

Epidemiology of Research for Temporomandibular Disorders

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A systematic review was performed in response to a request by the National Institute of Dental Research to evaluate in broad terms the strength of evidence regarding therapy for temporomandibular disorders (TMD). This report describes the epidemiology of research for TMD in broad terms indicating the total number of citations, the proportion related to therapy, and the distribution according to study design and language or country of origin. Med-line and hand searching of article bibliographies and of selected journals produced the set of citations evaluated. From 1980 to 1992, there were more than 4,000 references to TMD, of which about 1,200 regarded therapy. Forty-one percent of the 1,200 references were classified as reviews and only 15% were clinical studies. Less than 5% (n = 51) were randomized controlled trials. This review identified a vast amount of literature on TMD with articles published in several different languages, indicating a worldwide interest in this problem. Because assimilation of this literature cannot be expected of the average practitioner treating patients who have TMD, or of most researchers in this area, it is likely not being used to its maximum potential. The literature on therapy for TMD consists primarily of uncontrolled observations of patients such as uncontrolled clinical trials, case series, case reports, and simple descriptions of techniques. It is generally agreed that such uncontrolled observations, while contributing to knowledge about therapy of TMD, are subject to considerable bias and thus difficult to interpret. If treatment of TMD is going to follow the trend in medicine to base patient-care decisions on evidence rather than expert opinion or pathophysiologic rationales, then more rigorously controlled clinical trials of most therapies will be necessary.

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As trends in health care require that decisions be based on evidence or data rather than expert opinion or clinical best guesses,¹ efforts are needed to systematically identify what evidence is available and process it to make the findings more accessible to clinicians treating patients. One example of how this has been done is the Oxford Database of Perinatal Trials, a database of 600 systematic reviews based on more than 7,000 randomized controlled trials (RCTs) in the field of pregnancy and childbirth.² The focus is on RCTs rather than other sources of data because RCTs are generally recognized as the most reliable source of information regarding the effectiveness of health care practices. This database differs from traditional textbooks or reviews in that

an extensive search to identify all RCTs evaluating particular practices is continuously being carried out, and the results of these RCTs are summarized and presented in a systematic and explicit manner. The database is published in both book and electronic formats so that updates can be made in a timely fashion. The International Cochrane Collaboration is replicating this database for all of health care.³

Studying the epidemiology of research of a particular area according to issues of design and scientific inference can be useful in several ways.⁴ A careful and systematic review can help to identify which areas have adequate data to answer research questions and where gaps in evidence exist. Classification of research reports can identify critical issues such as the relative frequencies of the use of various designs over time or across features, such as source of funding, country of origin, institution, journal, or type of therapy. This information can be used to assess the state of knowledge of a particular clinical area, identify the use or underuse of appropriate research methods, and contribute to the understanding of the development of science in a particular discipline.

The questions asked in many clinical research projects require the detection of differences so small, or involve the potential for such considerable confounding, that even the most astute and experienced clinician might not be able to observe them. Although rigorous scientific research designs are needed to answer these questions, they unfortunately are not always utilized. This has been demonstrated in many areas in the medical and dental literature.⁴⁻⁸ Fletcher and Fletcher⁶ found that the frequency of weak research designs actually increased in three general medical journals during the 30-year period from 1946 to 1976. Similarly, Solomon and McLeod⁷ classified clinical studies in three medical surgical journals for the years 1980 and 1990 and found no overall increase in the proportion of stronger clinical trial designs.

In a review of the *American Journal of Orthodontics and Dentofacial Orthopedics* sampling the years 1976, 1981, and 1986, Tulloch et al⁸ found a more promising trend: experimental research designs increased in number and proportion from four of 66 studies in 1976 to 12 of 64 studies in 1986. However, the review⁸ also found that case reports continued to represent the most frequently published format and that the majority of studies reported findings from uncontrolled observations. Although uncontrolled clinical studies, case reports, and case series can provide some evidence

that there is potential benefit from a treatment, only controlled clinical trials can reliably identify if and how much benefit is related to the particular therapy and not to the natural history or cyclical nature of the disease, or to the placebo effect. Since the research design used to study a clinical problem can influence the knowledge gained, classification of research reports according to issues of design can help assess the state of the art and development of science in a particular discipline or clinical area. A number of characteristics of clinical studies should be considered when classifying reports.

Research Classification

Experimental Versus Observational

The first distinction in classifying studies is whether they are experimental or observational. In observational studies, patients are simply observed over time without any intentional intervention; in experimental studies, subjects are observed following some intentional intervention.

Experimental studies can be either controlled or uncontrolled. Uncontrolled experimental studies in which comparisons are made either with historic controls or with population-based results can only provide weak evidence regarding therapy effectiveness.⁹ These studies are still widely used in developmental research, such as in phase I drug trials, to identify unexpected results or obtain initial baseline data, but they should not generally be considered an alternative to controlled studies. Controlled studies, especially randomized controlled studies, provide the strongest evidence for therapy effectiveness.

There is an association between the degree of control in a study and estimates of effectiveness.¹⁰⁻¹² Weaker designs, because of bias, provide more optimistic estimates of effectiveness than do more rigorously controlled designs. Uncontrolled trials are more likely than controlled trials to not only say a treatment is effective, but also to overestimate the magnitude of the effect.

Cross-Sectional Versus Longitudinal

The second distinction relates to whether the study follows subjects over some period of time (longitudinal), or simply collects information at one particular time period (cross-sectional). In general, cause-and-effect relationships can only be evaluated with longitudinal study designs.

Prospective Versus Retrospective

The third distinction considers the time perspective in longitudinal studies. If data is collected from the initial condition continuing forward in time, it is a prospective study. If data is collected after the initial time point backward in time, it is a retrospective study. Randomized controlled trials by design are prospective. Because many case series or uncontrolled clinical trials are retrospective, the ability to infer treatment effectiveness from them is limited.

Control of Bias

One of the most important aspects of clinical research is the consideration of how bias may be operating to affect the results and conclusions of studies. Bias can occur in five main areas of clinical research:

1. Selection of subjects to participate in the study
2. Allocation of subjects to the treatment and control groups
3. Assessment of treatment effect
4. Analysis of results
5. Reporting

The RCT has become the standard by which all other designs are judged precisely because of its ability to control bias.¹³ The several features of RCTs that work to minimize bias, including randomization, blinding, sample size determination, and the use of appropriate outcome measures and statistical analysis, are extensively discussed elsewhere.^{12,14-17} The reporting of clinical research has recently been identified as a source of additional biases. One bias involves the actual presentation of methods and results in a published report.^{12,14-26} Another, publication bias, relates to the rate of publication of research studies.²⁷⁻²⁹ This type of bias has been primarily identified as the failure of "negative studies" to reach print; thus, the studies that do reach publication, the "positive studies," are not a good representation of the universe of studies on a particular topic. The published literature is thus biased in favor of demonstrating a difference. This type of bias is especially worrisome when case reports or case series are being considered as evidence for the effectiveness of a therapy. Patients who do not respond positively to a therapy are less likely to remain for follow-up or be reported with a case series. These uncontrolled observations are particularly prone to bias showing a positive effect. Publication bias can also occur due to repeated publication of the same

data. Many studies have multiple publications based on the same or on a subset of the same data, either over time as data is collected, or with emphasis on subgroup analyses or with different outcome variables.^{30,31} This bias also serves to overestimate the positive effects of therapy when it is difficult to identify whether multiple reports are based on the same data set.

The present article is based on a systematic review of the literature performed in response to a request by the National Institute of Dental Research to determine the strength of evidence regarding therapy for temporomandibular disorders (TMD). Findings from a literature search for 1966 to 1992 are described in terms of the total number of citations, the proportion related to therapy, and the distribution according to research design and language and/or country of origin. A companion report (unpublished) considers in greater detail the subset of studies that are randomized controlled trials (RCTs) in terms of quality of the trials and content of the treatments evaluated.

The objective of the present systematic review was to identify all references to therapy for TMD and describe the epidemiology of research in this area by classifying the reports found.

Materials and Methods

Numerous reports have demonstrated that when searches are limited to electronic databases, a large proportion of relevant trials, often as many as half, may be missed.³²⁻³⁴ The current study used three methods to find clinical studies:

1. Medline searching
2. Review of the bibliographies of clinical studies and review articles
3. Hand searching of selected journals

The general findings from the Medline search are presented to provide an overview of the volume and distribution of papers by study type related to therapy of TMD for both English language and non-English language papers. Also reported are more specific findings from hand searching of four journals for the year 1991.

Medline Search

The subject heading words used to identify relevant citations for this analysis using the Medline database for the years 1966 to 1992 were: *temporomandibular joint diseases*; *temporomandibular joint syndrome*; and *myofascial pain syn-*

dromes. To identify clinical studies, the following terms were used: *treatment; clinical trials; comparative studies; case reports; and randomized controlled trials*. The resulting list of articles was reviewed and classified according to the following broad categories to study trends in the methods used to evaluate therapies for TMD:

1. Non-English: Medline can separate the English from non-English language publications.
2. Reviews: Articles identified by Medline as review articles, or by reading the abstract or full article.
3. Reports of techniques: Articles that describe a method, surgical technique, or instrumentation with or without an associated case report or case series.
4. Clinical studies: Articles describing RCTs, nonrandomized, or uncontrolled clinical trials.
5. Case reports/case series: Articles reporting a single case, or a series of cases.
6. Editorials: Articles that discuss issues without providing a traditional review of the literature.
7. Letters: Letters to the editor are identified by Medline.
8. Management: Articles that address issues of reimbursement or payment for TMD services, practice patterns for TMD, litigation, or legislation related to TMD.
9. Other: Articles that did not fit any of the above categories. Examples include epidemiologic reports, interviews with experts, or articles that could not be classified.

In an effort to identify as many randomized controlled trials as possible, full copies of studies identified as clinical trials by Medline and of most of the review articles were obtained. The reference lists of these papers were examined to identify any clinical studies missed by the Medline search. Further, an individual review by hand of each of the major journals that publish clinical studies of therapy for TMD was carried out to identify additional studies and to look at general trends in the use of study designs by journal and over time. The data reported in the classification scheme refer generally to references retrieved from the Medline search; therefore, it must be acknowledged that these findings are not exact due to limitations in Medline indexing and retrieval. Although classification categories were made purposefully broad and considerable effort was made to try to classify articles accurately, some misclassification has likely occurred and the proportions presented should be taken as trends rather than exact numbers. More specific categorization was not within the objectives of this project.

Hand Search of Four Journals

To gain more specific insight into the composition of the literature to which clinicians are likely to be exposed most recently, four journals that are either dedicated entirely to the study of craniomandibular disorders (*Journal of Craniomandibular Disorders; Facial and Oral Pain and Journal of Craniomandibular Practice*), or regularly contain references to TMD (*Journal of Prosthetic Dentistry and Journal of Oral and Maxillofacial Surgery*), were hand searched for the year 1991, the most recent complete year of publication. A number of study characteristics were considered, including study design, country of origin, and study subject characteristics.

Results

Table 1 reports the total number of references to therapy identified by the Medline search by Medline grouping of years. The number of references to TMD therapy increased dramatically from the period of 1966 to 1971 to the period of 1989 to 1992. At the time of this search (July 1992), the period 1989 to 1992 was incompletely entered into the database for the years 1991 and 1992, so additional references for 1992 are expected. During the 6-year period from 1966 to 1971, 108 references were identified for TMD therapy compared with the most recently completed 3-year period 1986 to 1988, when 391 references were retrieved. From 1980 onward, a greater distinction was made in classifying references according to the disease classifications *temporomandibular joint diseases, temporomandibular joint syndromes, and myofascial pain syndromes*. There is some overlap in references as can be seen, for example, in the 1980 to 1982 data. A total of 204 references to TMD therapy were identified: 196 under *temporomandibular joint diseases*; 156 under *temporomandibular joint syndromes*; and 164 under *myofascial pain syndromes*.

The number of references pertaining to therapy is compared with the total number of references to TMD (Table 2). The growth in the total number of references in this clinical area, from 541 references in the time span of 1980 to 1982 to more than 1,300 references in the 3-year period of 1986 to 1988, is even more striking.

Results of the classification of references identified by the Medline search from 1980 to 1992 are reported in Table 3. The number of articles published in a language other than English is about

Table 1 Medline Search for Articles Referring to Therapy of TMD

Years	No. of years	Total No. of articles	TMJ diseases	TMJ syndrome	Myofascial pain dysfunction
1966 to 1971	6	108	108	108	108
1972 to 1976	5	155	155	155	155
1977 to 1979	3	135	135	135	135
1980 to 1982	3	204	196	156	164
1983 to 1985	3	376	364	233	245
1986 to 1988	3	391	363	163	191
1989 to 1992	3+	313	286	143	171

From 1980 onward, greater distinction was made in classification of references according to disease category. Several articles are indexed under more than one disease category; therefore, the total number of articles for each year is not the simple sum of articles under each disease category.

Table 2 Medline Search for TMD Articles

Years	Total No. of articles	TMJ diseases*		TMJ syndrome*		Myofascial pain dysfunction*	
		Total	Therapy	Total	Therapy	Total	Therapy
		1980 to 1982	204	541	196	380	156
1983 to 1985	376	1,027	364	567	233	604	245
1986 to 1988	391	1,329	363	478	163	567	191
1989 to 1992	313	1,275	286	423	143	494	171

Several articles are indexed under more than one disease category, therefore, the total number of articles for each year is not the simple sum of articles under each disease category.

*Total = total number of references to TMD; Therapy = number of references to therapy of TMD.

Table 3 Classification* of References to TMD Therapy

Years	Total No. of articles	Non-English	Reports of technique			Case reports/series				
			Reviews	Clinical studies	Editorials	Letters	Mgt [†]	Other		
1980 to 1982	204	85	56	22	15	7	6	5	3	5
1983 to 1985	376	109	114	34	51	24	7	19	4	14
1986 to 1988	391	114	109	41	55	36	5	19	5	9
1989 to 1992	313	101	78	35	29	20	3	24	9	5
Total	1284	409	357	132	150	87	21	67	21	33
Percent [‡]		32	41	15	17	10	2	8	2	4

*The categories are not mutually exclusive; for example, some articles were reports of techniques followed by report of a case, or series of cases.

†The percent reported for non-English is the percent of total references. For all other categories, it is the percent of English language references.

‡Mgt = management.

one third of the total, indicating a worldwide interest in this problem. Of the articles published in English, review articles represent the largest proportion, ranging from 37% (78 of 212) in the period of 1989 to 1992, to 47% (56 of 119) in the period of 1980 to 1982. Reports of techniques comprise 15% (132 of 875) of the references, and those of clinical studies comprise 17% (150 of

875). Case reports and case series make up approximately 10% (87 of 875) of references.

The 409 references to TMD therapy published during 1980 to 1992 in a language other than English were categorized. It should be noted that in addition to the articles considered in the present study, a considerable number of the references published in English describe research performed

Table 4 Classification of Non-English References to TMD Therapy By Language

Language	1980 to 1982	1983 to 1985	1986 to 1988	1989 to 1992	Total	Percent
German	31	22	23	21	97	24
Japanese	11	36	13	4	64	16
Italian	5	12	14	26	57	14
French	5	4	7	12	28	7
Scandinavian	2	9	11	6	28	7
Spanish	4	0	11	5	20	5
Other Slavic	10	3	1	3	17	4
Chinese	3	1	9	4	17	4
Russian	5	4	1	4	14	3
Other	9	17	24	17	67	16
Total	85	108	114	102	409	

Table 5 Classification of Non-English References to TMD Therapy

Years	Total No. of papers	Reviews	Techniques, case reports, case series*				Dx†	Other
			Clinical studies	Mgt†	Dx†	Other		
1980 to 1982	85	39	34	9	0	0	1	
1983 to 1985	109	53	50	2	1	2	1	
1986 to 1988	114	48	51	12	0	2	1	
1989 to 1992	101	41	42	15	2	0	1	
Total	409	181	177	38	3	4	4	
Percent		44	43	9	< 1	1	1	

*Reports of techniques and case reports/series are combined in this classification because distinction between them was too difficult using only titles and abstracts.

†Mgt = management; Dx = diagnosis.

in non-English speaking countries. Thus the non-English language literature represents only a portion of the worldwide interest in TMD.

The distribution of non-English language references for 1980 to 1992 is reported in Table 4 by language. The greatest number of references are in German, Japanese, and Italian. In Table 5, the non-English language references are classified by study type. Reports of techniques and case reports/case series are combined in this table because distinction between these was too difficult using information from the titles and/or abstracts only. The distribution of references is very similar to the English language references for reviews (44% versus 41%), but represents more reports of techniques, case reports/case series (43% versus 25%), and fewer clinical studies (9% versus 15%).

The results of the search of journals by hand are summarized in Tables 6 and 7. In Table 6, the articles are classified by research design, and the same trend toward a predominance of review articles and reports of uncontrolled observations (case reports/series, reports of techniques) exists as in

the overall Medline search. Some general characteristics of the 14 case series reported in these journals during 1991 are as follows. The mean number of subjects was 41, with a range from three to 109 subjects. The mean percentage of females was 87%, with a range from 82% to 94%. The mean age for these series was 31 years, with a range from 15 to 65 years.

In Table 7, the articles are grouped by country of origin as cited by Medline. The majority (66%) of reports are from the United States, with 20% from Europe, and 7% from Australia or Asia. All articles in these journals are published in English.

Randomized Controlled Trials

Based on the initial Medline search, a follow-up review of bibliographies, and a hand search of selected journals, 51 RCTs of therapy for TMD were identified. These trials included assessment of splint therapy (26 trials), biofeedback/relaxation therapy (12 trials), occlusal adjustment (six trials), transcutaneous electrical nerve stimulation (three

Table 6 Classification* of References to TMD Therapy Found by Hand Searching Four Journals, 1991

Journal	Total No. of articles	Reviews	Reports of technique	Clinical study	Case reports/ series	Anatomy/ physiology	Epi [†]	Mgt [†]	Dx [†]	Other
J Craniomand Pract	36	11	3	9	8	1	1	3	1	1
J Craniomandib Disord										
Facial Oral Pain	32	5	2	7	5	3	7	2	2	0
J Prosthet Dent	20	4	4	0	1	6	3	0	3	0
J Oral Maxillofac Surg	24	3	4	2	10	3	2	0	2	0
Total	112	23	13	18	24	13	13	5	9	1
Percent		20	12	16	21	12	12	4	8	<1

*The categories are not mutually exclusive, for example, some articles were reports of techniques followed by report of a case, or series of cases.

†Epi = epidemiology; Mgt = management; Dx = diagnosis.

Table 7 Classification of References to TMD Therapy Found by Hand Searching Four Journals, 1991

Journal	USA	Europe	Australia/Asia	Other
J Craniomand Pract	23	8	0	2
J Craniomandib Disord				
Facial Oral Pain	21	8	2	0
J Prosthet Dent	16	1	2	1
J Oral Maxillofac Surg	14	6	4	0

trials), and intra-articular injections (three trials). These trials were found in more than a dozen different journals. The lack of controlled evaluation of any surgical procedures was striking.

Discussion

To understand what is known about a particular clinical problem, it is important to look broadly at the content of the literature pertaining to that topic as well as specifically at the evidence available in well-designed clinical studies. There is a vast and growing amount of literature on TMD, with only a small proportion referring to therapy. To put into perspective what is known about treatment effectiveness from well-designed clinical studies, we report here a description of the total number of references available through Medline, the distribution across broad categories of study design, and some specific findings from additional hand searching of four journals to obtain a better understanding of what clinicians are likely to encounter when reading the literature. Since well-

controlled clinical studies make up such a small proportion (less than 5%) of the references to TMD, it is likely that clinicians are influenced more by the predominant uncontrolled, potentially biased reports they encounter. It is essential to consider the composition of the literature when trying to understand the state of science in this area and how and why clinicians make the decisions they do regarding the diagnosis and treatment of TMD.

Review of references to TMD from the electronic bibliographic database Medline and hand searching of four journals for the year 1991 identifies a number of important points and issues for further consideration:

(1) There is a vast and growing amount of literature on TMD. From 1980 to 1992, more than 4,000 references to TMD were identified using Medline. For practitioners to keep abreast of even a fraction of this literature would take a heroic effort. The fact that the 55 randomized controlled trials were found in more than a dozen different journals complicates the task of identifying reliable information even further.

(2) Of those 4,000 references, approximately one third are published in a language other than English, indicating a worldwide interest in TMD. Because Medline only indexes a fraction of non-English language journals, there is likely a substantially greater number of references than those found by this review. Failure to take into account this portion of the scientific literature may result in a biased estimate of treatment effectiveness.

(3) It is important to consider this distribution of references in terms of the current state of our understanding of TMD. First, references pertaining to therapy represent only about one third of the total references to TMD during the time period evaluated (1,284 of 4,172 total references). The

other two thirds must be composed of epidemiologic studies, anatomy, physiology, pathology, and other categories. Second, of the articles pertaining to therapy of TMD, only approximately 15% to 20% report data on the effect of therapy on patients (clinical studies and case reports/series). Third, most of the articles reporting treatment effects on patients are observational studies, not experimental. Thus, virtually all of the evidence regarding therapy for TMD is likely to be subject to considerable bias. This bias can influence many aspects of the study, including the selection of subjects for the study, the allocation of subjects to treatment, and the evaluation of response. This nearly total lack of clinical studies that control bias in the collection of data on treatment effectiveness is striking.

(4) The 51 randomized controlled trials focused primarily on conservative, nonsurgical therapies for TMD. It is important to consider this distribution of evaluations relative to the utilization of therapies by providers to assess whether there is sufficient evidence to support current clinical practice and identify areas where clinical trials are needed.

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Resumen

Epidemiología sobre la investigación de Desórdenes Temporomandibulares

Se realizó una revisión sistemática como respuesta al pedido solicitado por el Instituto Nacional de Investigación Dental, de evaluar en términos amplios la solidez de la evidencia relacionada a la terapia para desórdenes temporomandibulares (DTM). Este reporte describe la epidemiología de la investigación de los DTM en términos generales indicando el número total de menciones, la proporción relacionada a la terapia, y la distribución de acuerdo al diseño del estudio y lenguaje o país de origen. La serie de menciones evaluadas fue obtenida por medio del servicio de Medline; también se buscaron manualmente bibliografías de artículos y revistas seleccionadas. Desde 1980 hasta 1992, se encontraron más de 4,000 referencias relacionadas a los DTM, de las cuales alrededor de 1,200 consideraron el aspecto terapéutico. El 41% de las 1,200 referencias fueron clasificadas como revisiones y sólo 15% fueron estudios clínicos. Menos del 5% (n = 51) fueron estudios controlados distribuidos al azar. Esta revisión identificó una gran cantidad de literatura sobre DTM con artículos publicados en varios idiomas diferentes, lo cual indica un interés mundial en este problema. Debido a que no se puede esperar la asimilación de esta literatura por parte de un dentista promedio que trate pacientes con DTM, como tampoco de la mayoría de los investigadores en esta área, lo más probable es que no esté siendo utilizada al máximo. La literatura sobre la terapia para los DTM se relaciona principalmente a participantes en estudios clínicos no controlados, series de casos, reportes de casos, y simples descripciones de técnicas. En general se acepta que tales observaciones no controladas, en tanto que contribuyen al conocimiento sobre la terapia de los DTM, están sujetas a un prejuicio considerable y por lo tanto es difícil interpretarlas. Si el tratamiento de los DTM va a seguir la tendencia de la medicina que consiste en basar las decisiones sobre el cuidado del paciente en la evidencia existente en lugar de opiniones de expertos o razones patofisiológicas, entonces será necesario efectuar más estudios clínicos controlados rigurosamente, sobre la mayoría de las terapias.

Zusammenfassung

Epidemiologie der Forschung über Myoarthropathien des Kausystems

Auf Anfrage des National Institute of Dental Research wurde eine systematische Übersicht über das Beweismaterial zur Therapie der Myoarthropathien des Kausystems (MAP) erstellt. Dieser Bericht beschreibt in groben Zügen die Epidemiologie der MAP-Forschung, die totale Anzahl der Literaturstellen, den Bezug zur Therapie und die Verteilung hinsichtlich Studiendesign, Sprache und Ursprungsland. Medline- und Handsuche nach Bibliographien aus Artikeln und aus ausgewählten Journals ergab die Liste der zu bearbeitenden Literaturstellen. Zwischen 1980 und 1992 konnten über 4000 Bezüge zu MAP gefunden werden, 1200 hiervon betrafen die Therapie. 41% der 1200 Referenzen waren Reviews und nur 15% klinische Studien. Weniger als 5% (n = 51) waren kontrollierte randomisierte Untersuchungen. Die Übersicht identifizierte eine grosse Menge von MAP-Literatur in vielen verschiedenen Sprachen, was auf ein weltweites Interesse schliessen lässt. Es kann vom Praktiker, der MAP-Patienten behandelt, oder von den meisten Forschern nicht erwartet werden, dass sie diese Literatur aufarbeiten, man muss also annehmen, dass sie nicht maximal ausgenutzt wird. Die Literatur über MAP-Therapie besteht hauptsächlich aus unkontrollierten klinischen Studien, Fallserien, Fallberichten und einfachen technischen Beschreibungen. Man stimmt generell darin überein, dass solche unkontrollierten Beobachtungen einer erheblichen Parteilichkeit unterliegen und daher schwer zu interpretieren sind. Wenn die Behandlung von MAP dem Trend in der Medizin folgt und Therapieentscheidungen aufgrund von Beweismitteln statt aufgrund von Expertenmeinungen oder pathophysiologischen Überlegungen gefällt werden, so werden für die meisten Therapieformen strikte kontrollierte klinische Untersuchungen nötig werden.