ORIGINAL ARTICLES

HOMEOPATHIC TREATMENT OF HEADACHES: A SYSTEMATIC REVIEW OF THE LITERATURE

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ABSTRACT

Objective: To systematically review published prospective trials relating to the homeopathic treatment of tension type, cervicogenic, and migraine headache.

Data Sources: Pre-MEDLINE, MEDLINE, MANTIS, Cochrane Database of Systematic Reviews, and AMED were searched from the initial indexing year of each database through May 2002. Studies were further identified through a manual search of obtained article references.

Study Selection: English and non-English randomized clinical trials and prospective observational trials were included if there were at least ten subjects in the homeopathic portion of the trial and, for randomized clinical trials, if there was a placebo group. Treatment in these studies included single dose and individualized homeopathic prescription. Case studies, homeopathic provings, unpublished material, non-peer reviewed papers, and studies that combined multiple homeopathic remedies, introduced other complementary and alternative medicine therapies and/or introduced additional medical therapy for patients in the homeopathic treatment groups were excluded.

Data Extraction: Qualitative data were extracted from each paper and entered into an evidence table.

Data Synthesis: A critical evaluation list of 20 methodological items and their operational definitions was used, resulting in a validity score determined for each paper.

Results: Six papers met criteria for inclusion. Three out of the six papers studied migraine headache, two studied cervicogenic and tension type headache, and one included all types of headaches. Four studies were randomized clinical trials, and two were prospective observational studies. Validity scores ranged from 25.0% to 63.4%. Homeopathy was superior to placebo in one randomized clinical trial and equal to placebo in three randomized trials. In no study was homeopathy less effective than placebo in treating headache, or harmful. Two prospective observational studies demonstrated improvement in patients receiving homeopathic care.

Conclusion: There is insufficient evidence to support or refute the use of homeopathy for managing tension type, cervicogenic, or migraine headache. The studies reviewed possessed several flaws in design. Given these findings, further research is warranted to better investigate the effectiveness of homeopathic treatment of headaches. (J Chiropr Med 2004;3:45–52)

KEY WORDS: Homeopathy; Headache; Review of the Literature

INTRODUCTION

Background

Headache is experienced by approximately 90% of adults at some time during their lives (1). Approximately 4% of the American adult population suffers from daily headaches (2,3). Headache is the seventh leading presenting complaint in ambulatory medical care in the United States and accounts for 18.3 million outpatient visits per year (4). Today, patients have a wide choice of health care practitioners to choose from to help manage their headaches. Medical care for headaches primarily consists of over the counter and prescriptive medication intervention (5,6). For a number of reasons, including the side effects from strong medication prescribed for many types of headaches (7), many patients search for complementary and alternative medicine (CAM) treatments, homeopathy being one CAM choice (8,9).

Homeopathy is a 200-year-old health care system, founded by Samuel Hahnemann, MD (10). Homeopathic treatment and its use of a case-by-case, or indi-

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vidualized, method of clinical practice is time consuming. In selecting a course of care, homeopaths often use a method called "classical" or "constitutional" prescribing, whereby the specific aspects of a homeopathic remedy are carefully matched to the specific aspects of the patient's complaints. With this method, the specific selection of the remedies depends not only on symptoms and the disease itself, but also on the temperament, constitution, disposition, vitality and lifestyle of the patient. This approach is thought to result in high patient satisfaction, as well as improved outcomes (9). There are over 3,000 available remedies (11). The most commonly available strength is 30C potency, which is highly diluted.

The purpose of this paper is to systematically review peer-reviewed, published prospective trials relating to the use of homeopathic treatment for symptomatic headaches and focuses on the three most common types of headache, as determined by the International Headache Society: tension type headache, cervicogenic headache and migraine headache (12).

METHODS

Data Sources and Study Selection

Five databases were searched according to the strategy in Table 1. Studies were further identified through a manual search of obtained article references. Additionally, three authors of retrieved articles were located and contacted, with no reply obtained.

Randomized clinical trials and prospective observational studies were included if they had at least ten subjects in the homeopathic portion of the trial. Treatment in these studies included single dose and individualized, classical homeopathic prescription. English and non-English articles were included.

Studies that used homeopathic preparations containing multiple homeopathic remedies or potencies, in single remedy dose, introduced other CAM therapies and/or introduced additional medical therapy for patients in the homeopathic treatment groups were excluded. Case studies and homeopathic provings were excluded since they lack adequate evidence or prospective designs that aid in establishing a cause and effect relationship. Homeopathic provings are empirical studies where healthy subjects self-report the symptoms they feel are produced by taking homeopathic preparations. No unpublished material or non-peer reviewed literature were included in this research in an effort to focus this review on publications that have met the scrutiny of peer-review.

Data Extraction

The following were extracted from each paper and entered into a Microsoft Excel 1998 for MacIntosh spreadsheet: author; headache type; study design; sample size; duration; intervention; and outcomes. Each study was analyzed to see if the care provided to patients in homeopathic treatment groups was typical of homeopathic practice.

TABLE 1
SEARCH STRATEGIES

DATABASE	YEARS SEARCHED	SEARCH STRINGS USED	# STUDIES IN SEARCH
PRE-MEDLINE/MEDLINE*	JANUARY 1964–MAY 2002	HOMEOPATHY & HEADACHE	9
		HOMEOPATHY & MIGRAINE HEADACHE	15
		HOMEOPATHY & TENSION HEADACHE	0
		HOMEOPATHY & CERVICOGENIC HEADACHE	0
MANUAL AND NATURAL THERAPIES INDEXING SYSTEM (MANTIS)*	1880–MAY 2002	HOMEOPATHY & HEADACHE	26
		HOMEOPATHY & MIGRAINE HEADACHE	19
		HOMEOPATHY & TENSION HEADACHE	0
		HOMEOPATHY & CERVICOGENIC HEADACHE	0
		HOMEOPATHY & OCCIPITAL HEADACHE	0
COCHRANE*	THROUGH MAY 2002	HOMEOPATHY & HEADACHE	0
ALLIED AND COMPLEMENTARY MEDICINE DATABASE (AMED)*	1985–APRIL 2002	HOMEOPATHY & HEADACHE	58
		HOMEOPATHY & MIGRAINE	39
		HOMEOPATHY & CERVICOGENIC HEADACHE	1
		HOMEOPATHY & TENSION HEADACHE	0

* THE TERM "HOMEOPATHY" WAS COMBINED WITH EACH OF THE FOLLOWING WORDS AND YIELDED NO HITS: SINUS HEADACHE, PREGNANCY, POST TRAUMATIC, OCCIPITAL HEADACHES.

Assessment of Methodological Quality of Included Papers

A critical evaluation list of 20 methodological items and their operational definitions was used to assess each paper (see Appendix). Fourteen of the items addressed validity issues, yielding a validity score, and six items concerned descriptive information. The validity score was calculated based upon the number of points awarded to each item. For items not applicable to a particular study, a rating of "not applicable" (NA) was awarded to that item and it was not calculated into the validity score. This scoring system is a modification of previously used instruments, and is based on work done by Bronfort and colleagues (13). The evaluation list was nominally modified to make it clearer to read and use. Modifications included the conversion of Bronfort et al's questions into sentences and some minor syntax and grammar corrections. This methodological tool was used due to its precedence; it has been used in two additional meta-analyses published in high quality, scientific journals (14,15). Since the evaluation list focused on issues related to the internal validity of clinical trial designs, it seemed reasonably applicable to homeopathic studies. The methodological scoring of the studies was performed by the two authors independently. Differences in scores were resolved through consensus by the two reviewers. The validity scores of the individual studies were used as part of the evidence determination.

RESULTS

Characteristics of Papers Reviewed

Six studies were included in this review (16–21). A summary of the characteristics of these papers is presented in Table 2.

Three of the six papers studied migraine headache (16,18,21) while two studied cervicogenic and tension type headache (19,20). The remaining study included all types of headaches (17). Four of the six studies were randomized controlled trials (16,18,19,21) and two were prospective observational studies (17,20). Sample size ranged from 18 to 98 subjects. Five of the six studies had a four to six month study duration (16–19,21) while one study had a one year duration (20).

Interventions in five of the six studies were individualized homeopathic prescriptions (17–21). The remaining study had a single dose of a 30c potency given four times over a two week period (16); this study limited remedies to eight commonly used headache remedies and excluded subjects that did not present with headaches requiring one of these remedies. Of the five studies mentioned above, one of these studies individualized a homeopathic prescription that had been agreed upon by a practitioner group to minimize remedy selection error (17).

TABLE 2
CLINICAL TRIALS OF HOMEOPATHY FOR HEADACHE

AUTHOR	HEADACHE	STUDY DESIGN	SAMPLE SIZE	DURATION	INTERVENTION	OUTCOMES
WALACH 1997 (19)	CHRONIC HEADACHE	RANDOMIZED CONTROLLED TRIAL	98	6 WEEKS BASELINE 3 MONTHS TREATMENT	INDIVIDUALIZED HOMEOPATHIC PRESCRIPTION	BOTH HOMEOPATHIC AND PLACEBO REDUCTION IN ALL CATEGORIES*
STRAUMSHEIM 1997 (18)	MIGRAINE	RANDOMIZED CONTROLLED TRIAL	73	1 MONTH BASELINE 4 MONTHS TREATMENT	INDIVIDUALIZED HOMEOPATHIC PRESCRIPTION	BOTH HOMEOPATHIC AND PLACEBO REDUCTION IN ALL CATEGORIES*
BRIGO 1991 (16)	MIGRAINE	RANDOMIZED CONTROLLED TRIAL	60	4 MONTHS	SINGLE DOSE 30C/4X IN 2 WKS	SUPERIOR TO PLACEBO ALL CATEGORIES*
WHITMARSH 1997 (21)	MIGRAINE	RANDOMIZED CONTROLLED TRIAL	60	4 MONTHS	INDIVIDUALIZED HOMEOPATHIC PRESCRIPTION	CHANCE DIFFERENCE IN ALL CATEGORIES*. BOTH GROUPS IMPROVED.
MUSCARI-TOMAIOLI 2001 (17)	ALL TYPES	PROSPECTIVE OBSERVATIONAL	53	4–6 MONTHS	INDIVIDUALIZED HOMEOPATHIC PRESCRIPTION	>60% IMPROVEMENT
WALACH 2001 (20)	CHRONIC HEADACHE	PROSPECTIVE OBSERVATIONAL	18	1 YEAR	INDIVIDUALIZED HOMEOPATHIC PRESCRIPTION	>30% IMPROVEMENT HOMEOPATHIC GROUP, MOST WITHIN 12 WKS

* CATEGORIES: FREQUENCY, INTENSITY, SEVERITY AND LEVEL OF MEDICATION.

The outcomes from the homeopathic intervention covered the following categories: frequency, intensity, severity, duration and level of medication necessary for attacks. For the randomized trials one study showed (unspecified percent) homeopathic remedy group improvement (16), the remaining three studies showed improvement in homeopathic and placebo groups (18,19,21). For the prospective, observational studies one study found greater than 60% improvement in homeopathic subjects (17) and the other study found greater than 30% improvement in the homeopathic subjects (20).

Quality Assessment

The critical evaluation list contains 20 items (A–T) of which 14 (B–G, J, L–N, P–S) are classified as validity items related to the quality of the scientific rigor of the research and six (A, H, I, K, O and T) as information items. The Appendix contains a description of each item.

Validity scores derived from the quality assessment criteria ranged from 25.0% to 64.3% for the clinical trials and the observational studies scored 44.4% and 55.5% (Table 3). Four studies possessed groups that were comparable at baseline (16,18,19,21); the two prospective observational studies did not include this type of comparison as it is not part of the research design (17,20). In one case, the number of subjects reported in the text did not match the number of subjects listed in the data table (18). One of the four randomized trials adequately described the randomization procedure (19), two studies partially described randomization (16,18), one did not adequately describe randomization (21), and randomization was not applicable to the two prospective observational studies (17,20).

All studies included at least one main outcome measure pertaining to headache (16–21). Quality of life and other health parameters that changed during the course of homeopathic care were noted in some studies in addition to the primary outcomes. Improvements in emotional and gastrointestinal complaints (17) and hopelessness, anxiety and stress were reported (20). With the exception of one study that employed the SF-36 questionnaire (17), quantifiable outcome measures for such factors were not reported.

Three papers adequately described methods to illustrate that the patients were blinded to the degree possible (16,18,19) and three did not (17,20,21). Three of the six studies provided information which established that treatment providers were blinded to the degree possible (16,18,19), one study partially described provider blinding (17) and two did not (20,21). One study adequately demonstrated that the assessment of primary outcome measures was unbiased (19), two partially explained this (17,18) and three did not (16,20,21). None of the studies adequately addressed the impact of the amount of provider contact, provider enthusiasm or number of intervention sessions (16–21). The study hypothesis was clearly presented in one paper (20), partially in four (16–19) and not presented in one study (21).

The choice of statistical test(s) for the main results was partially appropriate in two studies (18,19) inappropriate in two (16,21) and not applicable for two (17,20). Adequate statistical power to detect an *a priori* determined between-group difference was adequately performed in one paper (21), partially performed in one (18), not described in two (16,19) and not applicable in the two prospective observational studies (17,20).

Dropouts were partially described and accounted for in three of the four clinical trials (18,19,21), not adequately described for one (16) and adequately described in the two observational studies (17,20). An intention-to-treat analysis was indicated in all four of the clinical trials, yet only one partially described this

TABLE 3
METHODOLOGICAL QUALITY SCORES OF CLINICAL TRIALS EVALUATING HOMEOPATHIC TREATMENT OF HEADACHES

	VALIDITY ITEMS																			
REF#	B	C	D	E	F	G	J	L	M	N	P	Q	R	S	SCORE %	A	H	I	K	O	T
19	+	+	+	+	+	+	–	P	P	–	P	–	P	+	64.3	+	P	P	–	P	+
18	+	P	+	+	+	P	–	P	P	P	P	–	–	+	57.1	+	P	P	+	–	P
16	+	P	+	+	+	–	–	P	–	–	–	NA	–	–	38.5	+	+	P	–	–	P
21	+	–	+	–	–	–	–	–	–	+	P	–	–	–	25.0	+	–	P	–	–	+
17	NA	NA	+	–	P	P	–	P	NA	NA	+	+	NA	P	55.5	+	+	+	+	NA	+
20	NA	NA	+	–	–	–	–	+	NA	NA	+	–	NA	+	44.4	+	–	P	+	NA	+

'+' = YES, '–' = NO, 'P' = UNCLEAR, 'NA' = NOT APPLICABLE.
SEE APPENDIX FOR CRITERIA DESCRIPTION.

process (19). Finally, three of the six studies appeared to make adjustments for the number of statistical tests (two or more) when establishing cut-off probability levels for each test (18,19,20), one was partially described (17) and two did not describe such adjustments (16,21).

All six studies contained inclusion and exclusion criteria that were clearly defined (16–21). Two studies included adequate post-intervention follow-up of at least three months (16,17), two studies had partially adequate follow up (18,19) and two studies did not (20,21). One study (17) adequately described all interventions with a defined protocol, the remaining five studies partially described these interventions (16,18–21). Three papers clearly made comparisons to existing efficacious or commonly practiced treatment option(s) (17,18,20) while three studies did not (16,19,21). One of the studies partially included or calculated confidence intervals (19), three did not (16,18,21) and this was not applicable in the two observational studies (17,20). Four of the six studies stated valid conclusions which were directly related to the primary objectives of the study (17,19–21) and two received partial scores (16,18).

DISCUSSION

Interpretation of Results

For several years, researchers of homeopathy have continued to investigate whether homeopathy is superior to placebo. This review found that for headaches homeopathy was superior to placebo in one randomized trial (16) and equal to placebo in three (17,20,21). In no studies reviewed was homeopathy found less effective than placebo in treating headache, or harmful. While not randomized controlled trials, both prospective observational studies reported improvement in at least thirty percent of patients receiving homeopathic care (17,20).

Prior systematic reviews investigating the effectiveness of homeopathy for various conditions have reported similar results. While one review of the literature reported that homeopathy was superior to placebo for a variety of conditions, it clearly noted that the methodological quality of the reviewed studies was highly variable (22). A 1997 meta-analysis indicated that while some improvements in patient outcomes have been noted in some trials, there is not sufficient evidence to demonstrate that homeopathy is clearly efficacious for any single condition and again commented on the need for better quality trials (23). A more recent systematic review reported that homeopathy was not effective in the prophylaxis of migraine headaches and further noted the paucity of literature available for review (24). The present review concurs with earlier studies and indicates that the debate continues whether homeopathy acts as a placebo or an effective intervention.

Investigators should seriously consider the quality of future studies if the effectiveness of homeopathy is ever to be determined. Controlled clinical studies are useful in bridging the gap between empirical homeopathic reports and a peer-reviewed, scientific evidence base. However, the validity scores for the studies reviewed in this paper ranged from 25.0% to 64.3% for the randomized clinical trials, and from 44.4% to 55.5% for the prospective observational studies. Therefore, finding a research model with both high relevance to homeopathic practice and rigorous research protocols is a challenge.

The need for pilot studies has been mentioned in homeopathic literature (17) because they render research of higher quality and greater adherence to scientific standards (22). Pilot studies aid the researcher in identifying the most serious problems which might occur in the planned full study. Because of the planning invested in pilot studies, the monitoring and evaluation that takes place later in the larger study is easier to conduct (25). Five of the six studies reviewed here utilized no pilot study to assist in developing an internally valid study design. One study (17) was a prospective observational study, which was designed as a pilot study. Based upon our evaluation of the literature, we concur with other authors. Investment in this crucial planning process may have yielded studies with higher validity scores.

The majority of studies reviewed in this study suffered from poor report format and writing style. Pertinent information was often scattered in a disorganized fashion throughout articles, making it difficult to read and extract information for this review. With the exception of two studies (18,20), hypotheses/objectives were not clearly delineated. With a weak hypothesis and sometimes vague conclusions, it was difficult to assume validity of a study due to the resulting poor study design or poor reporting. Adherence to a research protocol such as that detailed in the CONSORT statement (26) would greatly benefit future clinical trials and systematic reviews. The CONSORT statement contains a checklist and flow diagram which has been adopted by leading medical journals and major international editorial groups to facilitate critical appraisal and interpretation of RCTs.

Another area of weakness in the studies reviewed was the lack of consistent blinding of the subjects, practitioners, and assessors. To determine the initial remedy

prescription and follow up intervention there is a high level of contact between the subjects and the providers. Therefore, it is a difficult task to blind the subjects and the practitioners in this setting. Added problems which may be associated with or result from this flaw must be factored into the research design and may include: additional input from enthusiastic practitioners, follow-up which provides for an in-depth and sometimes repeated conversation with the patient, and a succession of different medicines (20).

With a high level of contact between the subjects and the homeopaths, things such as verbal clues, encouragement and empathy may be used by some homeopaths more than others. Such factors should be accounted for in future studies to better elicit whether homeopathy demonstrates effectiveness over placebo. Blinding of the homeopath may be achieved to some degree by the use of a pharmacist who is blinded to the rest of the study. This pharmacist could dispense active remedies and placebos to patients who are randomly assigned to one of the two groups without communication with homeopaths involved in the study (17,27).

Protocols used to select specific homeopathic remedies were not adequately described in most of the studies we reviewed (16,19–21). A description of the homeopathic remedy selection protocol must be included to inform the reader of how and why the homeopathic treatment was selected and the degree to which it reflects actual homeopathic practice. Classical homeopathy uses various prescription methods such as keynote, totality or essence. Regardless of method, the goal of classical homeopathy is to find the most suitable individual remedy (10,17). A suggested protocol, similar to the design used by Muscari-Tomalioli (17) could include consensus of all participating doctors on two remedies most likely to be correct. Such a study would not accept patients for whom consensus is not reached (17). Additionally, authors need to account for the pharmacological effects of traditional medicines if patients are taking them during clinical trials and describe how this is factored into the homeopathic remedy selection.

Study duration ranged from one month to one year in the studies we reviewed; only one study was of greater duration than three months (19). Study design should take into account the type of therapeutic intervention; homeopathy is considered a "gentle" or "soft" therapeutic intervention. The treatment effects may generally be expected to be small and the improvements in patients' conditions may not be observable until after a longer period of treatment. The length of study should consider this variable. Suggested solutions for this would be long-term trials with large numbers of subjects (20). Another argument for longer treatment duration is that if the patients have been chronically ill, therapeutic results may not present in a short-duration study (19).

Some of the greatest problems in the studies reviewed resided in the selection and use of statistical methods. Randomization procedures were poorly described in the clinical trials, causing one to ponder whether the studies were truly randomized clinical trials. Given that the choice of statistical test was only partially described in two studies, there remains much skepticism as to whether or not the reported differences between groups were accurate.

Study Limitations

The production of credible homeopathic research is a recent phenomenon. It is taking some time for the holistic, homeopathic field to reconcile how it can conduct research that is true to its philosophy but also withstands the scrutiny of reductionistic experimental research. With homeopathic research in its infancy, there is little research to review. Therefore, this study was restricted by the limited quantity of homeopathic clinical trials currently available in the peer-reviewed literature that met the inclusion criteria. While the possibility remains that we are subject to publication bias, we feel that our search criteria incorporated the indexing systems most likely to contain relevant information and we did review the references from each article obtained for further potential studies.

A potential flaw of making conclusions from a review of the limited and unfavorable literature currently available is that it could lead towards a premature negative bias. Another flaw of this study is that clinical trials investigating multiple headache types were reviewed. This is a potential problem because many variables are investigated, which is uncharacteristic of systematic reviews.

Poor reporting methods by the authors of the studies reviewed may have inadvertently introduced a source of error into this review because information to be extracted was difficult to find. To account for this, items were located within each study in a sequential, deliberate manner progressing from criterion A through T of the scoring tool.

The scoring method utilized in appraising the papers, while adapted from a reputable source (13), may require further detail and refinement in future analyses. It seemed to adapt well to homeopathic trials, however, it

is unknown if any validity of the scoring method is lost through this adaptation.

Problems with statistical methodology and reporting by the authors of the studies reviewed introduce bias into the interpretation of these studies. As such, caution is exercised when interpreting the data as it pertains to the relative effectiveness or efficacy of homeopathy for headaches.

CONCLUSION

There is insufficient evidence to support or refute the use of homeopathy for tension type headache, cervicogenic headache and migraine headache. The studies reviewed, overall, showed many flaws in design and there were few studies to review. The present review found that homeopathy was superior to placebo in one randomized clinical trial and equal to placebo in three. In no study was homeopathy found to be less effective than placebo in treating headache, or harmful. Two prospective observational studies demonstrated improvement in patients receiving homeopathic care. Given the insufficient quality and quantity of the literature, further research is warranted to better investigate the effectiveness of homeopathic treatment of chronic headaches.

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REFERENCES

1. Rasmussen BK. Epidemiology of headache in a general population-a prevalence study. J Clin Epidemiol 1991;44:1147–57
2. Castillo J, Munoz P, Guitera V, Pascual J. Epidemiology of chronic daily headache in a population sample. Headache 1999;39:190–6
3. Scher A, Stewart W, Liberman J, Lipton R. Prevalence of frequent headache in a population sample. Headache 1998;38:497–506
4. Current estimates for the National Heath Interview Survey. United States, 1984. Vital & Health Statistics-Series 10: Data From the National Health Survey; 1986;156:1–191
5. Edmeads J, Findlay H, Tugwell P, Pryse-Phillips W. Impact of migraine and tension-type headache on life-style, consulting behavior, and medication use: A Canadian population survey. Can J Neurol Sci 1993;20:131–7
6. Pollmann W, Keide M, Pfaffenrath V. Headache and the cervical spine: a critical review. Cephalgia 1991;17:801–16
7. Pryse-Phillips W, Dodick D, Edmeads J, et al. Guidelines for nonpharmacologic management of migraine in clinical practice. Can Med Assoc J 1997; 156:1273–87
8. Kessler RC, Davis R, Foster D, et al. Long-term trends in the use of complementary and alternative medical therapies in the United States. Ann Int Med 2001;135:262–8
9. Eisenberg D, Kessler R, Van Rompay M, et al. Perceptions about complementary therapies relative to conventional therapies among adults who use both: Results from a national survey. Ann Int Med 2001;135:344–51
10. Hahnemann S. Organon of medicine. 5th ed. New Dehli, India: B Jain Publishers; 1994
11. Clarke J. A dictionary of practical materia medica, vol 1–3. New Dehli, India: B Jain Publishers; 1994
12. IHS, Headache Classification Committee. Classification for headache disorders, cranial neuralgias and facial pain. Cephalgia 1988;7(Suppl):1–96
13. Bronfort G, Assendelft W, Evans R, Haas M, Bouter L. Efficacy of spinal manipulation for chronic headache: a systematic review. J Manipulative Physiol Ther 2001;24:457–66
14. Koes BW, Assendelft W, van der Hejiden GH, Bouter LM, Kinpschild PG. Spinal manipulation and mobilization for back and neck pain: a blinded review. BMJ 1991;303:1298–1303
15. Assendelft W, Koes BW, Geert JMG, van der Heijden GH, Bouter LM. The effectiveness of chiropractic for treatment of low back pain: An update and attempt at statistical pooling. J Manipulative Physiol Ther 1995;19: 499–507
16. Brigo B, Serpelloni G. Homeopathic treatment of migraine: A sixty case, double-blind, controlled study (homeopathic remedy vs. placebo). Berlin J Research Homeo 1991;1:98–102
17. Muscari-Tomaioli G, Allegri F, Miali E, et al. Observational study of quality of life in patients with headache, receiving homeopathic treatment. Br Hom J 2001;90:189–97
18. Straumsheim P, Borchgrevink C, Mowinckel P, Kierulf H, Hafslund C. Homeopathic treatment of migraine: a double blind, placebo controlled trial of 68 patients. Br Hom J 2000;89:4–7
19. Walach H, Haeusler W, Lowes T, et al. Classical homeopathic treatment of chronic headaches. Cephalgia 1997;17:119–26
20. Walach H, Lowes T, Mussbach W, et al. The long-term effects of homeopathic treatment of chronic headaches: one year follow-up and single case time series analysis. Br Hom J 2001;90:63–72
21. Whitmarsh T, Coleston-Shields D, Steiner T. Double-blind randomized placebo-controlled study of homeopathic prophylaxis of migraine. Cephalgia 1997;17:600–4
22. Linde K, Melchart D. Randomized controlled trials of individualized homeopathy: a state-of-the-art review. J Alt Comp Med 1998;4:371–4
23. Linde K, Clausius N, Ramirez G, et al. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. Lancet 1997; 350:834–43
24. Ernst E. Homeopathic prophylaxis of headaches and migraine? A systematic review. J Pain Symptom Management 1999;18:353–7
25. Gaus W, Hogel J. Studies on the efficacy of unconventional therapies. Problems and designs. Arzneimittelforshung 1995;45:88–92
26. Altman D, Shultz K, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Int Med 2001;134:663–94
27. Whitmarsh T. More lessons from migraine. Br Homeo J 1989;1:1–2

APPENDIX
CRITERIA FOR QUALITY ASSESSMENT OF STUDIES REVIEWED

SCORING:

- YES SCORE (+) IS ONLY USED WHEN ALL DESCRIBED INDIVIDUAL ITEM CRITERIA ARE MET. A YES SCORE = 1 POINT.
- NO SCORE (–) IS ONLY USED WHEN IT IS CLEAR FROM THE ARTICLE THAT NONE OF THE DESCRIBED INDIVIDUAL ITEM CRITERIA ARE MET. A NO SCORE = 0 POINTS.
- UNCLEAR/PARTLY (P) IS USED WHEN THE DOCUMENTATION OR DESCRIPTION IS INSUFFICIENT TO ANSWER ANY OR ALL OF THE DESCRIBED INDIVIDUAL ITEM CRITERIA. AN UNCLEAR/PARTLY SCORE = _ POINT.
- NOT APPLICABLE (NA) IS NON APPLICABLE AND NOT INCLUDED IN PERCENT SCORES.
- VALIDITY SCORE (VS) IS THE PERCENTAGE SCORE OF THE APPLICABLE VALIDITY ITEMS.

CRITERIA:

A. INCLUSION AND EXCLUSION CRITERIA ARE CLEARLY DEFINED AND STATED EXPLICITLY. THE SCORE IS UNCLEAR/PARTLY IF A MORE DETAILED DESCRIPTION WAS NEEDED, OR ONLY INCLUSION OR EXCLUSION CRITERIA WERE CLEARLY DEFINED.

B. THE GROUPS ARE COMPARABLE AT BASELINE. IF THE GROUPS ARE DIFFERENT, APPROPRIATE ADJUSTMENTS SHOULD BE MADE DURING THE STATISTICAL ANALYSIS. COMPARABILITY SHOULD BE PRESENT ESPECIALLY FOR MAIN OUTCOMES, BUT ALSO FOR IMPORTANT CLINICAL AND DEMOGRAPHIC VARIABLES, SUCH AS AGE, GENDER, DURATION AND SEVERITY OF CONDITION, AND KNOWN PROGNOSTIC INDICATORS.

C. THE RANDOMIZATION PROCEDURE IS ADEQUATELY DESCRIBED AND APPROPRIATE. A NO SCORE IS GIVEN IF IT IS ONLY NOTED THAT RANDOMIZATION WAS USED. A YES SCORE IS GIVEN IF THE RANDOMIZATION PROCESS IS DESCRIBED (I.E., RANDOMLY GENERATED LISTS, OPAQUE ENVELOPES), THE METHOD USED (E.G. SIMPLE, BLOCK, STRATIFICATION, MINIMIZATION) MUST BE APPROPRIATE, AND THE CONCEALMENT OF RANDOMIZATION MUST BE DESCRIBED EXPLICITLY. AN UNCLEAR/PARTLY SCORE IS GIVEN WHEN ONE OR TWO OF THESE CRITERIA ARE MET.

D. AT LEAST ONE MAIN OUTCOME MEASURE RELEVANT TO THE CONDITION UNDER STUDY MUST BE USED. THE RELIABILITY AND VALIDITY OF THE OUTCOME MEASURE SHOULD BE DOCUMENTED BY EITHER INVESTIGATION, APPROPRIATE REFERENCES, OR BE GENERALLY ACCEPTED (E.G. VAS SCALES, OSWESTRY, OR ROLAND-MORRIS DISABILITY SCALES). IF ALL OF THE ABOVE CONDITIONS ARE NOT MET, A NO SCORE IS GIVEN.

E. THE SUBJECTS MUST BE BLINDED TO THE DEGREE POSSIBLE AND DISCUSSION REGARDING THE EFFECTIVENESS OF THE BLINDING PROCEDURE SHOULD BE PROVIDED. IF THIS CRITERION DOES NOT APPLY TO A STUDY (E.G., A COMPARISON OF A DRUG AND PHYSICAL THERAPY), THE SCORE IS 'NA'. A SCORE OF UNCLEAR/PARTLY IS THE HIGHEST ATTAINABLE IN EITHER OF THE FOLLOWING SITUATIONS:
   1. THE PRESENCE OF EITHER "OPTIMAL BLINDING" OR "EFFECTIVENESS OF BLINDING" IS NOT DOCUMENTED.
   2. IF AT LEAST ONE STUDY INVOLVES A "BLINDABLE" INTERVENTION, THEN THE EFFECTIVENESS OF THE BLINDING MUST BE DOCUMENTED.

F. IT SHOULD BE ESTABLISHED THAT TREATMENT PROVIDERS WERE BLINDED TO THE DEGREE POSSIBLE, AND THAT THIS BLINDING WORKED.

G. ASSESSMENT OF THE PRIMARY OUTCOMES MUST BE UNBIASED. IF APPLICABLE, ACTIONS TAKEN TO BLIND THE ASSESSMENT OF OUTCOMES SHOULD BE DESCRIBED. EFFECTIVENESS OF BLINDING MUST BE DOCUMENTED. DOCUMENTATION REGARDING PROVIDERS' OR INVESTIGATORS' INFLUENCE ON HOW SUBJECTS SCORED THEIR OWN OUTCOMES SHOULD BE PRESENTED.

H. THE POST-INTERVENTION FOLLOW-UP PERIOD SHOULD BE ADEQUATE AND CONSISTENT WITH THE NATURE OF THE CONDITION UNDER STUDY. THE MINIMUM FOLLOW-UP PERIOD IS ONE MONTH FOR ACUTE CONDITIONS AND THREE MONTHS FOR CHRONIC CONDITIONS IN ORDER TO RECEIVE A YES SCORE. A MINIMUM OF TWO WEEKS FOR ACUTE CONDITIONS AND ONE MONTH FOR CHRONIC CONDITIONS MUST BE MET FOR AN UNCLEAR/PARTLY SCORE. THIS CRITERION MAY NOT APPLY TO SOME STUDIES (E.G., CROSSOVER DESIGNS).

I. INTERVENTIONS SHOULD BE ADEQUATELY DESCRIBED AND ALL INTERVENTIONS SHOULD FOLLOW A DEFINED PROTOCOL. IT SHOULD BE POSSIBLE TO REPLICATE THE SAME TREATMENT IN A CLINICAL SETTING.

J. DIFFERENCES IN ATTENTION BIAS BETWEEN GROUPS SHOULD BE CONTROLLED AND EXPLICITLY DESCRIBED. TIME, PROVIDER ENTHUSIASM AND NUMBER OF INTERVENTION SESSIONS MUST BE EQUIVALENT AMONG STUDY GROUPS.

K. COMPARISON OF THE INTERVENTION SHOULD BE MADE TO EXISTING EFFICACIOUS OR COMMONLY PRACTICED TREATMENT OPTION(S). IF A PLACEBO CONTROLLED STUDY, A COMPARISON TO AN EXISTING EFFICACIOUS STANDARD SHOULD BE MADE PREVIOUSLY.

L. THE PRIMARY STUDY OBJECTIVE (HYPOTHESIS) IS CLEARLY DEFINED IN TERMS OF GROUP CONTRASTS, OUTCOMES, AND TIME POINTS *A PRIORI*. (MANY STUDIES PRESENT BIASED POSTHOC CONCLUSIONS.)

M. THE CHOICE OF STATISTICAL TEST(S) FOR THE MAIN RESULTS IS APPROPRIATE. THE MAIN ANALYSIS SHOULD BE CONSISTENT WITH THE DESIGN AND THE OUTCOME VARIABLES USED.

N. ADEQUATE STATISTICAL POWER (BETA = 0.2 WITH ALPHA = 0.05) TO DETECT AN *A PRIORI* DETERMINED CLINICALLY IMPORTANT BETWEEN-GROUP DIFFERENCE BETWEEN PRIMARY OUTCOMES IS ESTABLISHED AT RANDOMIZATION. THIS MAY INCLUDE ADJUSTMENT OF MULTIPLE TESTS AND/OR OUTCOME MEASURES.

O. CONFIDENCE INTERVALS (CI), OR DATA ALLOWING CI TO BE CALCULATED, ARE PRESENTED.

P. ALL DROPOUTS ARE DESCRIBED FOR EACH STUDY GROUP SEPARATELY AND ACCOUNTED FOR IN THE ANALYSIS OF THE MAIN OUTCOMES. ANALYSIS OF IMPACT OF DROPOUTS OR WORST/BEST CASE ANALYSIS IS INCLUDED. ALMOST ALL STUDIES WITH APPROPRIATE FOLLOW-UP PERIODS THAT EVALUATE THE EFFECTS OF THERAPEUTIC MANAGEMENT OF A CONDITION WILL HAVE SOME ATTRITION (>5%). IF THERE ARE NO DROPOUTS, AN EXPLANATION OR ADDRESS OF THIS ASPECT MUST BE INCLUDED TO OBTAIN A YES SCORE, OTHERWISE, THIS ITEM DOES NOT APPLY TO THE STUDY. AN EXAMPLE OF A 'NA' SCORE WOULD BE A STUDY IN WHICH THERE IS ONE INTERVENTION AND THE OUTCOMES ARE COLLECTED IN THE SAME SESSION.

Q. ALL MISSING DATA FROM EACH STUDY GROUP MUST BE DESCRIBED AND ACCOUNTED FOR SEPARATELY IN THE ANALYSIS OF THE MAIN OUTCOMES. ANALYSIS OF THE IMPACT OF MISSING DATA SHOULD BE PRESENTED. ALMOST ALL STUDIES THAT EVALUATE THE EFFECTS OF THERAPEUTIC MANAGEMENT OF A CONDITION WILL HAVE MISSING DATA (>5%). IF THERE IS NO MISSING DATA, THIS CRITERION IS NOT APPLICABLE.

R. IF INDICATED, AN INTENTION-TO-TREAT ANALYSIS SHOULD BE USED. IN STUDIES WITH DOCUMENTED FULL COMPLIANCE WITH ALLOCATED TREATMENTS, AND NO DIFFERENTIAL CO-INTERVENTION BETWEEN GROUPS, A YES SCORE CAN APPLY. IN SINGLE SESSION STUDIES (E.G., STUDIES WITH ONE INTERVENTION AND OUTCOMES COLLECTED IN SAME SESSION) THIS CRITERION IS NOT APPLICABLE.

S. ADJUSTMENTS ARE MADE FOR THE NUMBER OF STATISTICAL TESTS (2 OR MORE) WHEN ESTABLISHING THE CUT-OFF POINT FOR THE *P*-LEVEL FOR EACH TEST. IF APPLICABLE, IT SHOULD BE DOCUMENTED THAT THIS MAY HAVE INFLUENCED THE OUTCOME OF THE STUDY (AVOIDANCE OF INCREASING RISK OF TYPE I ERRORS) AND APPROPRIATE STATISTICAL ADJUSTMENTS SHOULD BE MADE (E.G. BONFERRON'S OR SIMILAR TYPE OF ADJUSTMENTS). IF INDICATED ADJUSTMENT(S) WERE INCAPABLE OF CHANGING THE MAIN RESULT/OUTCOME OF THE STUDY, OR IF THE STUDY INVOLVED ONLY ONE TEST AT ONE POINT IN TIME, THIS CRITERION IS NOT APPLICABLE.

T. CONCLUSIONS ARE STATED THAT ARE VALID AND DIRECTLY RELATED TO THE PRIMARY OBJECTIVE(S) OF THE STUDY. A *PRIORI* TESTABLE HYPOTHESES SHOULD BE TESTED AND PRIORITIZED APPROPRIATELY IN THE CONCLUSIONS (ALSO SEE CRITERION L).