 [-0.89; 0.49]	.
Pharm	Relax+Educ+Other	0	.	.	.	0.15 [-0.78; 1.09]	0.15 [-0.78; 1.09]	.
Pharm	Relax+Pharm+CBT+Tailored	1	122	.	1.27 [0.67; 1.88]	1.72 [-0.20; 3.64]	1.32 [0.74; 1.89]	0.6629
Pharm	TAU	0	.	.	.	-0.59 [-1.18; -0.01]	-0.59 [-1.18; -0.01]	.
Relax	Relax+CBT	0	.	.	.	-0.00 [-0.59; 0.58]	-0.00 [-0.59; 0.58]	.
Relax	Relax+CBT+Educ	1	75	.	-0.19 [-0.85; 0.47]	-0.04 [-0.68; 0.61]	-0.11 [-0.57; 0.35]	0.7415
Relax	Relax+CBT+Tailored	0	.	.	.	-0.16 [-0.83; 0.50]	-0.16 [-0.83; 0.50]	.
Relax	Relax+Educ	0	.	.	.	0.10 [-0.44; 0.64]	0.10 [-0.44; 0.64]	.
Relax	Relax+Educ+Other	0	.	.	.	0.46 [-0.38; 1.29]	0.46 [-0.38; 1.29]	.
Relax	Relax+Pharm+CBT+Tailored	0	.	.	.	1.62 [0.95; 2.29]	1.62 [0.95; 2.29]	.
Relax	TAU	2	112	0.0%	-0.35 [-0.85; 0.16]	-0.20 [-0.86; 0.46]	-0.29 [-0.69; 0.11]	0.7267
Relax+CBT	Relax+CBT+Educ	0	.	.	.	-0.11 [-0.68; 0.46]	-0.11 [-0.68; 0.46]	.
Relax+CBT	Relax+CBT+Tailored	0	.	.	.	-0.16 [-0.97; 0.65]	-0.16 [-0.97; 0.65]	.
Relax+CBT	Relax+Educ	0	.	.	.	0.10 [-0.53; 0.74]	0.10 [-0.53; 0.74]	.
Relax+CBT	Relax+Educ+Other	0	.	.	.	0.46 [-0.45; 1.37]	0.46 [-0.45; 1.37]	.
Relax+CBT	Relax+Pharm+CBT+Tailored	0	.	.	.	1.62 [0.81; 2.44]	1.62 [0.81; 2.44]	.
Relax+CBT	TAU	2	100	56.8%	-0.39 [-0.92; 0.13]	0.09 [-0.91; 1.08]	-0.29 [-0.75; 0.18]	0.4024
Relax+CBT+Educ	Relax+CBT+Tailored	0	.	.	.	-0.05 [-0.81; 0.70]	-0.05 [-0.81; 0.70]	.
Relax+CBT+Educ	Relax+Educ	1	115	.	0.19 [-0.41; 0.79]	0.23 [-0.42; 0.89]	0.21 [-0.23; 0.65]	0.9317
Relax+CBT+Educ	Relax+Educ+Other	0	.	.	.	0.57 [-0.24; 1.37]	0.57 [-0.24; 1.37]	.
Relax+CBT+Educ	Relax+Pharm+CBT+Tailored	0	.	.	.	1.73 [0.97; 2.49]	1.73 [0.97; 2.49]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Relax+CBT+Educ	TAU	3	372	42.1%	-0.20 [-0.59; 0.19]	-0.10 [-0.84; 0.64]	-0.18 [-0.52; 0.16]	0.8146
Relax+CBT+Tailored	Relax+Educ	0	.	.	.	0.26 [-0.54; 1.06]	0.26 [-0.54; 1.06]	.
Relax+CBT+Tailored	Relax+Educ+Other	0	.	.	.	0.62 [-0.40; 1.64]	0.62 [-0.40; 1.64]	.
Relax+CBT+Tailored	Relax+Pharm+CBT+Tailored	1	124	.	1.78 [1.17; 2.40]	.	1.78 [1.17; 2.40]	.
Relax+CBT+Tailored	TAU	0	.	.	.	-0.13 [-0.84; 0.58]	-0.13 [-0.84; 0.58]	.
Relax+Educ	Relax+Educ+Other	1	49	.	0.25 [-0.48; 0.99]	1.63 [-0.94; 4.20]	0.36 [-0.35; 1.06]	0.3124
Relax+Educ	Relax+Pharm+CBT+Tailored	0	.	.	.	1.52 [0.72; 2.32]	1.52 [0.72; 2.32]	.
Relax+Educ	TAU	1	108	.	-0.27 [-0.88; 0.34]	-0.52 [-1.15; 0.11]	-0.39 [-0.83; 0.05]	0.5673
Relax+Educ+Other	Relax+Pharm+CBT+Tailored	0	.	.	.	1.16 [0.14; 2.18]	1.16 [0.14; 2.18]	.
Relax+Educ+Other	TAU	0	.	.	.	-0.75 [-1.54; 0.05]	-0.75 [-1.54; 0.05]	.
Relax+Pharm+CBT+Tailored	TAU	0	.	.	.	-1.91 [-2.62; -1.20]	-1.91 [-2.62; -1.20]	.

Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; CI=confidence interval; Educ=education; Hypno=hypnotherapy; k=number of studies; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; n=number of participants; Pharm=pharmacologic; Relax=relaxation therapy; SMD=standardized mean difference; TAU=treatment-as-usual

The 18 behavioral interventions comprise eight behavioral components. The most common components were relaxation and education, which were used in 32% and 23% of study arms, respectively (Figure G-4). CBT was only evaluated in combination interventions, while hypnotherapy and ACT were only evaluated alone (Figure G-5).

Figure G-4. Components cross-table, adults, migraine/headache frequency

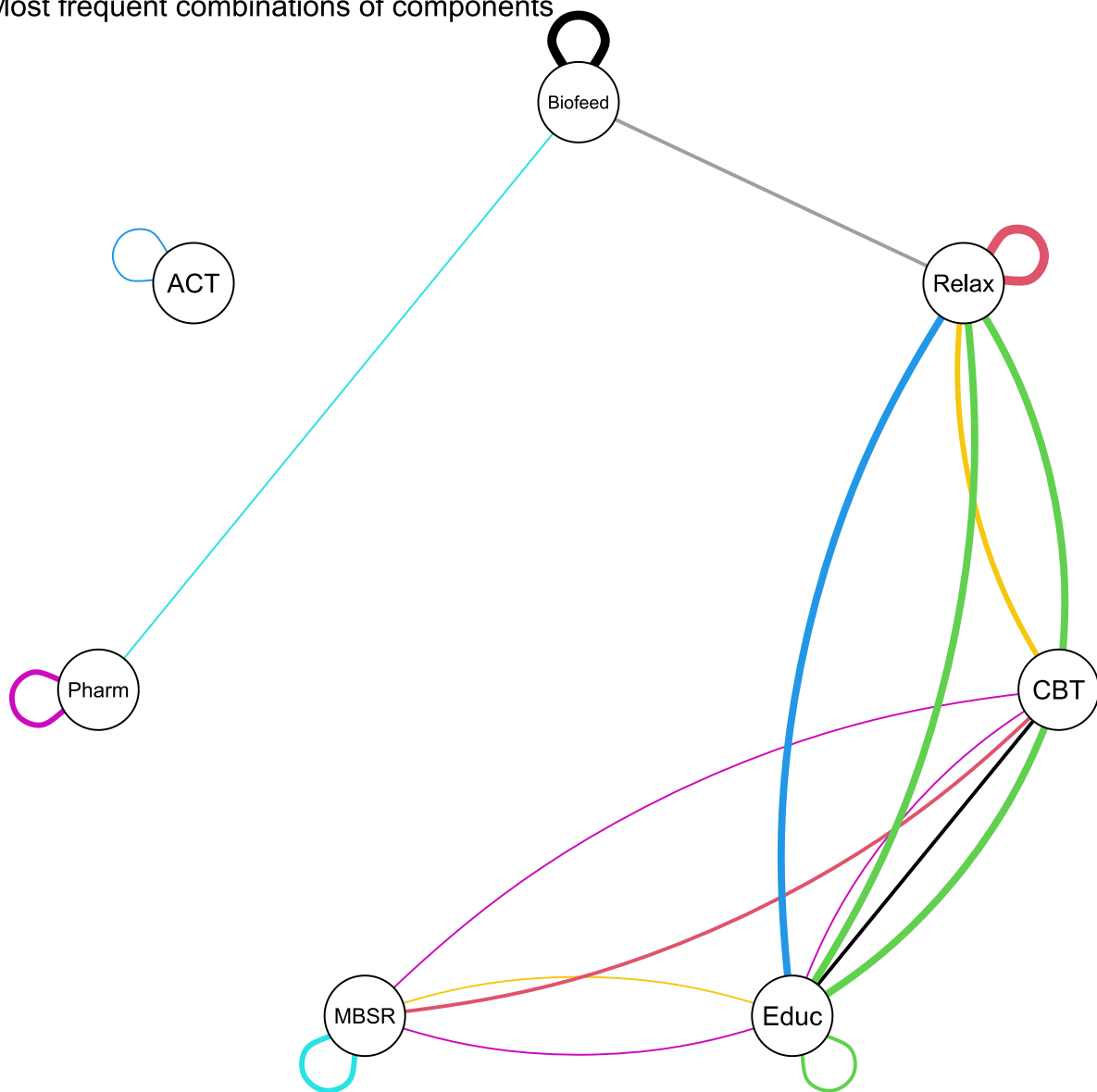


Total number of study arms: 65

Components cross-table visualizing the number of arms that include a component or any pair of two components for migraine frequency in adults. Parentheses in the diagonal elements denote the proportions of study arms that include the component, while in the non-diagonal elements denote the proportion of study arms that include the corresponding pair of components out of those study arms that include the component in the corresponding row. The intensity of the color is proportional to the relative frequency of the corresponding component (combination). Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy; TAU=treatment-as-usual

Figure G-5. Components network graph, adults, migraine/headache frequency

Most frequent combinations of components



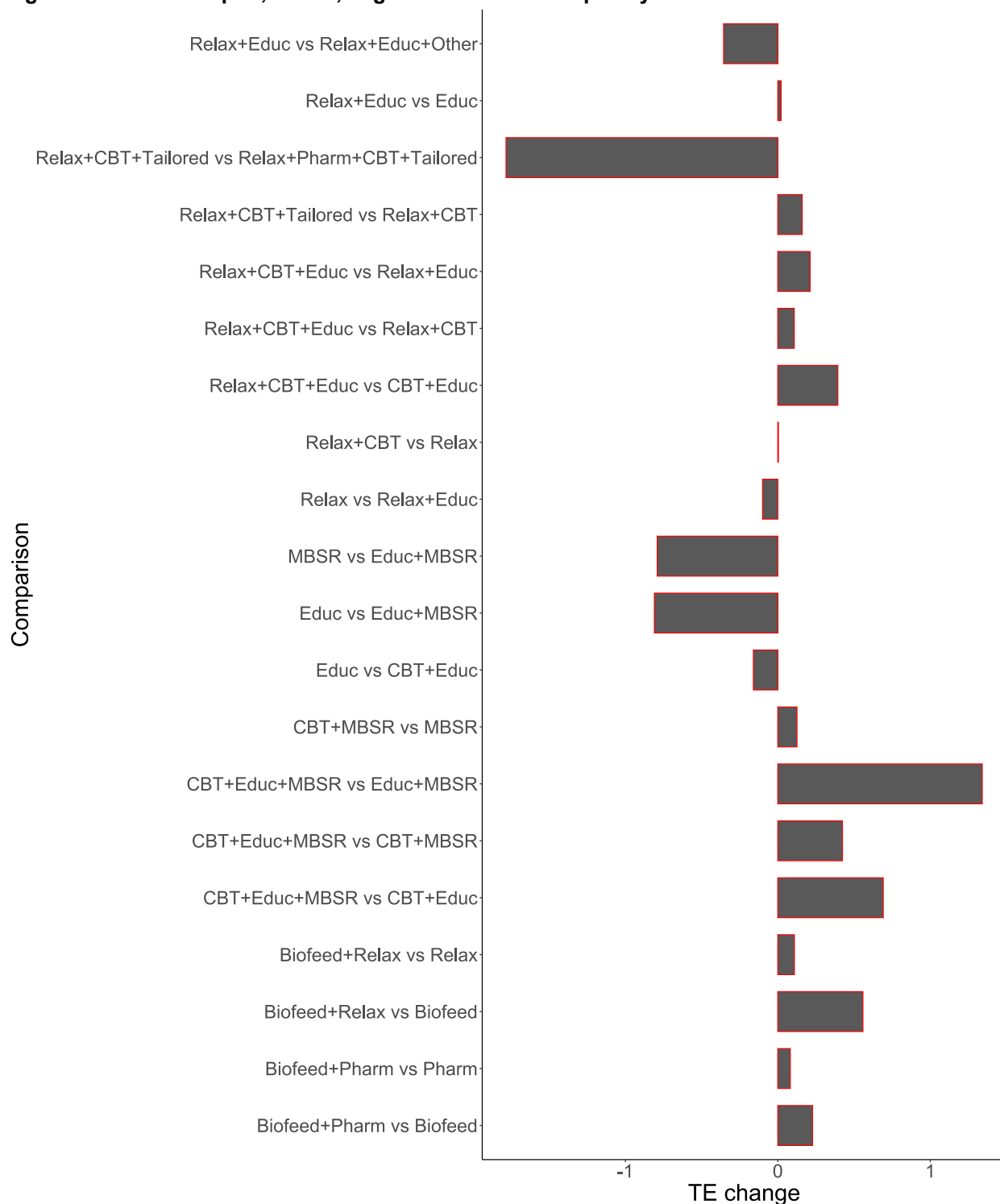
Components network graph for migraine frequency in adults. Thickness of the line is proportional to the number of arms containing the corresponding component combination while colors refer to different interventions. Loops from and to the same component indicate arms where the component was evaluated alone. Abbreviations: ACT=acceptance and commitment therapy; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; MBSR=mindfulness-based stress reduction; Pharm=pharmacologic; Relax=relaxation therapy

To evaluate the impact of individual behavioral components on migraine frequency, we attempted to fit a component NMA model assuming the effects of the individual components were additive; however, the test for additivity indicated that an additive model was not a good fit for the data (standard NMA model: $Q = 25.05$, degrees of freedom [df] = 14; additive model: $Q = 63.24$, df = 23; difference: $Q = 38.20$, $p < 0.0001$).

We also employed an alternative approach using visualizations of the standard NMA results to evaluate the importance of individual components. The waterfall plot shows the differences in estimated effects between interventions which are identical except for the presence or absence of a particular component (Figure G-6). The components heat plot shows the median effect of interventions in the network containing a particular component, as well as the median effect of different pairs of component combinations (Figure G-7). The violin plot shows the range of effects for all interventions containing a particular component (Figure G-8). All presented effects are relative to TAU.

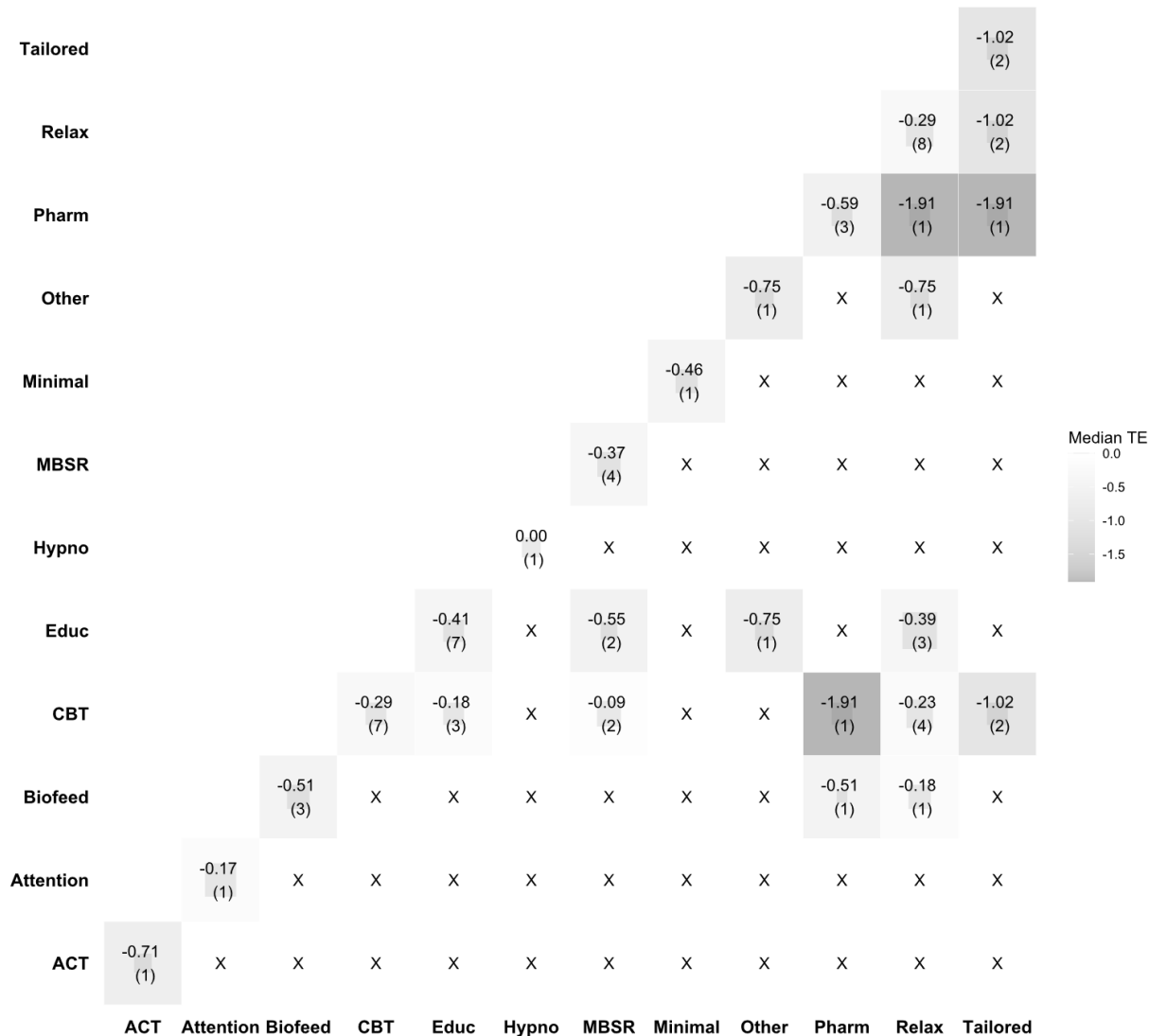
Despite biofeedback having a large effect on its own, when added to other interventions (pharmacological and relaxation), it appears to have a minimal impact on the effect of those interventions (Figure G-6). When relaxation training is added to education, it appears to have a minimal effect, while when added to biofeedback or CBT + education, the effectiveness decreases. The discrepancies in these effects likely contributed to the violation of the additivity assumption in the components NMA model. It is also notable that two behavioral components, CBT and relaxation training, that appear in the most effective intervention, relaxation training + pharmacologic + CBT + tailored, have much smaller effects outside of that particular combination, suggesting that these components are not particularly effective on their own or in most combinations (Figure G-7, Figure G-8).

Figure G-6. Waterfall plot, adults, migraine/headache frequency



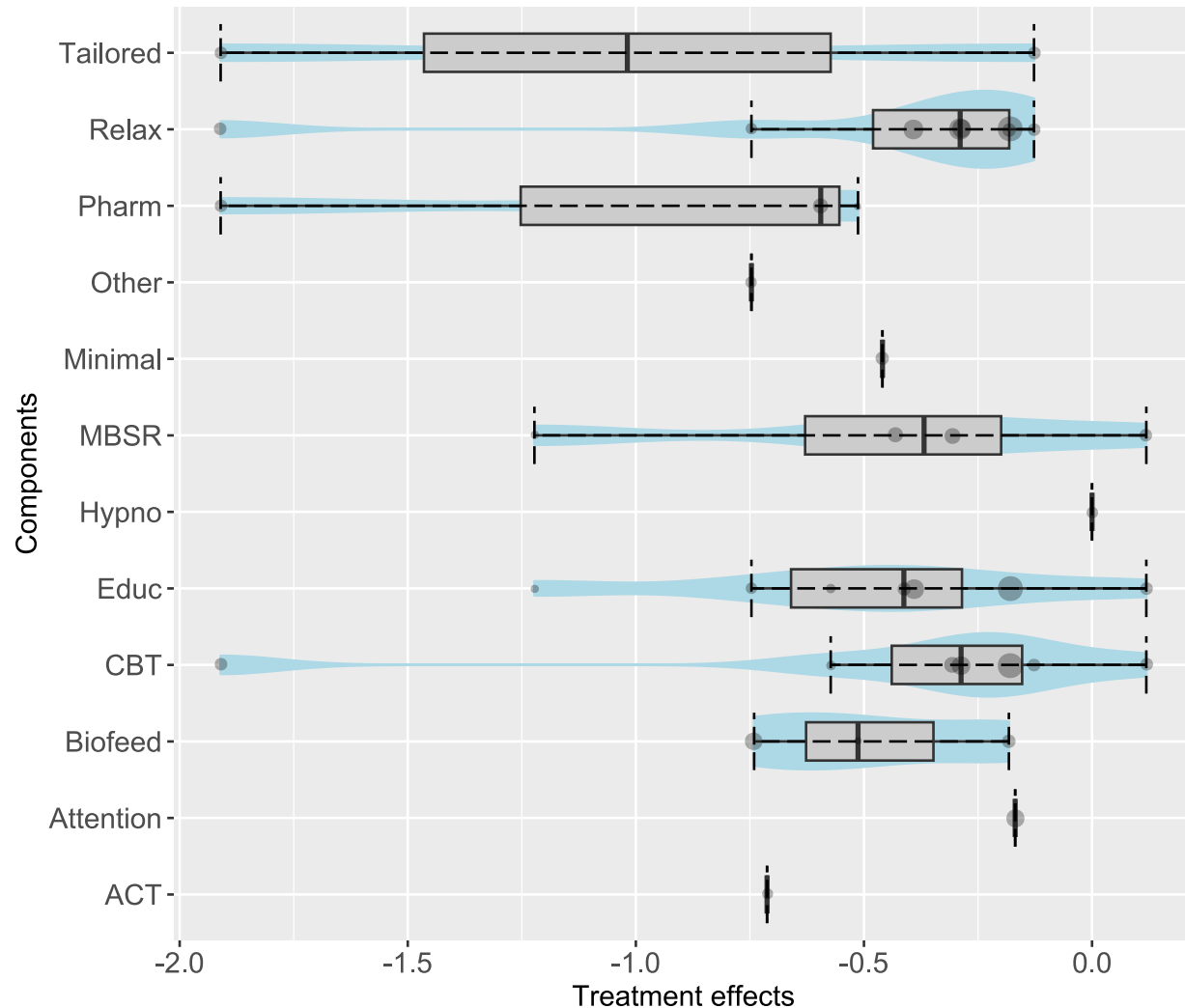
Waterfall plot for migraine frequency in adults showing the comparisons that differ by a single component using network meta-analysis effects relative to treatment-as-usual. Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy; TE=treatment effect

Figure G-7. Components heat plot, adults, migraine/headache frequency



Components heat plot for migraine frequency in adults. Each cell refers to a combination of components and presents the median network meta-analysis effects of interventions that include that combination of components relative to treatment-as-usual. Gray boxes are proportional to the estimates' precision. Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy; TE=treatment effect

Figure G-8. Violin plot, adults, migraine/headache frequency



Violin plots displaying the distribution of effects of the components used for migraine frequency in adults, using network meta-analysis effects relative to treatment-as-usual. Dots are proportional to the precision of the relative effect estimates.

Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; Pharm=pharmacologic; Relax=relaxation therapy

Network Meta-Analysis, Adults, Migraine Disability

After excluding the disconnected smaller networks, the network of studies evaluating behavioral interventions in adults for migraine disability included 17 studies (1818 patients). There are 14 distinct interventions, of which 12 included at least one behavioral component and two were controls (attention control or TAU) (Figure G-9). The most common comparator was TAU, which was used as the reference treatment for the analysis.

We first evaluated the effect of all interventions on migraine disability using the standard NMA approach. Two behavioral interventions displayed statistically significant improvements compared to TAU: hypnotherapy alone and relaxation training + CBT + education + other (Figure G-10, Table G-2). Note that “other” refers to a non-behavioral and non-pharmacological active component (such as exercise). Hypnotherapy also significantly improved disability over all other interventions except for CBT + education+MBSR, education + ACT, and relaxation training + CBT + education + other. Beyond TAU, relaxation training + CBT + education + other significantly improved disability measures over ACT, relaxation training + education, biofeedback + relaxation training + CBT + education, relaxation training + CBT + education, and biofeedback.

To assess incoherence, we used the node-splitting and design-by-treatment interaction approaches. Neither approach provided clear evidence of incoherence in the network (node-splitting: p-values ranged from 0.312 to 0.523 (Table G-2); design-by-treatment interaction: p-value = 0.651).

Figure G-9. Detailed network graph of evidence base for adults, migraine disability

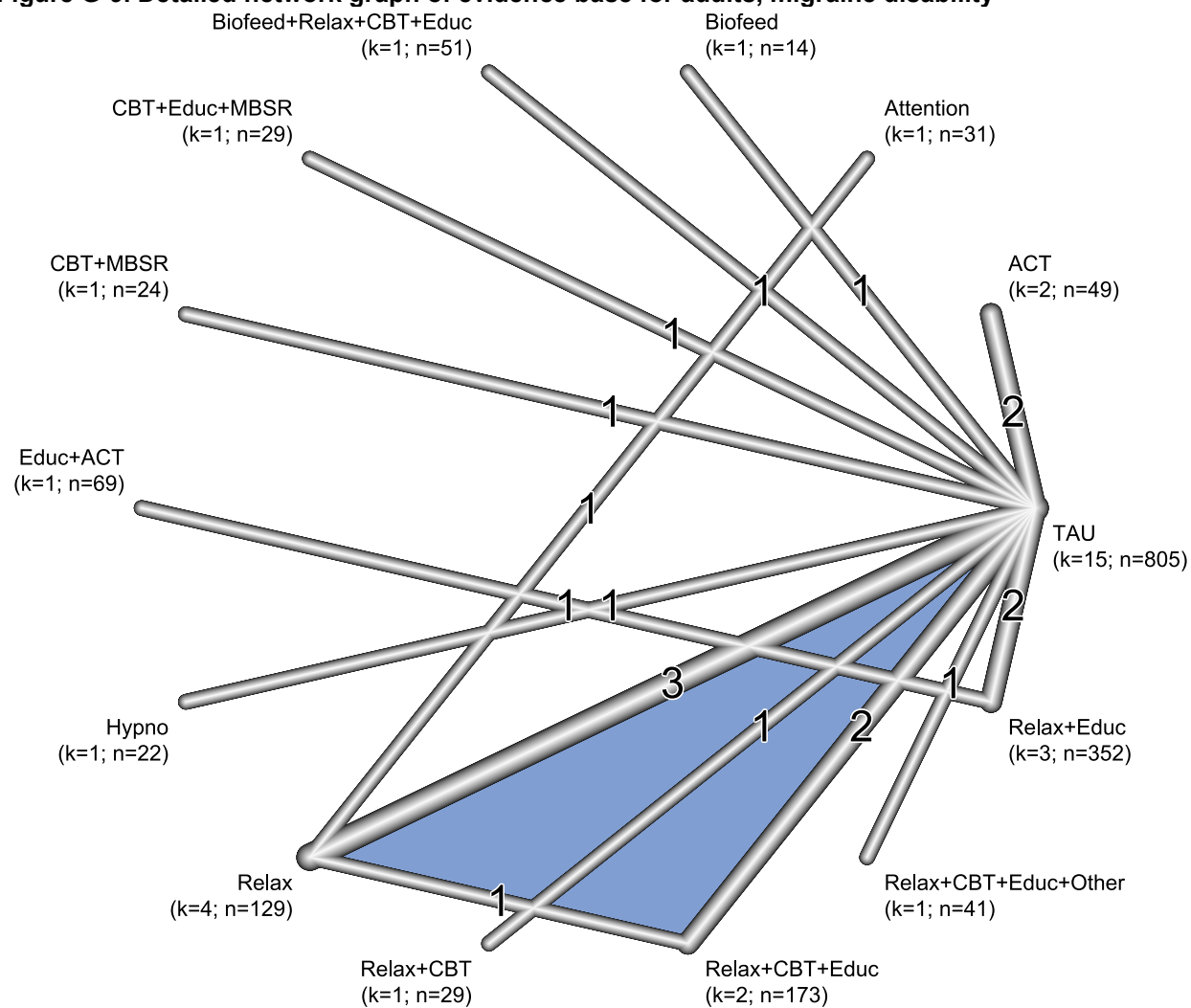
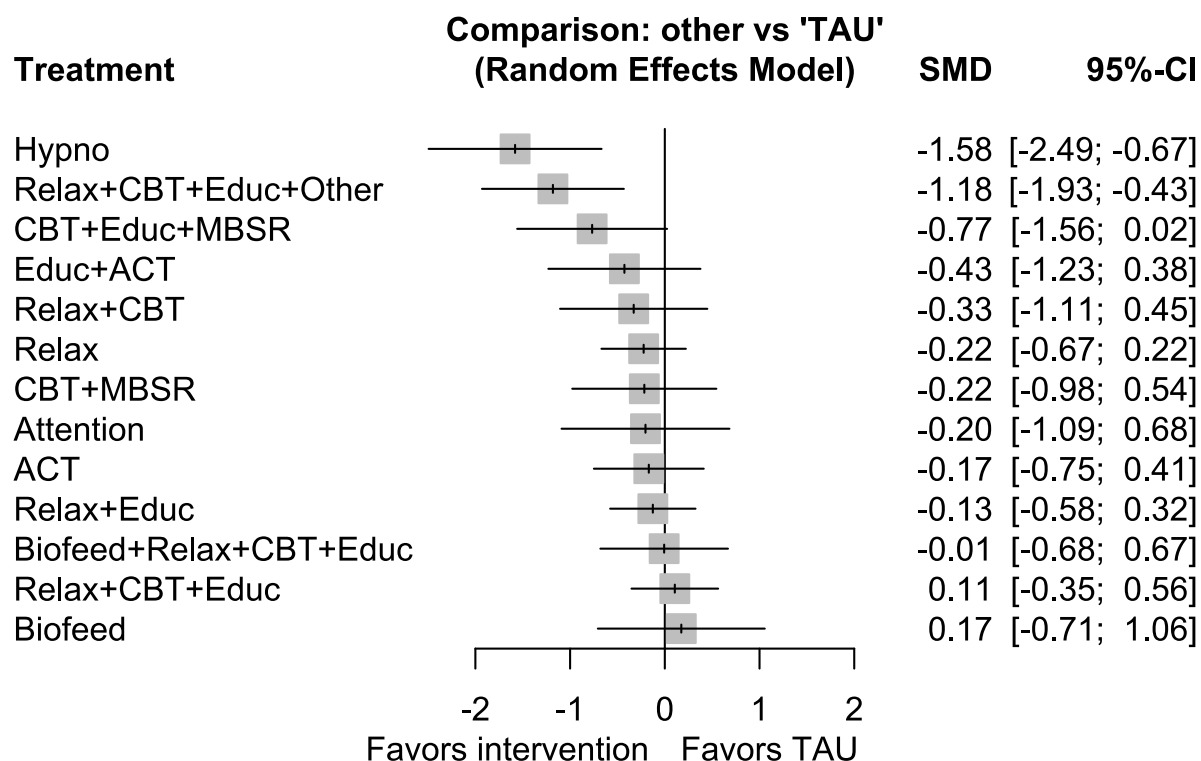


Figure G-10. Forest plot of network results for all interventions compared to TAU, adults, migraine disability



Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; CI=confidence interval; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Relax=relaxation therapy; SMD=standardized mean difference; TAU=treatment-as-usual

Table G-2. Direct, indirect, and network estimates for adults, migraine disability

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
ACT	Attention	0	.	.	.	0.04 [-1.02; 1.09]	0.04 [-1.02; 1.09]	.
ACT	Biofeed	0	.	.	.	-0.34 [-1.40; 0.71]	-0.34 [-1.40; 0.71]	.
ACT	Biofeed+Relax+CBT+Educ	0	.	.	.	-0.16 [-1.05; 0.73]	-0.16 [-1.05; 0.73]	.
ACT	CBT+Educ+MBSR	0	.	.	.	0.60 [-0.38; 1.58]	0.60 [-0.38; 1.58]	.
ACT	CBT+MBSR	0	.	.	.	0.05 [-0.91; 1.00]	0.05 [-0.91; 1.00]	.
ACT	Educ+ACT	0	.	.	.	0.26 [-0.73; 1.25]	0.26 [-0.73; 1.25]	.
ACT	Hypno	0	.	.	.	1.41 [0.33; 2.49]	1.41 [0.33; 2.49]	.
ACT	Relax	0	.	.	.	0.05 [-0.68; 0.79]	0.05 [-0.68; 0.79]	.
ACT	Relax+CBT	0	.	.	.	0.16 [-0.81; 1.13]	0.16 [-0.81; 1.13]	.
ACT	Relax+CBT+Educ	0	.	.	.	-0.27 [-1.01; 0.46]	-0.27 [-1.01; 0.46]	.
ACT	Relax+CBT+Educ+Other	0	.	.	.	1.01 [0.07; 1.96]	1.01 [0.07; 1.96]	.
ACT	Relax+Educ	0	.	.	.	-0.04 [-0.78; 0.69]	-0.04 [-0.78; 0.69]	.
ACT	TAU	2	96	86.0%	-0.17 [-0.75; 0.41]	.	-0.17 [-0.75; 0.41]	.
Attention	Biofeed	0	.	.	.	-0.38 [-1.63; 0.87]	-0.38 [-1.63; 0.87]	.
Attention	Biofeed+Relax+CBT+Educ	0	.	.	.	-0.20 [-1.31; 0.92]	-0.20 [-1.31; 0.92]	.
Attention	CBT+Educ+MBSR	0	.	.	.	0.56 [-0.63; 1.75]	0.56 [-0.63; 1.75]	.
Attention	CBT+MBSR	0	.	.	.	0.01 [-1.16; 1.18]	0.01 [-1.16; 1.18]	.
Attention	Educ+ACT	0	.	.	.	0.22 [-0.97; 1.42]	0.22 [-0.97; 1.42]	.
Attention	Hypno	0	.	.	.	1.38 [0.10; 2.65]	1.38 [0.10; 2.65]	.
Attention	Relax	1	59	.	0.02 [-0.75; 0.79]	.	0.02 [-0.75; 0.79]	.
Attention	Relax+CBT	0	.	.	.	0.12 [-1.05; 1.30]	0.12 [-1.05; 1.30]	.
Attention	Relax+CBT+Educ	0	.	.	.	-0.31 [-1.26; 0.64]	-0.31 [-1.26; 0.64]	.
Attention	Relax+CBT+Educ+Other	0	.	.	.	0.98 [-0.18; 2.14]	0.98 [-0.18; 2.14]	.
Attention	Relax+Educ	0	.	.	.	-0.08 [-1.07; 0.92]	-0.08 [-1.07; 0.92]	.
Attention	TAU	0	.	.	.	-0.20 [-1.09; 0.68]	-0.20 [-1.09; 0.68]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Biofeed	Biofeed+Relax+CBT+Educ	0	.	.	.	0.18 [-0.93; 1.29]	0.18 [-0.93; 1.29]	.
Biofeed	CBT+Educ+MBSR	0	.	.	.	0.94 [-0.24; 2.13]	0.94 [-0.24; 2.13]	.
Biofeed	CBT+MBSR	0	.	.	.	0.39 [-0.77; 1.55]	0.39 [-0.77; 1.55]	.
Biofeed	Educ+ACT	0	.	.	.	0.60 [-0.59; 1.79]	0.60 [-0.59; 1.79]	.
Biofeed	Hypno	0	.	.	.	1.75 [0.49; 3.02]	1.75 [0.49; 3.02]	.
Biofeed	Relax	0	.	.	.	0.40 [-0.59; 1.39]	0.40 [-0.59; 1.39]	.
Biofeed	Relax+CBT	0	.	.	.	0.50 [-0.67; 1.68]	0.50 [-0.67; 1.68]	.
Biofeed	Relax+CBT+Educ	0	.	.	.	0.07 [-0.92; 1.06]	0.07 [-0.92; 1.06]	.
Biofeed	Relax+CBT+Educ+Other	0	.	.	.	1.36 [0.20; 2.51]	1.36 [0.20; 2.51]	.
Biofeed	Relax+Educ	0	.	.	.	0.30 [-0.69; 1.29]	0.30 [-0.69; 1.29]	.
Biofeed	TAU	1	36	.	0.17 [-0.71; 1.06]	.	0.17 [-0.71; 1.06]	.
Biofeed+Relax+CBT+Educ	CBT+Educ+MBSR	0	.	.	.	0.76 [-0.28; 1.80]	0.76 [-0.28; 1.80]	.
Biofeed+Relax+CBT+Educ	CBT+MBSR	0	.	.	.	0.21 [-0.81; 1.23]	0.21 [-0.81; 1.23]	.
Biofeed+Relax+CBT+Educ	Educ+ACT	0	.	.	.	0.42 [-0.63; 1.47]	0.42 [-0.63; 1.47]	.
Biofeed+Relax+CBT+Educ	Hypno	0	.	.	.	1.57 [0.44; 2.71]	1.57 [0.44; 2.71]	.
Biofeed+Relax+CBT+Educ	Relax	0	.	.	.	0.22 [-0.59; 1.02]	0.22 [-0.59; 1.02]	.
Biofeed+Relax+CBT+Educ	Relax+CBT	0	.	.	.	0.32 [-0.71; 1.35]	0.32 [-0.71; 1.35]	.
Biofeed+Relax+CBT+Educ	Relax+CBT+Educ	0	.	.	.	-0.11 [-0.93; 0.70]	-0.11 [-0.93; 0.70]	.
Biofeed+Relax+CBT+Educ	Relax+CBT+Educ+Other	0	.	.	.	1.17 [0.17; 2.18]	1.17 [0.17; 2.18]	.
Biofeed+Relax+CBT+Educ	Relax+Educ	0	.	.	.	0.12 [-0.69; 0.93]	0.12 [-0.69; 0.93]	.
Biofeed+Relax+CBT+Educ	TAU	1	124	.	-0.01 [-0.68; 0.67]	.	-0.01 [-0.68; 0.67]	.
CBT+Educ+MBSR	CBT+MBSR	0	.	.	.	-0.55 [-1.65; 0.55]	-0.55 [-1.65; 0.55]	.
CBT+Educ+MBSR	Educ+ACT	0	.	.	.	-0.34 [-1.47; 0.79]	-0.34 [-1.47; 0.79]	.

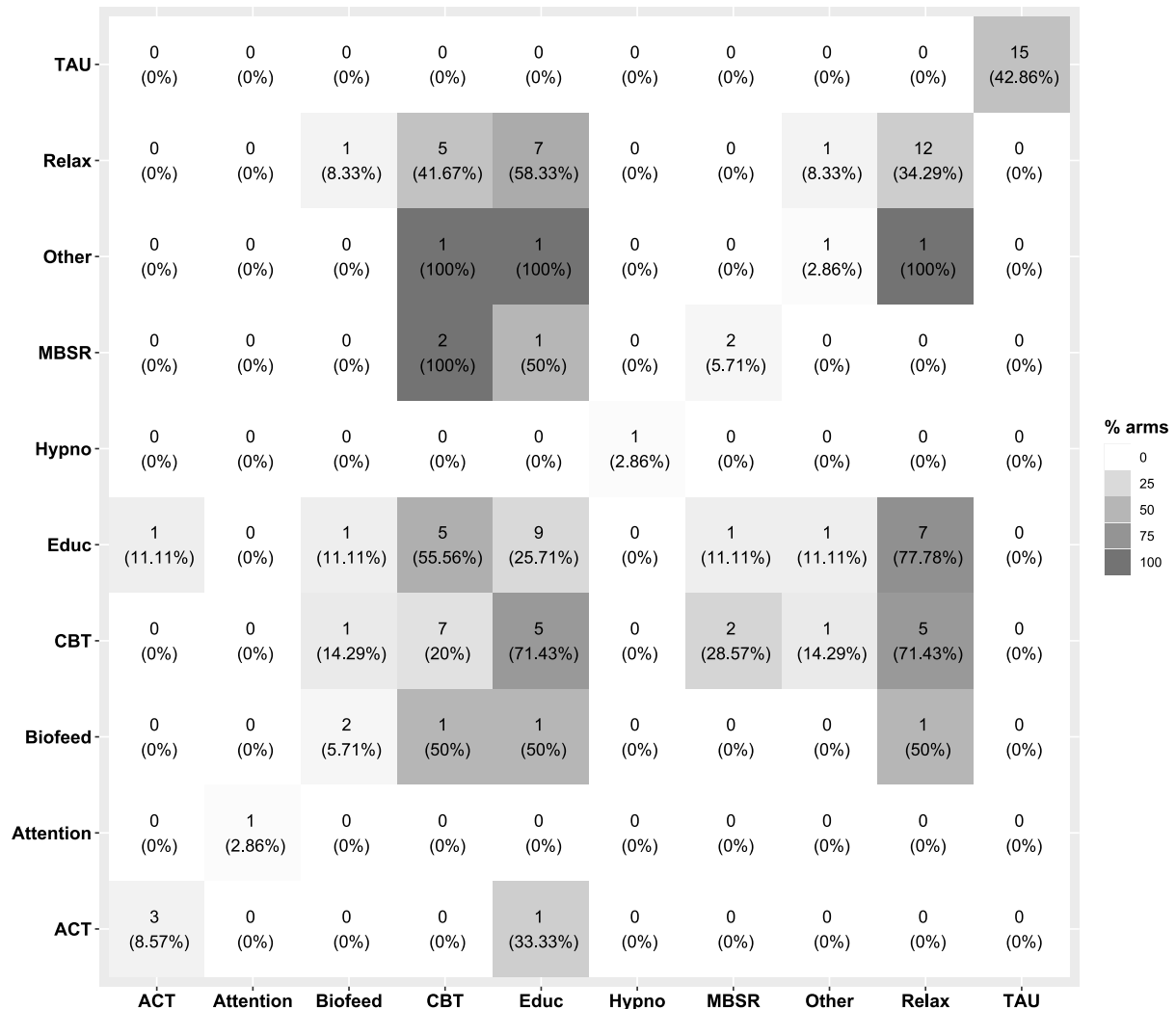
Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
CBT+Educ+MBSR	Hypno	0	.	.	.	0.81 [-0.39; 2.02]	0.81 [-0.39; 2.02]	.
CBT+Educ+MBSR	Relax	0	.	.	.	-0.54 [-1.45; 0.36]	-0.54 [-1.45; 0.36]	.
CBT+Educ+MBSR	Relax+CBT	0	.	.	.	-0.44 [-1.55; 0.67]	-0.44 [-1.55; 0.67]	.
CBT+Educ+MBSR	Relax+CBT+Educ	0	.	.	.	-0.87 [-1.79; 0.04]	-0.87 [-1.79; 0.04]	.
CBT+Educ+MBSR	Relax+CBT+Educ+Other	0	.	.	.	0.41 [-0.68; 1.50]	0.41 [-0.68; 1.50]	.
CBT+Educ+MBSR	Relax+Educ	0	.	.	.	-0.64 [-1.55; 0.27]	-0.64 [-1.55; 0.27]	.
CBT+Educ+MBSR	TAU	1	55	.	-0.77 [-1.56; 0.02]	.	-0.77 [-1.56; 0.02]	.
CBT+MBSR	Educ+ACT	0	.	.	.	0.21 [-0.90; 1.32]	0.21 [-0.90; 1.32]	.
CBT+MBSR	Hypno	0	.	.	.	1.36 [0.18; 2.55]	1.36 [0.18; 2.55]	.
CBT+MBSR	Relax	0	.	.	.	0.01 [-0.87; 0.89]	0.01 [-0.87; 0.89]	.
CBT+MBSR	Relax+CBT	0	.	.	.	0.11 [-0.98; 1.20]	0.11 [-0.98; 1.20]	.
CBT+MBSR	Relax+CBT+Educ	0	.	.	.	-0.32 [-1.21; 0.57]	-0.32 [-1.21; 0.57]	.
CBT+MBSR	Relax+CBT+Educ+Other	0	.	.	.	0.96 [-0.10; 2.03]	0.96 [-0.10; 2.03]	.
CBT+MBSR	Relax+Educ	0	.	.	.	-0.09 [-0.97; 0.79]	-0.09 [-0.97; 0.79]	.
CBT+MBSR	TAU	1	48	.	-0.22 [-0.98; 0.54]	.	-0.22 [-0.98; 0.54]	.
Educ+ACT	Hypno	0	.	.	.	1.15 [-0.06; 2.37]	1.15 [-0.06; 2.37]	.
Educ+ACT	Relax	0	.	.	.	-0.20 [-1.12; 0.72]	-0.20 [-1.12; 0.72]	.
Educ+ACT	Relax+CBT	0	.	.	.	-0.10 [-1.22; 1.02]	-0.10 [-1.22; 1.02]	.
Educ+ACT	Relax+CBT+Educ	0	.	.	.	-0.53 [-1.46; 0.39]	-0.53 [-1.46; 0.39]	.
Educ+ACT	Relax+CBT+Educ+Other	0	.	.	.	0.75 [-0.34; 1.85]	0.75 [-0.34; 1.85]	.
Educ+ACT	Relax+Educ	1	134	.	-0.30 [-0.96; 0.36]	.	-0.30 [-0.96; 0.36]	.
Educ+ACT	TAU	0	.	.	.	-0.43 [-1.23; 0.38]	-0.43 [-1.23; 0.38]	.
Hypno	Relax	0	.	.	.	-1.36 [-2.37; -0.34]	-1.36 [-2.37; -0.34]	.
Hypno	Relax+CBT	0	.	.	.	-1.25 [-2.45; -0.05]	-1.25 [-2.45; -0.05]	.

Intervention	Comparator	k	n	I ²	Direct Estimate	Indirect Estimate	Network Meta-Analysis	Incoherence P-Value
Hypno	Relax+CBT+Educ	0	.	.	.	-1.69 [-2.71; -0.67]	-1.69 [-2.71; -0.67]	.
Hypno	Relax+CBT+Educ+Other	0	.	.	.	-0.40 [-1.58; 0.78]	-0.40 [-1.58; 0.78]	.
Hypno	Relax+Educ	0	.	.	.	-1.45 [-2.47; -0.44]	-1.45 [-2.47; -0.44]	.
Hypno	TAU	1	40	.	-1.58 [-2.49; -0.67]	.	-1.58 [-2.49; -0.67]	.
Relax	Relax+CBT	0	.	.	.	0.11 [-0.79; 1.00]	0.11 [-0.79; 1.00]	.
Relax	Relax+CBT+Educ	1	75	.	-0.58 [-1.31; 0.16]	0.00 [-0.85; 0.86]	-0.33 [-0.89; 0.23]	0.3121
Relax	Relax+CBT+Educ+Other	0	.	.	.	0.96 [0.09; 1.83]	0.96 [0.09; 1.83]	.
Relax	Relax+Educ	0	.	.	.	-0.10 [-0.73; 0.54]	-0.10 [-0.73; 0.54]	.
Relax	TAU	3	253	50.5%	-0.18 [-0.65; 0.28]	-0.77 [-2.49; 0.96]	-0.22 [-0.67; 0.22]	0.5234
Relax+CBT	Relax+CBT+Educ	0	.	.	.	-0.43 [-1.34; 0.47]	-0.43 [-1.34; 0.47]	.
Relax+CBT	Relax+CBT+Educ+Other	0	.	.	.	0.85 [-0.23; 1.93]	0.85 [-0.23; 1.93]	.
Relax+CBT	Relax+Educ	0	.	.	.	-0.20 [-1.10; 0.70]	-0.20 [-1.10; 0.70]	.
Relax+CBT	TAU	1	56	.	-0.33 [-1.11; 0.45]	.	-0.33 [-1.11; 0.45]	.
Relax+CBT+Educ	Relax+CBT+Educ+Other	0	.	.	.	1.29 [0.41; 2.16]	1.29 [0.41; 2.16]	.
Relax+CBT+Educ	Relax+Educ	0	.	.	.	0.23 [-0.41; 0.87]	0.23 [-0.41; 0.87]	.
Relax+CBT+Educ	TAU	2	352	0.0%	0.04 [-0.44; 0.52]	0.94 [-0.76; 2.63]	0.11 [-0.35; 0.56]	0.3175
Relax+CBT+Educ+Other	Relax+Educ	0	.	.	.	-1.05 [-1.93; -0.18]	-1.05 [-1.93; -0.18]	.
Relax+CBT+Educ+Other	TAU	1	77	.	-1.18 [-1.93; -0.43]	.	-1.18 [-1.93; -0.43]	.
Relax+Educ	TAU	2	580	36.9%	-0.13 [-0.58; 0.32]	.	-0.13 [-0.58; 0.32]	.

Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; CI=confidence interval; Educ=education; Hypno=hypnotherapy; k=number of studies; MBSR=mindfulness-based stress reduction; n=number of participants; Relax=relaxation therapy; SMD=standardized mean difference; TAU=treatment-as-usual

The 12 behavioral interventions comprise seven behavioral components. The most common components were relaxation and education, which were used in 34% and 26% of study arms, respectively (Figure G-11). CBT, MBSR, and education were only evaluated in combination interventions, while hypnotherapy was only evaluated alone (Figure G-12).

Figure G-11. Components cross-table, adults, migraine disability

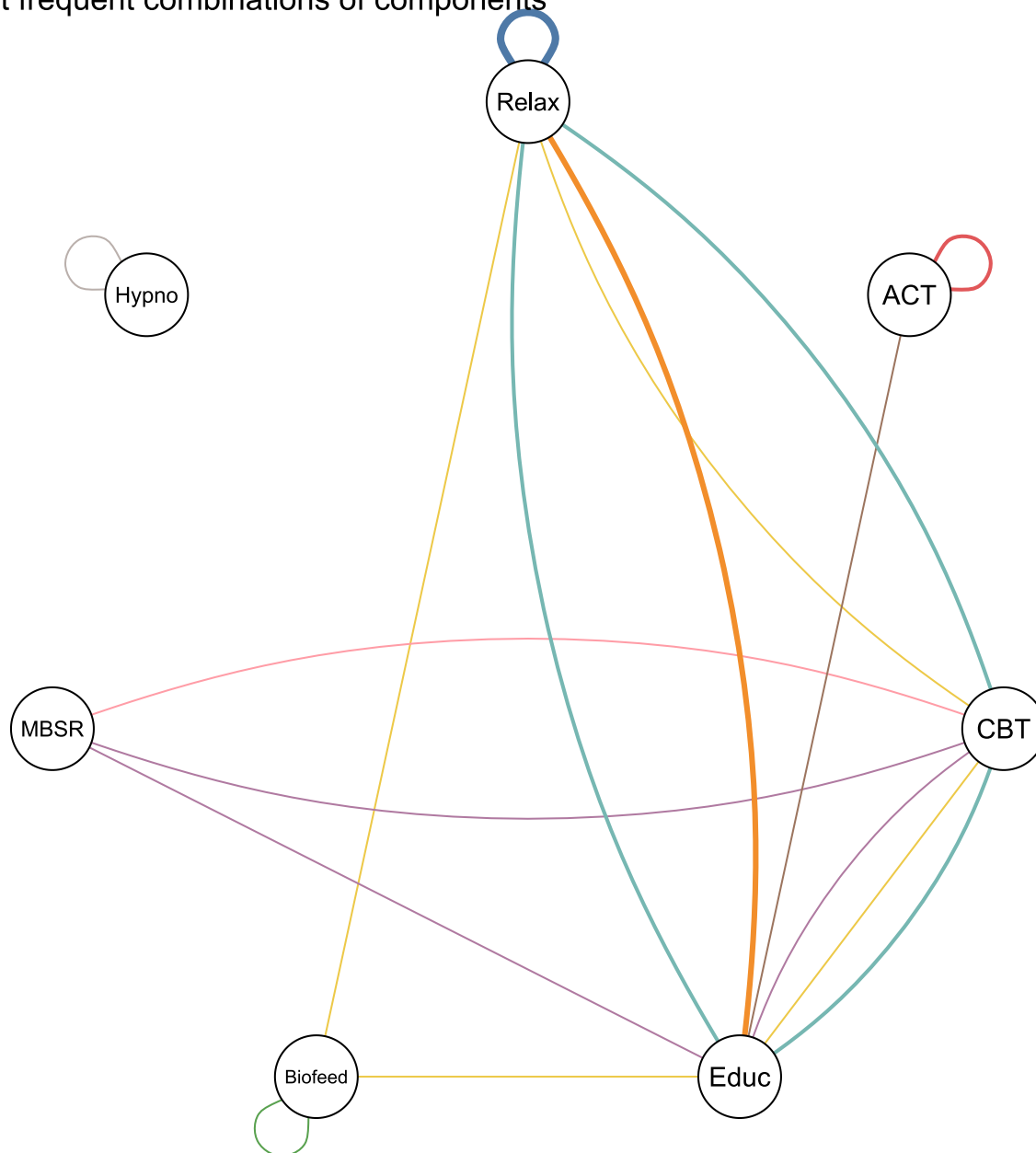


Total number of study arms: 35

Components cross-table visualizing the number of arms that include a component or any pair of two components for migraine disability in adults. Parentheses in the diagonal elements denote the proportions of study arms that include the component, while in the non-diagonal elements denote the proportion of study arms that include the corresponding pair of components out of those study arms that include the component in the corresponding row. The intensity of the color is proportional to the relative frequency of the corresponding component (combination). Abbreviations: ACT=acceptance and commitment therapy; Attention=attention control; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; k=number of studies; MBSR=mindfulness-based stress reduction; Minimal=minimal intervention; n=number of participants; Relax=relaxation therapy; TAU=treatment-as-usual

Figure G-12. Components network graph, adults, migraine disability

Most frequent combinations of components

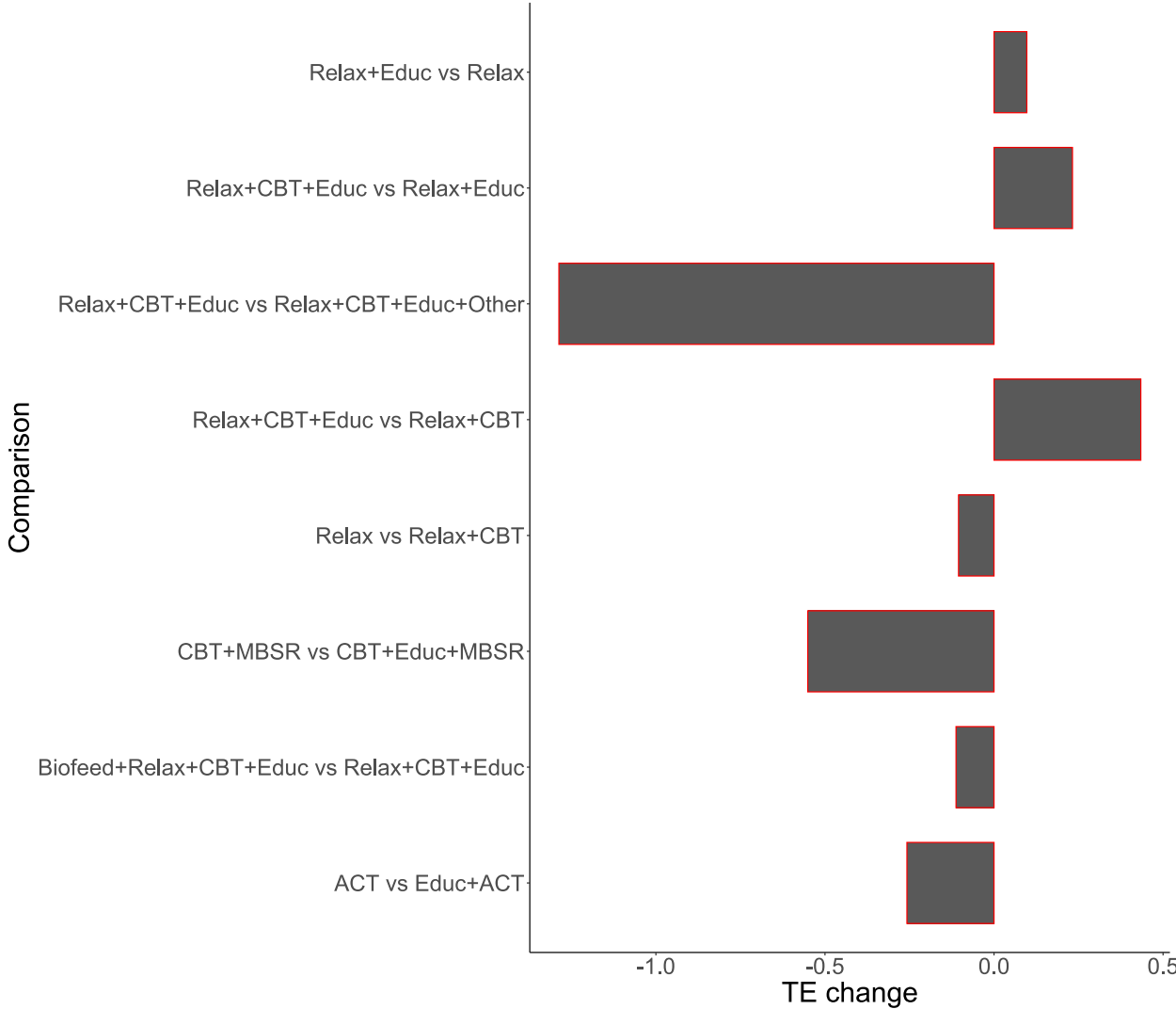


Components network graph for migraine disability in adults. Thickness of the line is proportional to the number of arms containing the corresponding component combination while colors refer to different interventions. Loops from and to the same component indicate arms where the component was evaluated alone.

To evaluate the impact of individual behavioral components on migraine disability, we attempted to fit a component NMA model assuming the effects of the individual components were additive. Although the test for additivity was not statistically significant (standard NMA model: $Q = 14.10$, $df = 5$; additive model: $Q = 19.20$, $df = 9$; difference: $Q = 5.10$, $p = 0.278$), visualization

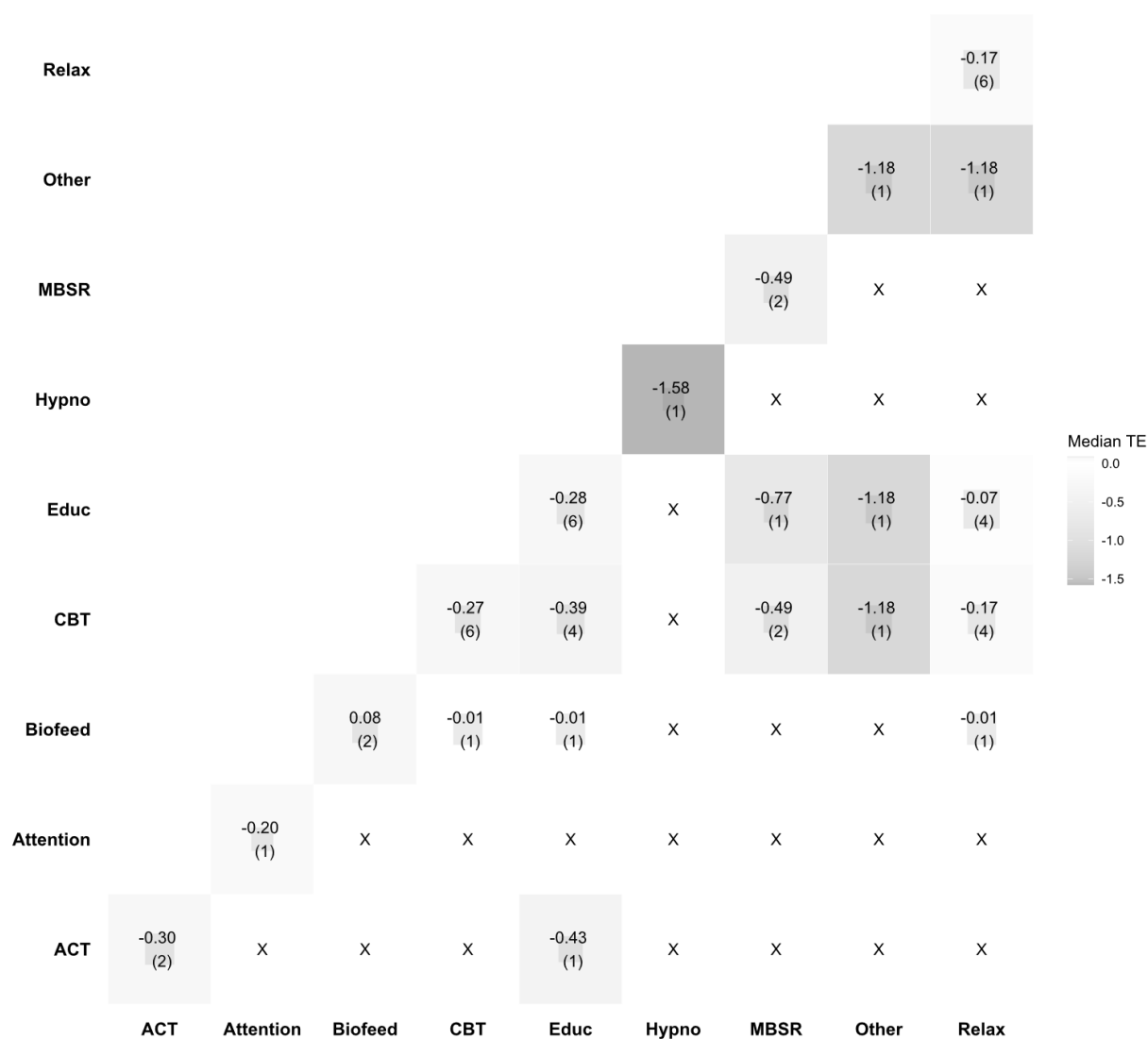
of the standard NMA results in a waterfall plot led us to believe that the additivity assumption may not be justified (Figure G-13). Adding education to ACT and CBT + MBSR appears to increase effectiveness, while adding it to relaxation training + CBT decreases effectiveness. Adding CBT to relaxation increases effectiveness but adding it to relaxation training + education reduces effectiveness. Finally, adding education to relaxation training increases effectiveness, while it decreases effectiveness when added to relaxation training + CBT. From the components heat plot (Figure G-14) and violin plot (Figure G-15), it is notable that CBT, education, and relaxation training only appear to be really effective when used in the relaxation training + CBT + education + other combination intervention.

Figure G-13. Waterfall plot, adults, migraine disability



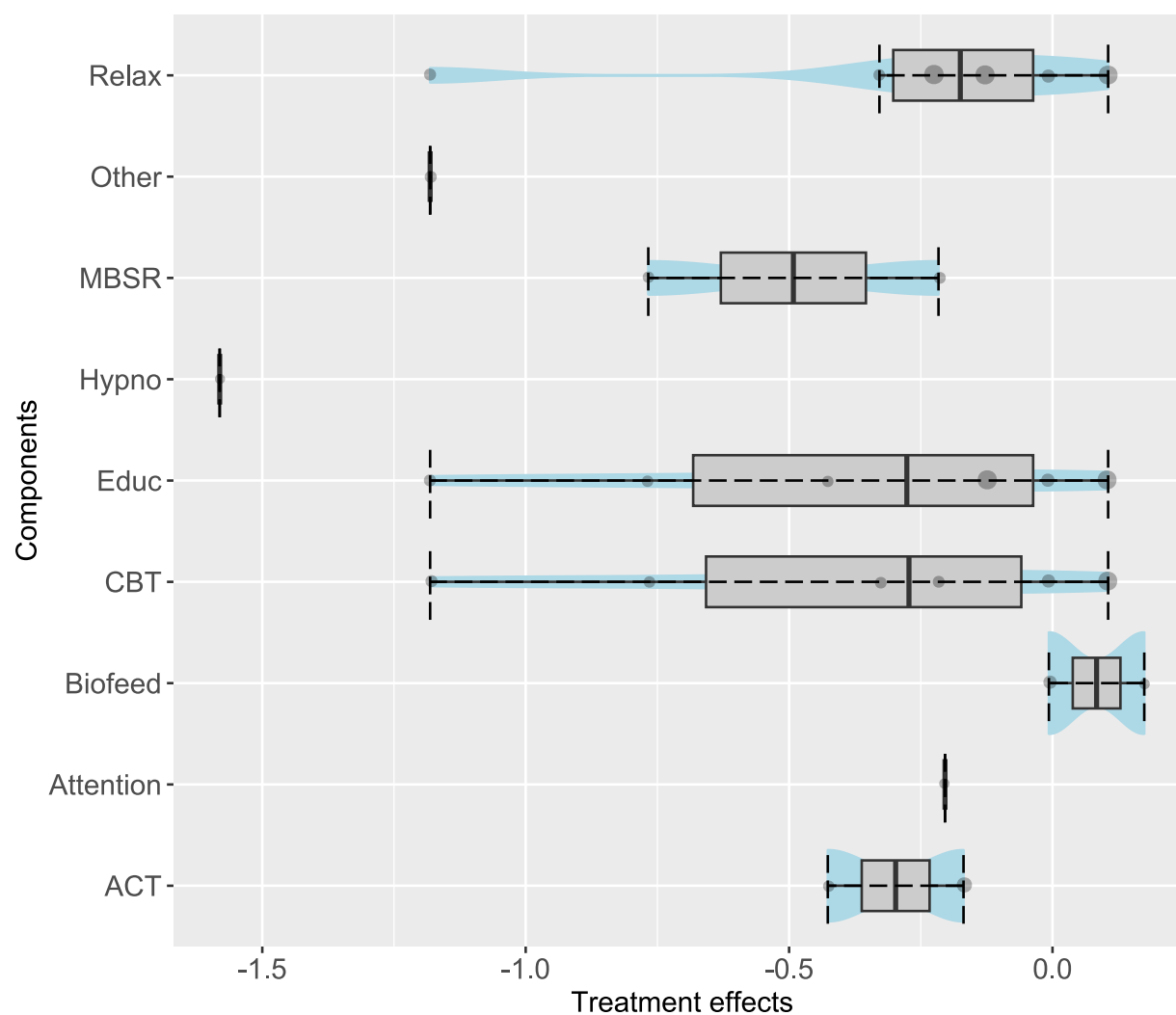
Waterfall plot for migraine disability in adults showing the comparisons that differ by a single component using network meta-analysis effects relative to treatment-as-usual. Abbreviations: ACT=acceptance and commitment therapy; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; MBSR=mindfulness-based stress reduction; Relax=relaxation therapy; TE=treatment effect

Figure G-14. Components heat plot, adults, migraine disability



Components heat plot for migraine disability in adults. Each cell refers to a combination of components and presents the median network meta-analysis effects of interventions that include that combination of components relative to treatment-as-usual. Gray boxes are proportional to the estimates' precision.

Figure G-15. Violin plot, adults, migraine disability



Violin plot evaluating the effectiveness of the components used for migraine disability in adults, using network meta-analysis effects relative to treatment-as-usual. Dots are proportional to the precision of the relative effect estimate. Abbreviations: ACT=acceptance and commitment therapy; Biofeed=biofeedback; CBT=cognitive behavioral therapy; Educ=education; Hypno=hypnotherapy; MBSR=mindfulness-based stress reduction; Relax=relaxation therapy