

Evidenced-Based Guidelines For Migraine Headache: Behavioral and Physical Treatments

J. Keith Campbell MD

Emeritus Professor of Neurology, Department of Neurology, Mayo Medical School and Mayo Clinic, Rochester, MN

Donald B. Penzien, PhD

Associate Professor and Director, UMC Head Pain Center, Department of Psychiatry and Human Behavior, University of Mississippi Medical Center, Jackson, MN

Eric M. Wall, MD, MPH

Regional Medical Director, Lifewise, A Premera Health Plan, Portland, OR

US Headache Consortium:§

American Academy of Family Physicians

American Academy of Neurology

American Headache Society

American College of Emergency Physicians*

American College of Physicians-American Society of Internal Medicine

American Osteopathic Association

National Headache Foundation

§The US Headache Consortium participants: J. Keith Campbell, MD; Frederick G. Freitag, DO; Benjamin Frishberg, MD; Thomas T. Gilbert, MD, MPH; David B. Matchar, MD; Douglas C. McCrory, MD, MHSc; Donald B. Penzien, PhD; Michael P. Pietrzak, MD, FACEP; Nabih M. Ramadan, MD; Jay H. Rosenberg, MD; Todd D. Rozen, MD; Stephen D. Silberstein, MD, FACP; Eric M. Wall, MD, MPH; William B. Young, MD.

*Endorsement by ACEP means that ACEP agrees with the general concepts in the guidelines and believes that the developers have begun to define a process of care that considers the best interests of patients with migraine headache

Copyright © by the American Academy of Neurology: Licensed to the members of the US Headache Consortium

Behavioral and Physical Treatments

A. Introduction

Some headache sufferers may prefer nonpharmacological treatment in the primary management of their problem *before* medication is employed. While all have at one time or another used medications to treat their headaches, some do not always respond to traditional drug therapies. In addition, some pharmacological treatments may not be suitable for patients who have particular coexisting conditions. The well-documented variation in individual response to medication further complicates pharmacological therapy.^{1,2} Consequently, many patients seek additional types of treatment to help manage migraine and other types of headache. Although these patients are not necessarily dissatisfied with conventional therapies, many of them find nonpharmacological methods to be more congruent with their own values, beliefs, and philosophical orientations.³

Over the past two decades, several behavioral treatments for migraine prevention have been used widely as independent therapies or combined with pharmacological therapy. Most treatments are classified into three broad categories: relaxation training, biofeedback therapy (often administered in conjunction with relaxation training), and cognitive-behavioral training (also known as stress-management training). Interest in the use of physical treatment as preventive therapy for migraine has also grown in the US and includes procedures such as acupuncture, cervical manipulation, and mobilization therapy. These therapies may be particularly well suited as treatment options for headache sufferers who have one or more of the following characteristics:

- (a) patient preference for nonpharmacological interventions;
- (b) poor tolerance for specific pharmacological treatments;
- (c) medical contraindications for specific pharmacological treatments;
- (d) insufficient or no response to pharmacological treatment;
- (e) pregnancy, planned pregnancy, or nursing;
- (f) history of long-term, frequent, or excessive use of analgesic or acute medications that can aggravate headache problems (or lead to decreased responsiveness to other pharmacotherapies); and
- (g) significant stress or deficient stress-coping skills.

Aims of the Guideline

The objective of the US Headache Consortium is to develop scientifically sound, clinically relevant practice guidelines on chronic headache in the primary care setting. These headache Guidelines review the evidence published in the literature and propose diagnostic and therapeutic recommendations to improve the care and satisfaction of migraine patients. This specific document focuses evidenced-based treatment recommendations for behavioral and physical therapies currently used for acute treatment or prevention of migraine.^{§§} The basis for this Guideline is the *Agency for Health Care Policy and Research (AHCPR) Technical Review*, which focused on behavioral and physical treatments for migraine.⁴ Recommendations are based on meta-analyses across multiple studies that tested selected behavioral and physical techniques

^{§§}This statement is provided as an educational service of the US Headache Consortium member organizations. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. These organizations recognize that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

specifically in migraine patients. Evidence supporting or denying their efficacy for migraine is reviewed in the Summary of Evidence below (and in Table 1), and specific treatment recommendations follow. Additional details of methodologies and analyses are described in the *Evidence-Based Treatment Guidelines for Migraine Management: Overview of Program Description and Methodology*.⁵ Specific studies included in the meta-analysis with variables analyzed are detailed in Table 2.

Goals of Behavioral and Physical Treatments for Migraine

In most instances, behavioral and physical interventions are used for preventing migraine episodes rather than for alleviating symptoms once an attack has begun. Although these modalities may be effective as monotherapy, they are more commonly used in conjunction with pharmacological management. The specific long-term goals for using these treatment modalities for migraine prevention include:

- reduced frequency and severity of headache,
- reduced headache-related disability,
- reduced reliance on poorly tolerated or unwanted pharmacotherapies,
- enhanced personal control of migraine, and
- reduced headache-related distress and psychological symptoms.

B. Summary of the Evidence

The principal findings of the *AHCPR Technical Review on Behavioral and Physical Treatments for Migraine*⁴ are summarized below. The report reviewed and analyzed published

reports of randomized, controlled trials and other prospective, comparative clinical trials of behavioral and physical treatments for migraine. Measures of headache index (a composite score of headache frequency, severity, and/or duration) and headache frequency reported as group means were used to calculate standardized mean differences. The number of patients obtaining at least a 50% reduction in headache index frequency or severity was recorded and used to calculate odds ratios. Further methodological details are found in the *AHCPR Technical Review*.⁴

Behavioral Treatments

Overall, 355 behavioral and physical treatment articles were identified, of which 70 controlled trials of behavioral treatments for migraine were reviewed. Only 39 of these trials met all of the criteria for inclusion in the *AHCPR Technical Review* and analysis. To be considered for inclusion, studies needed to be prospective, controlled trials of behavioral or physical treatments aimed at the prevention of attacks of migraine headaches or the relief of symptoms of individual episodes of headache in patients with migraine. Studies were included only if allocation to treatment groups was randomized or quasi-randomized. The treatments considered in the *AHCPR Technical Review* included relaxation training, biofeedback training, cognitive-behavioral (or stress-management) therapy, hypnosis, and various combinations of these interventions. This review is limited to these treatments, recognizing that other modalities have been employed but were beyond the scope of the *AHCPR Technical Review*. The relaxation techniques considered included those that train patients to control muscle tension and those that teach patients to use mental relaxation and/or visual imagery to achieve treatment goals. The biofeedback interventions considered were standard thermal (hand-warming) and electromyographic (EMG) biofeedback training. For relaxation and biofeedback, only those techniques that involved at least some formal

training by a therapist were included. Treatments considered under the heading of cognitive-behavioral therapy were those involving a psychotherapeutic intervention that had as its primary goal to teach skills for identifying and controlling stress and minimizing the effects of stress. Hypnotic treatments were considered only when hypnotic induction and suggestion were aimed primarily at headache control.

Eighteen of the 39 trials included in the *AHCPR Technical Review* investigated outcome data and variance data, thereby permitting calculation of standardized effect-size estimates. Effect size represents the difference between groups with respect to outcomes of interest (in this case, change in headache index or headache frequency) divided by the standard deviation in that measure. Effect size is a commonly used measure for quantifying study outcomes in the meta-analysis. Greater effect size is presumed to be related to greater clinical improvement. Effect sizes from individual trials were then combined in a meta-analysis that used a multi-variable, random-effects model to estimate a summary effect size for each type of treatment, controlling for the study. For the purposes of this meta-analysis, the behavioral interventions considered were grouped into eight categories based in part on statistical considerations and in part on clinical considerations (taking into account the way that interventions are actually combined in clinical use). The resulting categories for meta-analysis were: control ("no treatment," also called "wait-list"), psychological placebo (including sham biofeedback), relaxation training, thermal biofeedback training, thermal biofeedback training plus relaxation, EMG biofeedback training, cognitive-behavioral therapy, and cognitive-behavioral therapy plus thermal biofeedback training (see Table 1).[‡]

[‡] Only one study evaluating hypnosis for treatment of migraine was included in the *AHCPR Technical Review*.

Because fewer than half of the trials that met the inclusion criteria for the *AHCPR Technical Review* permitted effect-size calculation, the sample of studies included in the meta-analysis may be subject to selection bias. Therefore, in addition to the standardized effect-size meta-analysis, treatment efficacy was also evaluated using percent improvement scores for: (a) studies included in the meta-analysis of standardized effect sizes and (b) those not included in the standardized effect-size meta-analysis (see Table 1).

Comparisons of behavioral treatments with drug treatments were not included in the meta-analysis, but are discussed below.

Relaxation training: For the purposes of the analysis, all relaxation techniques (principally progressive muscle relaxation [PMR], autogenic training, and meditation or passive relaxation) were considered together. This was done on the basis of one trial that compared PMR and autogenic training, which found that the type of training used made no significant difference in headache index.⁶ A total of 10 trials yielded an average mean improvement of 32% in headache index or frequency from pre- to post-treatment.⁷⁻¹⁶ Mean improvement of 41% was demonstrated among five studies that provided sufficient data for inclusion in the standard effect-size meta-analysis (Table 1).^{7-10,16} Relaxation training obtained a statistically significant and moderately large effect size of 0.55.

Hypnotherapy: In one trial, hypnotherapy (six sessions) was compared with prochlorperazine (Stemetil® 10 mg/day first month, then 20 mg/day for 11 months).¹⁷ During the first six months, patients in the hypnotherapy group had reduced headache frequency compared with prochlorperazine, and this difference reached statistical significance during months 6-12 of

treatment. A second study tested the effects of self-hypnosis compared with thermal biofeedback plus relaxation therapy. Both approaches showed significant improvement compared to pretreatment for headache index, but no significant difference between treatment groups was found.

Thermal biofeedback training: Five trials showed an average of 37% improvement in headache activity.^{11,12,18-20} The three studies providing data for standardized effect sizes obtained a more modest effect size (0.38), and failed to support a significant clinical benefit.¹⁸⁻²⁰ However, studies not included in the standardized meta-analysis reported higher mean improvement scores, suggesting potential study selection bias.^{11,12}

Thermal biofeedback plus relaxation training: Ten studies assessing the clinical benefits of combinations of biofeedback and relaxation training therapy for migraine found a mean average improvement of 33% in headache activity.^{7,8,10,13,15,21-25} The results from the effect-size meta-analysis were based on 8 of the 10 studies, which reported significant and roughly equivalent outcomes for studies with and without standardized effect sizes.^{7,8,10,21-25} Thermal biofeedback plus relaxation training obtained a modest (0.40) but still statistically significant effect size.

Several studies compared thermal biofeedback plus relaxation training with other behavioral techniques with or without medication therapy. In one study, thermal biofeedback plus relaxation (three sessions in three months) was compared with thermal biofeedback plus relaxation therapy (three sessions in three months) plus propranolol (60-180 mg/day).²⁶ The headache index of patients receiving the combination of behavioral and drug treatments decreased significantly more than for the behavioral treatments alone group. A second study compared

thermal biofeedback plus relaxation training with ergotamine plus compliance training that focused on the appropriate use of ergotamine.²⁷ Both groups improved significantly from pre- to post-treatment, although neither group was better than the other. A third study tested the effects of thermal biofeedback plus relaxation plus cognitive-behavioral therapy as compared with long-acting propranolol.²⁸ Statistically significant improvements from baseline were seen for both groups, but no significant difference was noted between treatments. One study compared thermal biofeedback plus relaxation with drug therapy alone (propranolol plus analgesics).²⁹ Both treatments reduced the headache index from pre-treatment (54% and 45%, respectively), and no between-group comparisons were reported.

EMG biofeedback therapy: Five studies were analyzed, revealing a weighted average of 40% improvement in headache index.^{10,12,15,24,30} Meta-analysis using data from three of the five studies indicated a significant clinical improvement with electromyographic (EMG) biofeedback, with a moderately large effect size score of 0.77.^{10,24,30} Studies not included in the standardized meta-analysis reported lower mean improvement scores, suggesting potential study selection bias.

One study compared the effects of EMG biofeedback plus thermal biofeedback plus relaxation ("EMG biofeedback group") with propranolol or amitriptyline. The control group received a combination of ergotamine tartrate and analgesics as acute therapy only. The EMG biofeedback group did significantly better compared with the control group. Similar improvement was reported for amitriptyline plus biofeedback.³¹

Cognitive-behavioral therapy: Seven trials evaluated the clinical benefits of cognitive-behavioral therapy and revealed an average of 49% improvement in headache activity.^{7,14,16,32-34}

Results from a standardized meta-analysis using data from five of the seven trials suggest a significant clinical improvement with a moderately large effect size score of 0.54.^{7,16,32-34} Studies not included in the standardized meta-analysis reported higher mean improvement scores, suggesting a potential study selection bias.¹⁴

Cognitive-behavioral training and thermal biofeedback: Five trials evaluated this combination therapy and showed an average 38% improvement in headache activity. Standardized meta-analysis using data from all five studies found a more modest effect size score of 0.37 that failed to reach statistical significance.^{21,21,33,35}

Physical treatments

Thirteen reports (twelve trials) of physical treatments for migraine were included in the *AHCPR Technical Review*. The interventions tested were acupuncture,^{34,36-41} transcutaneous electrical nerve stimulation (TENS),^{42,43} occlusal adjustment,⁴⁴ cervical manipulation,⁴⁵ and hyperbaric oxygen.⁴⁶ Acupuncture uses fine needles to pierce the skin to relieve pain, induce anesthesia, and achieve therapeutic goals.⁴⁷ Researchers believe that stimulation with the needles allows pain-killing endorphins to be released into the patient's system thereby relieving pain.⁴⁸ TENS applies focused electrical shocks to areas of the body experiencing pain.⁴⁹ Cervical manipulation directs short- or long-term high velocity thrusts at one or more joints of the cervical spine. Occlusal adjustment involves dental procedures used to improve a patient's bite, thereby relieving muscle tension in the jaw that might induce or exacerbate migraine pain. Finally, hyperbaric oxygen therapy requires that the patient be placed in a hyperbaric chamber to increase pressurization of the blood gases.

Acupuncture: Seven small trials of acupuncture yielded mixed results.^{34,36-41} One study comparing acupuncture with control treatment ("no treatment" or wait-list) reported a significant improvement post-treatment with acupuncture (53% reduction in the frequency of disabling headache), but not with the control treatment (14% reduction); however, the significance of between-group differences was not tested.³⁴ Two trials comparing acupuncture with sham acupuncture found that the genuine intervention was significantly better at reducing headache intensity.^{36,41} One of the two trials, however, had serious methodological problems.³⁶ Another study, comparing acupuncture with sham TENS, found no significant difference between the two interventions: a reduction of 50% or more in headache frequency was reported by 32% of patients receiving acupuncture and 26% receiving sham TENS.³⁷

A single trial compared acupuncture with psychological therapy (aimed at training patients to observe and change psychological sensations associated with migraine attacks).³⁴ Both treatments reduced the frequency of disabling headache compared with pre-treatment levels (acupuncture by 53% and psychological therapy by 29%), but the statistical significance of the difference between the two treatments was not reported. The trial was not large enough to demonstrate equivalence of the two interventions.

Two trials compared acupuncture with drug therapies; in one case with the beta-blocker metoprolol,³⁸ and in the other with a variety of migraine prophylactic therapies.⁴⁰ Neither trial found any significant differences between acupuncture and the drug therapies tested. Neither trial was large enough to demonstrate equivalence of the two interventions.

TENS: Two studies of TENS provided little support for the efficacy of this treatment for patients with migraine. One trial found that standard TENS therapy was no better than subliminal TENS or sham TENS for the treatment of *acute* migraine.⁴² Another study reported limited results for the use of cranio-electrotherapy stimulation, and analysis of the potential efficacy of this procedure was not possible.⁴³

Occlusal adjustment: A single trial compared genuine and sham occlusal adjustment in patients with migraine and patients with mixed migraine and tension-type headache.⁴⁴ In the subgroup of migraine patients, no significant benefit was found for the genuine therapy compared with the sham treatment. Among patients with mixed migraine and tension-type headache, the genuine therapy showed a modest benefit, but statistically significant differences were not reported. Overall, the investigators concluded that for prevention of migraine, occlusal adjustment was not superior to the sham treatment. Additional benefits may be seen in patients with mixed headache types.

Cervical manipulation: A single trial of cervical mobilization (oscillation of a joint within its normal range of movement) and cervical manipulation (movement of a joint beyond its normal range of movement) provided little support for the use of these interventions for patients with chronic headache.⁴⁵ The study compared three interventions: cervical manipulation performed by a medical practitioner or physiotherapist, cervical manipulation performed by a chiropractor, and cervical mobilization performed by a medical practitioner or physiotherapist (used as a control). All three treatment groups were considered together. Post-treatment scores were significantly better than pre-treatment scores for headache frequency, severity, and disability, but not for

duration. Comparison between chiropractic manipulations and the control cervical mobilization showed no difference.

Other Nonpharmacological Treatments for Migraine

For centuries, a host of nonpharmacological treatment approaches have been used to treat a multitude of diseases and conditions, but limited studies have been done specifically in migraine. The *AHCPR Technical Review* limited its focus to behavioral and physical treatments for migraine. A few additional studies have been done in migraine that do not involve behavioral or physical treatments. Specifically, one study looked at the role of hyperbaric oxygen for treatment of migraine.

Hyperbaric oxygen: One small trial examined the efficacy of hyperbaric oxygen (two atmospheres of pressure) versus normobaric oxygen (one atmosphere of pressure) for the treatment of *acute* migraine.⁴⁶ All patients had experienced a severe, very severe, or "most severe ever" migraine attack. Clinical success was defined as a reduction in headache intensity to mild or none after 40 minutes of treatment. The results suggested a large and statistically significant difference in favor of hyperbaric oxygen.

C. Transition from Evidence to Guidelines

The empirical evidence that provides the basis for this Guideline was limited to studies included in the *AHCPR Technical Review*. The report included only published literature on reported randomized, controlled trials, published in English, and it evaluated adult migraine

patients. The effect-size data suggest that relaxation training, thermal biofeedback combined with relaxation training, and cognitive-behavioral therapy are all modestly effective in preventing migraine when compared to a wait list control.

The efficacy of drug treatments for migraine is generally established on the basis of double-blind comparisons with matching placebo. By contrast, most of the trials in the meta-analysis compared behavioral treatments with control (wait-list) conditions. Double-blinding is impossible for most behavioral interventions, and effective single-blinding is also difficult to achieve in most cases. Using "no treatment" controls (rather than credible placebo groups) and no blinding makes behavioral trials more prone to bias than are traditionally designed drug trials, and one might suspect to find a spurious statistically significant result (Type I error). However, the meta-analysis estimates the magnitude of this bias by estimating the effect size for a variety of "placebo" conditions. This effect size was not significantly different from control, and was less than half the size of the weakest effect observed among the behavioral interventions included in the meta-analysis. Therefore, this bias is too small to explain the results observed.

Generalizing results from the published trials is limited because most patients were recruited from specialized centers that treat patients (a) whose headaches are severe or (b) whose headaches have not responded to common pharmacologic therapies. Additionally, studies with small sample sizes (as used in most trials in this area) may lack sufficient statistical power to detect small but clinically meaningful results, and may limit generalizing about the findings.

These methodological issues, paired with the relatively small number of published controlled trials included in the meta-analysis, limit the strength of the recommendations that can be made regarding behavioral and physical treatments for migraine. As with pharmacological treatments, current research does not clearly identify those patients with the best potential for

responding to these treatments. Studies on how to integrate these treatment methodologies into existing pharmacological strategies are limited as well.

D. General Principles of Management

The general principles of management below are based on consensus rather than evidence available in the literature. The US Headache Consortium agreed that these general principles are important in improving the quality of care in patients with chronic headache.

Involving the migraine patient in developing a management plan for an often-disabling condition is not only empowering but critical to the success of treatment strategies, including those with behavioral and physical components. Migraine headache is a chronic condition with long-term management goals focused on reduction in attack frequency and severity.

When creating and maintaining a partnership, realistic patient expectations need to be established. Some behavioral and physical therapies offer modest reduction in migraine frequency, as do many pharmacological therapies. Much of the difficulty in managing patients with migraine stems from the disappointment that ensues when the patient's expectations of the benefits of treatment are not met. The patient can be assisted in establishing realistic treatment goals and recognizing treatment success. Some suggest that diary cards, flow charts, headache calendars, tracking days of disability or missed work or school, and providing treatment plans are useful tools to aid in this effort.

The key to optimizing multiple treatment approaches is careful coordination through communication between the provider and the patient. Specifically, this includes identifying all treatment modalities used (including those used for coexisting conditions) and designing a coordinated treatment plan that all parties acknowledge and accept (e.g., patient, family practitioner, internist, neurologist, and psychologist). Design and coordinate a treatment plan that everyone agrees with, and communicate that plan to the patient.

E. Specific Treatment Recommendations

As illustrated above, the number of studies that met entry criteria for review and analysis of behavioral and physical therapies is limited, and therefore allows for limited interpretation for evidence-supported treatment recommendations.

Findings: Relaxation training, thermal biofeedback combined with relaxation training, EMG biofeedback, and cognitive-behavioral therapy are all somewhat effective in preventing migraine when compared with controls. Given the evidence reviewed, no conclusions can be made regarding equivalence or superiority among specific behavioral treatments, or for specific behavioral treatments relative to other specific preventive pharmacological therapies.

Recommendation: Relaxation training, thermal biofeedback combined with relaxation training, EMG biofeedback, and cognitive-behavioral therapy may be considered as

treatment options for prevention of migraine (Grade A[§]). Specific recommendations regarding which of these to use for specific patients cannot be made.

Findings: Behavioral treatments have been directly compared and integrated with drug treatments as preventive therapy for migraine. The addition of propranolol conferred additional clinical benefits when added to: (1) thermal biofeedback plus relaxation plus cognitive-behavioral therapy, (2) thermal biofeedback plus relaxation, and (3) EMG biofeedback (amitriptyline also proved beneficial in a later trial).

Recommendation: Behavioral therapy (i.e., relaxation, biofeedback) may be combined with preventive drug therapy (i.e., propranolol, amitriptyline) for patients to achieve additional clinical improvement for migraine relief (Grade B[§]).

Findings: The empirical evidence pertaining to treatment of migraine with acupuncture is limited and the results are mixed. Very limited evidence evaluates hypnosis, TENS, cervical manipulation, occlusal adjustment, and hyperbaric oxygen as preventive or acute therapy for migraine.

[§] **Quality of the evidence**⁵⁰

- A. Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings.
- B. Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal. For instance, either few randomized trials existed, the trials that did exist were somewhat inconsistent, or the trials were not directly relevant to the recommendation. An example of the last point would be the case where trials were conducted using a study group that differed from the target group for the recommendation.
- C. The US Headache Consortium achieved consensus on the recommendation in the absence of relevant randomized controlled trials.

Recommendation: Evidenced-based treatment recommendations are not yet possible regarding the use of hypnosis, acupuncture, TENS, cervical manipulation, occlusal adjustment, and hyperbaric oxygen as preventive or acute therapy for migraine. For hyperbaric oxygen treatment, even if further studies confirmed efficacy results presented above, the lack of availability would limit practical clinical application of this treatment (Grade C^s).

F. Future Research

Additional studies need to be done on behavioral and physical therapies such as osteopathic manipulation, hypnosis, biofeedback, and relaxation therapy. Few studies to date provide head-to-head comparisons between behavioral and pharmacological treatments of migraine. Existing empirical literature does not adequately address the integration of behavioral and physical therapies into treatment plans for migraine patients. Studies have shown that these methods can be used effectively as sole or adjunctive therapy, but little is known about which types of migraine patients are most likely to be responsive to which treatment modalities (e.g., migraine associated with menses, migraine with aura, mild or severe migraine, or presence of specific coexistent conditions). Additional studies are needed to elucidate which patient characteristics will enhance or hinder treatment efficacy. For example, patient characteristics such as age, stress-coping skills, depression, or other psychological features may increase or decrease the likelihood of specific treatment success.

Future studies of behavioral or physical treatment should include populations derived from primary care settings (as opposed to a specialty headache clinic that treats more severe or

complicated migraine patients) so that the results may be more generalizable and useful to primary care practitioners.

The relative efficacy of behavioral and physical treatments, compared with medications with demonstrated efficacy for migraine or with other behavioral or physical treatment approaches, needs to be determined.

Defining appropriate control groups is critical in establishing clinically and statistically significant differences in treatments tested. New studies need to incorporate, as much as possible, adequate clinical trial designs that fall within the recommendations of the International Headache Society Committee on Clinical Trials on Migraine.⁵¹

Finally, component analysis studies should be undertaken to determine the extent to which the various elements of the therapeutic regimen contribute to the efficacy of the intervention. These components may include behavioral, pharmacologic, environmental, and social factors. Patients may receive any number of additional therapeutic interventions, some of which are readily quantifiable (e.g., medications), while others are more difficult to measure (e.g., supportive care). These factors may include increased time with or attention from healthcare providers or increased office visits; increased education (regarding triggers or compliance issues); or assistance with regular tracking of headaches, highlighting treatment successes. Additional prospective studies are needed to determine the role these various components play in achieving migraine management success.

Acknowledgments

The authors and US Headache Consortium wish to thank Starr Pearlman, PhD, Joanne Okagaki, and Rebecca Gray, DPhil, for their help in preparing this manuscript and for their

administrative support. We also wish to acknowledge the scientific advice of Drs. Jes Olesen, Jean Schoenen, Helene Massiou, Peer Tfelt Hansen, F. Cankat Tulunay, and Kai Jensen.

Funding and Support

The Evidenced-Based Guidelines for Migraine Headache were supported by: Abbott Laboratories, AstraZeneca, Bristol Myers Squibb, Glaxo Wellcome, Merck, Pfizer, Ortho-McNeil, and the AAN Education & Research Foundation, along with the seven participant member organizations.

G. References

1. Nies AS. Principles of therapeutics. In: Gilman AG, Rall TW, Nies AS, Taylor P, eds. *Goodman and Gilman's: The Pharmacological Basis of Therapeutics*. 8th ed. New York, NY: Pergamon Press, Inc; 1990:62-83.
2. Vesell ES. Pharmacogenetic approaches to the prediction of drug response. In: Braude MC, Chao HM, eds. *Genetic and Biological Markers in Drug Abuse and Alcoholism*. National Institute on Drug Abuse Research Monograph Series No. 66. Department of Health and Human Services. Washington, DC: US Government Printing Office; 1986: 25-40.
3. Astin JA. Why patients use alternative medicine: results of a national study. *JAMA*. 1998;279(19):1548-1553.
4. Goslin RE, Gray RN, McCrory DC, Penzien D, Rains J, Hasselblad V. *Behavioral and Physical Treatments for Migraine Headache*. Technical Review 2.2, February 1999. (Prepared for the Agency for Health Care Policy and Research under Contract No. 290-94-2025. Available from the National Technical Information Service; NTIS Accession No. 127946.)
5. McCrory DC, Matchar DB, Rosenberg JH, Silberstein SD. Evidenced-based guidelines for migraine headache: overview of program description and methodology. (<http://www.aan.com>)
6. Janssen K, Neutgens J. Autogenic training and progressive relaxation in the treatment of three kinds of headache. *Behav Res Ther*. 1986;24(2):199-208.
7. Barrios FX. Social skills training and psychosomatic disorders. In: Rathjen DP, Foreyt JP, eds. *Social Competence: Interventions for Children and Adults*. New York, NY: Pergamon; 1980:271-301.
8. Blanchard EB, Theobald DE, Williamson DA, Silver BV, Brown DA. Temperature biofeedback in the treatment of migraine headaches: a controlled evaluation. *Arch Gen Psychiatry*. 1978;35(5):581-588.
9. Brown JM. Imagery coping strategies in the treatment of migraine. *Pain*. 1984;18(2):157-167.
10. Daly EJ, Donn PA, Galliher MJ, Zimmerman JS. Biofeedback applications to migraine and tension headaches: a double-blinded outcome study. *Biofeedback Self Regul*. 1983;8(1):135-152.
11. Friedman H, Taub HA. Brief psychological training procedures in migraine treatment. *Am J Clin Hypn*. 1984;26(3):187-200.

12. Lacroix JM, Clarke MA, Bock JC, Doxey N, Wood A, Lavis S. Biofeedback and relaxation in the treatment of migraine headaches: comparative effectiveness and physiological correlates. *J Neurol Neurosurg Psychiatry*. 1983;46(6):525-532.
13. Machado HP, Gomez de Machado AML. The effectiveness of psychophysiological techniques in the treatment of migraine headaches: a cross-cultural study in a Honduran population. Unpublished manuscript (1985).
14. Mitchell KR, Mitchell DM. Migraine: an exploratory treatment application of programmed behaviour therapy techniques. *J Psychosom Res*. 1971;15(2):137-157.
15. Sargent J, Solbach P, Coyne L, Spohn H, Segerson J. Results of a controlled, experimental, outcome study of nondrug treatments for the control of migraine headaches. *J Behav Med*. 1986;9(3):291-323.
16. Sorbi M, Tellegen B. Differential effects of training in relaxation and stress-coping in patients with migraine. *Headache*. 1986;26(9):473-481.
17. Anderson JA, Basker MA, Dalton R. Migraine and hypnotherapy. *Int J Clin Exp Hypn*. 1975;23(1):48-58.
18. Gauthier J, Lacroix R, Côté, A, Doyon J, Drolet M. Biofeedback control of migraine headaches: a comparison of two approaches. *Biofeedback Self Regul*. 1985;10(2):139-159.
19. Kewman D, Roberts AH. Skin temperature biofeedback and migraine headaches: a double-blind study. *Biofeedback Self Regul*. 1980;5(3):327-345.
20. Mullinix JM, Norton BJ, Hack S, Fishman MA. Skin temperature biofeedback and migraine. *Headache*. 1978;17:242-244.
21. Blanchard EB, Appelbaum KA, Nicholson NL, Radnitz CL, Morrill B, Michultka D, Kirsch C, Hillhouse J, Dentinger MP. A controlled evaluation of the addition of cognitive therapy to a home-based biofeedback and relaxation treatment of vascular headache. *Headache*. 1990;30(6):371-376.
22. Blanchard EB, Appelbaum KA, Radnitz CL, et al. A controlled evaluation of thermal biofeedback and thermal biofeedback combined with cognitive therapy in the treatment of vascular headache. *J Consult Clin Psychol*. 1990;58(2):216-224.
23. Blanchard EB, Nicholson NL, Radnitz CL, Steffek BD, Appelbaum KA, Dentinger MP. The role of home practice in thermal biofeedback. *J Consult Clin Psychol*. 1991;59(4):507-512.
24. Lake A, Rainey J, Papsdorf JD. Biofeedback and rational-emotive therapy in the management of migraine headache. *J Appl Behav Anal*. 1979;12(1):127-140.

25. McGrady A, Wauquier A, McNeil A, Gerard G. Effect of biofeedback-assisted relaxation on migraine headache and changes in cerebral blood flow velocity in the middle cerebral artery. *Headache*. 1994;34(7):424-428.
26. Holroyd KA, France JL, Cordingley GE, Rokicki LA, Kvaal SA, Lipchik GL, McCool HR. Enhancing the effectiveness of relaxation-thermal biofeedback training with propranolol hydrochloride. *J Consult Clin Psychol*. 1995;63(2):327-330.
27. Holroyd KA, Holm J, Hursey KG, Penzien DB, Cordingley GE, Theofanous AG, Richardson SC, Tobin DL. Recurrent vascular headache: home-based behavioral treatment versus abortive pharmacological treatment. *J Consult Clin Psychol*. 1988;56(2):218-23.
28. Penzien D, Johnson C, Carpenter D, Holroyd K. Drug vs. behavioral treatment of migraine: long-acting propranolol vs. home-based self-management training [abstract]. *Headache*. 1990;30(5):300.
29. Sovak M, Kunzel M, Sternbach RA, Dalessio DJ. Mechanism of the biofeedback therapy of migraine: volitional manipulation of the psychophysiological background. *Headache*. 1981;21(3):89-92.
30. Bild R, Adams HE. Modification of migraine headaches by cephalic blood volume pulse and EMG biofeedback. *J Consult Clin Psychol*. 1980;48(1):51-57.
31. Mathew NT. Prophylaxis of migraine and mixed headache. A randomized controlled study. *Headache*. 1981;21(3):105-109.
32. Richardson GM, McGrath PJ. Cognitive-behavioral therapy for migraine headaches: a minimal-therapist-contact approach versus a clinic-based approach. *Headache*. 1989;29(6):352-357.
33. Sorbi M, Tellegen B. Multimodal migraine treatment: does thermal feedback add to the outcome? *Headache*. 1984;24:249-255.
34. Wittchen H. A biobehavioral treatment program (SEP) for chronic migraine patients. In: Holroyd KA, Schlote B, Zenz B, eds. *Perspectives in Research on Headache*. Toronto: Hogrefe; 1983:183-97.
35. Nicholson NL, Blanchard EB. A controlled evaluation of behavioral treatment of chronic headache in the elderly. *Behav Ther*. 1993;24(3):395-408.
36. Cecherelli F, Ambrosio F, Avila M, Duse G, Munari A, Giron GP. Acupuncture vs. placebo in the common migraine: a double blind study. *Cephalalgia*. 1987;7(Suppl 6):499-500.
37. Dowson DI, Lewith GT, Machin D. The effects of acupuncture versus placebo in the treatment of headache. *Pain*. 1985;21(1):35-42.

38. Hesse J, Møgelvang B, Simonsen H. Acupuncture versus metoprolol in migraine prophylaxis: a randomized trial of trigger point inactivation. *J Intern Med.* 1994;235(5):451-456.
39. Lenhard L, Waite PM. Acupuncture in the prophylactic treatment of migraine headaches: pilot study. *N Z Med J.* 1983;96(738):663-666.
40. Loh L, Nathan PW, Schott GD, Zilkha KJ. Acupuncture versus medical treatment for migraine and muscle tension headaches. *J Neurol Neurosurg Psychiatry.* 1984;47(4):333-337.
41. Vincent CA. A controlled trial of the treatment of migraine by acupuncture. *Clin J Pain.* 1989;5(4):305-312.
42. Solomon S, Guglielmo KM. Treatment of headache by transcutaneous electrical stimulation. *Headache.* 1985;25(1):12-15.
43. Sheftell F, Rapoport A, Kudrow L. Efficacy of cranial electrotherapy stimulation in the prophylactic treatment of migraine and chronic muscle contraction headaches. *Cephalalgia.* 1989;9(Suppl 10):379-380.
44. Forssell H, Kirveskari P, Kangasniemi P. Changes in headache after treatment of mandibular dysfunction. *Cephalalgia.* 1985;5(4):229-236.
45. Parker GB, Tupling H, Pryor DS. A controlled trial of cervical manipulation of migraine. *Aust N Z J Med.* 1978;8(6):589-593.
46. Myers DE, Myers RA. A preliminary report on hyperbaric oxygen in the relief of migraine headache. *Headache.* 1995;35(4):197-199.
47. Ingelfinger FJ, ed. *Dorland's Medical Dictionary.* Shorter ed. Philadelphia, PA:Saunders; 1980:15.
48. Tollison CD, Kunkel RS, eds. *Headache Diagnosis and Treatment.* Baltimore, MD: Williams and Wilkins; 1993:393.
49. Elkind A. *Migraines: Everything You Need To Know about Their Cause and Cure.* New York, NY: Avon Books; 1997:175.
50. Fiore MC, Bailey WC, Cohen SJ, et al. *Smoking Cessation.* Clinical Practice Guideline No 18. Rockville, MD: US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research. AHCPR Publication No. 96-0692. April 1996.
51. International Headache Society Committee on Clinical Trials in Migraine. Guidelines for controlled trials of drugs in migraine. First edition. *Cephalalgia.* 1991;11(1):1-12.

H. Tables and Figures

Table 1: Behavioral Treatment Migraine Efficacy Summary

Intervention	No Studies in analysis	Mean weighted % improvement (range)	Effect size (95% confidence interval)*
I. Studies included in effect size analysis			
"No treatment" (control)	12	5 (-20 - 19)	0
Placebo	4	9 (-7 - 37)	0.16 (-0.31-0.63)
Relaxation	5	41 (6.2-78)	0.55 (0.14-0.96)
Thermal biofeedback	3	30 (13-60)	0.38 (-0.18-0.94)
Thermal biofeedback + relaxation	8	33 (21-52)	0.40 (0.01-0.79)
EMG biofeedback	3	51 (36-58)	0.77 (0.24-1.3)
Cognitive-behavioral therapy	5	39 (29-51)	0.54 (0.13-0.94)
Cognitive-behavioral therapy + biofeedback	5	38 (21-46)	0.37 (-0.23-0.97)
II. Studies not able to calculate effect size			
"No treatment" (control)			Not measurable
Placebo			Not measurable
Relaxation	5	22 (3.4-62)	Not measurable
Thermal biofeedback	2	49 (24-86)	Not measurable
Thermal biofeedback + relaxation	2	32 (21-87)	Not measurable
EMG biofeedback	2	23 (20-24)	Not measurable
Cognitive-behavioral therapy	2	71 (68-76)	Not measurable
Cognitive-behavioral therapy + biofeedback	0	-	Not measurable
III. All studies identified for review			
"No treatment" (control)	12	5 (-20-19)	Not measurable
Placebo	4	9 (-7-37)	Not measurable
Relaxation	10	32 (3-78)	Not measurable
Thermal biofeedback	5	37 (13-86)	Not measurable
Thermal biofeedback + relaxation	10	33 (21-87)	Not measurable
EMG biofeedback	5	40 (20-58)	Not measurable
Cognitive-behavioral therapy	7	49 (29-76)	Not measurable
Cognitive-behavioral therapy	5	35 (21-46)	Not measurable

*An effect size may be interpreted as statistically significant if its 95% confidence interval excludes zero (null effect).

EMG, electromyography

+ biofeedback			
---------------	--	--	--

Table 2: Studies Included in the Analyses of Behavioral Treatments

	Control	Placebo	RLX	TBF	TBF + RLX	EMG BF	Cog	TBF + Cog	Excluded therapies
Barrios (1980) ⁷			4		4		4		
Bild and Adams (1980) ³⁰	4					4			BVP BF
Blanchard et al. (1990) ²¹	4				4 (home based)			4	
Blanchard et al. (1990) ²²	4	4			4			4	
Blanchard et al. (1991) ²³	4				4 (with and without home practice)				
Blanchard et al. (1978) ⁸	4		4		4				
Brown (1984) ⁹		4	4						RLX (stimulus therapy)
Daly et al. (1983) ¹⁰			4		4	4			
Gauthier et al. (1985) ¹⁸	4			4					BVP BF
Kewman and Roberts (1980) ¹⁹	4			4					TBF BF
Lake et al. (1979) ²⁴	4				4	4		4	
McGrady et al. (1994) ²⁵		4			4 (Contained few sessions of EMG BF)				
Mullinix et al. (1978) ²⁰		4		4					
Nicholson and Blandchard (1993) ³⁵	4							4	

	Control	Placebo	RLX	TBF	TBF + RLX	EMG BF	Cog	TBF + Cog	Excluded therapies
Richardson and McGrath (1989) ³²	4						4 (minimal therapist treatment) 4 (Clinic-based treatment)		
Sorbi and Tellegen (1984) ³³							4	4	
Sorbi and Tellegen (1986) ¹⁶			4				4		
Wittchen (1983) ³⁴	4						4		Acupuncture

Control indicates wait list control, Placebo indicates non-drug control condition, RLX indicates relaxation training, TBF indicates temperature biofeedback training, TBF + RLX indicates temperature biofeedback and relaxation training, EMG BF indicates electromyographic or EMG biofeedback training, Cog indicates cognitive-behavior therapy, TBF + Cog indicates temperature biofeedback training and cognitive-behavior therapy, BVP BF indicates blood volume pulse biofeedback training, TBF decrease indicates temperature biofeedback training to decrease hand temperature