research." They conclude that a low-tech and conservative approach is warranted in most patients. The NIDCR (2000) states that surgical treatments should be avoided where possible.

## VIII.OUTCOME MEASURES

There is a lack of a well-recognized or uniform set of outcome measures used for evaluating TMD interventions. Also, many outcome measures used in TMD studies have not been validated, i.e., shown to detect changes in TMD status in an accurate and reliable manner. This confounds attempts to integrate findings across the TMD literature, diminishing the ability to compare results of multiple studies of the same intervention and to generalize findings to clinical practice (LeResche et al. 1997; Stohler and Zarb 1999). In general, outcome measures fall into the categories of: pain or discomfort; motion and flexibility; clinical visualization; mental health/behavioral; and neurological, neuromuscular, and sleep. Outcome measures used in the TMD literature are shown in Table 2. The majority of studies identified in this review used measures of pain and jaw motion and flexibility to assess patient outcomes.

## Table 2: Outcome Measurement Tools Used in TMD Studies

| Outcome Measure | Method or Example |
|---|---|
| Pain and discomfort | Visual analog scales of pain (various); Subjective pain diary<br>Relative verbal pain descriptions; Pain Questionnaire; McGill Pain Questionnaire (MPQ) (Melzak 1987); West Haven-Yale Multidimensional Pain Inventory (MPI) (Kerns et al. 1985) |
| Motion and flexibility | Jaw opening, pain on palpation, joint noises, etc. |
| Clinical visualization | Radiographic imaging (e.g., CT, MRI) |
| Mental health and behavioral | SCL-90R measurement of psychological status (Derogatis 1992); Pittsburgh Sleep Quality Index (Buysse et al. 1989); Helkimo's Anamnestic Dysfunction Index (Helkimo 1974); Helkimo's Clinical Dysfunction Index (Helkimo 1974); Symptom Severity Index (SSI); Craniomandibular Index (including Dysfunction Index and the Muscle Index) (Fricton and Schiffman 1986); Beck Depression Inventory(BDI) (Beck et al. 1961); Oral-Parafunctional Habits Scale (Turk et al. 1996); Modified Symptom Severity Index |
| Neurological, neuromuscular, and sleep | Pressure algometer (to measure pressure pain thresholds); polysomnographic recording (of sleep patterns); electroencephalographic (EEG) and electromyographic (EMG) recorder; measurement of electrical activity (electrodes/monitor) |

Aside from the lack of standardized and validated outcome measures is the question of whether or not these measures capture the impact of TMD on the lives of patients. LeResche et al. (1997) have suggested use of more specific outcomes related to pain and its consequences, such as pain intensity, affective aspects of pain, pain-related coping, pain behaviors (i.e., expressive behaviors, activity limitation, and use of health services), and pain-related disability and life interference.

## IX. SELECTED IMPLICATIONS FOR STUDY DESIGN AND INTERPRETATION

One of the challenges posed by a vaguely defined and diverse patient population is the difficulty of establishing a uniform patient sample when drawing patients for a clinical trial from larger populations with apparent signs or symptoms for TMD. One implication of this is that investigators use very broad patient inclusion criteria, in which it is likely that patients with a wide variety of signs and symptoms, and perhaps an equally wide variety of underlying diseases or conditions, are included in a study of a treatment for TMD. If the particular treatment is truly beneficial for a particular subgroup of this broadly constituted patient sample, but is not beneficial for other subgroups, then the treatment effect is more likely to be diluted or masked by the larger non-responding patient population. Clinical trials with small sample sizes are particularly subject to this weakness. This decreases the internal validity of the study findings, which in this instance are more likely to be negative. The design, implementation, and

interpretation of clinical trials of TMD treatments is compromised by the absence of sufficient understanding of the etiology and course of TMD and diagnostic criteria that could be used for staging or other clinically meaningful distinctions among subgroups of TMD patients.

Conversely, the breadth of TMD symptoms and diagnostic ambiguity have implications for very restrictive inclusion criteria. Unless a study is drawing from a very large population, such as a managed care organization with hundreds of thousands of enrollees, it may be difficult to identify a treatment group of sufficient size to provide the statistical power to detect any true treatment effect. The findings of studies with such small groups are also more vulnerable to patient noncompliance and dropouts. To the extent that the treatment used in the study is found to be effective in the selected treatment group, these findings will have limited external validity to the broader TMD population. The management and interpretation of patient noncompliance and dropouts, regardless of the size of the trial, can compromise its rigor and the validity of its findings (Whitney and Dworkin 1997).

The latter implication of selection criteria is exemplified in a study by Ekberg et al. (1996) in which only 39 patients satisfied the selection criteria from an initial population of 2,012 TMD patients. Similarly large exclusions were noted in Ekberg et al. (1998b) with 60 subjects from 1,904 TMD patients, Goudot et al. (2000) with 62 subjects from 720 TMD patients, and Magnusson and Syren (1999) with 26 subjects from 1,344 TMD patients. In an RCT reported by Magnusson and Syren (1999), the investigators chose to forgo carrying out a statistical analysis due to patient dropouts and noncompliance with the established treatment regimen.

There are many instances where a body of evidence on the effects of a health care intervention on certain diseases or conditions comprises conflicting findings or inconclusive findings due to studies having sample sizes that are too small for detecting any true treatment effects. In such instances, it may be possible to pool study results or patient-level data using meta-analysis or other integration approaches. However, these usually require having a group of studies involving a particular intervention used in populations with the same or similar indications. The lack of clearly defined diagnostic criteria and interventions compromises efforts to integrate results from multiple studies or otherwise draw inferences about the effectiveness or cost of TMD treatments.

The potential discrepancy between the more "ideal" conditions in some RCTs and other investigations of TMD treatments conducted in research settings and the conditions of routine clinical settings in which TMD is managed may diminish the validity of some of the available literature. This is recognized by researchers and was emphasized by certain of the clinicians and researchers interviewed for this report. RCTs conducted under conditions and lacking sufficient duration may not add greatly to understanding "real-world" care, which often involve long-term treatment utilizing combinations of therapies and flexible pharmaceutical dosages (Stohler and Zarb 1999; Schiffman et al. 1996). While this is a common debate in clinical research, it is particularly relevant in this case due to the heterogeneous nature of TMD cases and treatments.

## X. STUDY METHODOLOGY

Two main tools were used to gather information for this report: stakeholder input and an extensive review of the literature. An initial review of the literature was used to help us identify relevant issues in the treatment of TMD and to inform the questions we developed for interviews of stakeholders and other experts. These discussions helped to guide the search strategy for the focused literature review.

### A. Stakeholder Input

Lewin solicited expert opinion from NIDCR staff, representative payers, provider associations, and patient advocacy groups. The purpose of this task was to gain input from stakeholders regarding available treatments, pertinent outcome measures (for safety/risk, morbidity, quality of life, etc.), economic measures (for costs, productivity, etc.), and relevant sources of evidence. The interviews served also to more clearly define the scope of this effort. An expert from the field of dentistry with peer-reviewed published research reports on TMD helped to guide our stakeholder outreach and review of the literature.

Stakeholders contacted included NIDCR staff, the medical directors of four major payers (Kaiser Permanente, NW Region; Arkansas Blue Cross and Blue Shield; Blue Cross and Blue Shield of Kansas; and United Healthcare), four provider associations (American Dental Association; American Academy of Head, Neck, and Facial Pain; American Chiropractic Association; and the Foundation for Chiropractic Education and Research), and patients (i.e., The TMJ Association). Lewin solicited the views of these stakeholders with regard to available treatments, the costs and effectiveness of these treatments, and relevant supporting evidence. Not all stakeholders who were contacted were interviewed. In some cases, stakeholders declined, some indicating that it was inappropriate for them to be interviewed on this subject (Table 3).

### Table 3: Stakeholders and Other Experts

| Stakeholder | Contact and Title | Interviewed |
|---|---|---|
| Center for Health Research, Kaiser Permanente, NW Region | Alex White, D.D.S., Oral Health Services Researcher | Yes |
| Blue Cross and Blue Shield of Kansas | S. Satya-Murti, M.D., Medicare Medical Director | Yes |
| United Healthcare | Dick Justman, M.D., National Medical Director | Yes |
| Arkansas Blue Cross and Blue Shield Association | Jim Adamson, M.D., Corporate Medical Director | Yes |
| The TMJ Association | Terrie Cowley, President | Yes |
| National Institute of Dental and Craniofacial Research (NIDCR) | Kenneth Gruber, Ph.D., Chief of Chronic Disease Branch | Yes |
| American Dental Association | No contact | Declined |
| American Chiropractic Association | No contact | Declined |
| Foundation for Chiropractic Education and Research | No contact | Declined |
| American Academy of Craniofacial Pain (formerly American Academy of Head, Neck, and Facial Pain) | Larry Tilley, D.M.D., President Elect | Yes |
| Private practice (Washington, DC) | Peter Neff, D.D.S., Sc.D. | Yes |

## B. Focused Literature Review

Articles relevant to the per-patient costs and efficacy of available treatments for TMD were systematically collected and reviewed for the period January 1996 through January 2001. Multiple search strategies in MEDLINE and the Cochrane database were used. We limited our search to articles in English (English abstracts for non-English articles were excluded) and to human trials only. We also limited the focus to articles in which the primary focus was treatment of TMD or costs associated with treatment of TMD. Specifically excluded were articles related only to complications resulting from treatment or the etiology and diagnosis of the TMD. Additional articles suggested during our stakeholder interviews that were not identified in our literature review but that met the inclusion criteria were included (e.g., Carlson et al. in press). Table 4 outlines the search terms used.

Further, we conducted a search of the ClinicalTrials.gov database, maintained by the National Library of Medicine (NLM), using the search term "temporomandibular joint disorders" to identify any studies currently in the planning stages. Three relevant studies were identified, which are noted below.

### 1. *Inclusion and Exclusion Criteria*

Selection criteria were chosen to limit the literature reviewed to only studies that concern the efficacy and/or the per-patient costs of treatment for TMD. Only studies that met all of the selection criteria were included in our review. We attempted to strike a balance in developing selection criteria that were broad enough to capture the breadth of TMD and its treatments, yet not so broad as to encompass cranio- or maxillofacial disorders and treatments that may be only marginally, or not at all, related to TMD, or that would yield a review containing information that is difficult to compare and synthesize (Khan et al.).

**Table 4: Literature Search Methods**

| Database Type | Database Name | Years | MeSH |
|---|---|---|---|
| National Library of Medicine | MEDLINE | 1996-Present | [Temporomandibular joint disorders *or*<br>Temporomandibular joint dysfunction syndrome *or*<br>Craniomandibular disorders *or*<br>Facial neuralgia]<br>AND<br>[Economics (subheading and MeSH) *or*<br>Costs *or*<br>Cost analysis *or*<br>Cost (text word) *or*<br>Cost-benefit analysis *or*<br>Cost effectiveness]<br>AND<br>[Therapeutics *or*<br>Treatment]<br>AND<br>[Randomized controlled trial *or*<br>Editorial *or*<br>Longitudinal study *or*<br>Clinical trial *or*<br>Meta-analysis *or*<br>Control *or*<br>Trial] |
| The Cochrane Collaboration | The Cochrane Library | 1996-present | Temporomandibular joint disorders<br>Randomized controlled trial<br>Clinical trial<br>Treatment |

## C. Organizing the Literature

During preparation of the literature review, we developed a matrix detailing the types of articles identified (Appendix A: Evidence Table). Articles reporting on treatment efficacy are organized by type of study (e.g., RCTs, nonrandomized trials with concurrent controls, etc.). The small number of articles reporting on cost of TMD precluded organization in this manner (see Overview of Cost Literature). Information collected on each article included the following.

- Title
- Author(s)
- Source
- Modality
- Sample size
- Study duration
- Follow-up
- Blinding
- Multi-site
- Sample characteristics
- Outcome measures
- Benefit of the study
- Cost of treatment (if stated)

After standardizing the information collected from each article, we organized the body of literature by study design. The categories of study type are based on use of an evidence-based approach in which greater study validity is attributed to more rigorous methodology. The classification of therapies was loosely adapted from the literature and from clinical educational documents prepared for patients (e.g., Stohler and Zarb 1999; The Staywell Company 2000).

Investigators use various study designs to determine the effectiveness of specific treatment approaches. While there are many variations of study designs, they can be categorized into several main, well-recognized groups that are distinguished by key methodological attributes such as being prospective vs. retrospective, controlled vs. uncontrolled, and randomized vs. nonrandomized. We categorized the literature into these categories, as follows, listed in general order of most to least rigorous design.

- Randomized controlled trial (RCT)
- Non-randomized trial with concurrent control
- Non-randomized trial with historical control

  Case control or adjusted cohort study
- Case series

  Case study or anecdote
- Expert opinion

In general, double-blinded, multi-site, large sample, randomized controlled trials (RCTs) are considered to be the gold standard of methodological rigor for determining treatment efficacy. These studies should also include sound inclusion and exclusion criteria to achieve uniformity, sufficient power to permit valid generalization, and appropriate handling of missing data and

patient dropouts (i.e., discussion or use of an intention-to-treat analysis). Of course, it is not always possible to conduct studies with all of these attributes; for example, while it is often possible and desirable to conduct single- or double-blinded studies of pharmaceutical therapies, it is usually not possible or acceptable to conduct blinded or placebo-controlled studies of surgical interventions. Furthermore, studies that are well designed are not necessarily well conducted.

Finally, in evaluating the evidence on effectiveness, we further classified articles by treatment methodology as described in section VII above. For example, all RCTs assessing behavioral interventions were evaluated, followed by articles examining behavioral interventions that were not RCTs.

## XI. FINDINGS

### A. Efficacy and effectiveness literature

#### *1. Overview*

Seventy-two studies were identified in our initial literature search. Of these, 27 were subsequently excluded, 10 of which were RCTs, because they did not meet our selection criteria (see below). An additional RCT was included in our review that was identified by one of our stakeholders and is currently in press. Of the non-RCTs excluded from review, 10 studies were outside the scope of our study, i.e., TMD was not the focus of the study. Five non-RCTs were excluded because they did not involve an intervention for TMD. One non-RCT was excluded because it was a pilot study, and one was excluded because it was in Italian.

In total, 15 RCTs, two nonrandomized trials with concurrent controls, one case control, one case series, 20 single case studies, and six expert opinions satisfied our inclusion and exclusion criteria. Table 5 provides the distribution of study type by year.

Table 5: Distribution of study type by year

| Study Type | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | Totals |
|---|---|---|---|---|---|---|---|
| Randomized clinical Trial | 4 | 3 | 2 | 3 | 2 | 1* | 15 |
| Nonrandomized trial with concurrent control | 1 | 1 | 0 | 0 | 0 | 0 | 2 |
| Nonrandomized trial with historical control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Case control or adjusted cohort study | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Case series | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| Single case study or anecdote | 2 | 3 | 4 | 10 | 1 | 0 | 20 |
| Expert opinion | 1 | 3 | 0 | 1 | 1 | 0 | 6 |
| Total | 9 | 10 | 7 | 14 | 4 | 1 | 45 |

* Carlson et al., in press

### 2. *Randomized Clinical Trials*

The initial search identified 25 reports of RCTs. Five were excluded because TMD was not the primary focus of the investigation; the subjects had other disorders, e.g., bruxism, headache, or arthritis (Marklund and Franklin 1996; Tegelberg and Kopp 1996; de Andre et al. 1998; Vallon and Nilner 1997; Treacy 1999) or the study was not specifically an investigation of an intervention for TMD (Nemeth et al. 2000; Rodrigues-Garcia et al. 1998; Kirveskari et al. 1998; Ekberg and Nilner 1999). One study was excluded because it was published in German (Umstadt et al. 1998). One study was excluded because it was an analysis of material already included in this review (Ekberg et al. 1998a).

Fifteen reports of RCTs of treatments for TMD were found that met our selection criteria. Of these, four studied the effectiveness of behavior modification techniques and/or physical therapy in treating TMD, four focused on the effectiveness of pharmaceutical management to treat TMD, four investigated the effectiveness of occlusal therapies, and three investigated the effectiveness of surgical techniques on TMD (Appendix A).

All but two of the study populations consisted of patients who had been referred for treatment for TMD symptoms (e.g., orofacial pain, TMJ locking, and/or clicking). In two studies (Denucci et al. 1998; Komiyama et al. 1999), the nature or basis of identifying the study population is not described. Information about previous TMD treatments was provided in the majority of studies. In three cases, explicit mention was made of previous treatment as an exclusionary criterion or that no patient in the study had previously been treated for TMD (Ekberg 1998b; Komiyama et al. 1999; Magnusson and Syren 1999). Three studies on surgical interventions note that non-

invasive measures were attempted before surgery was undertaken (Fridrich et al. 1996; Goudot et al. 2000; Miyamoto et al. 1999). Three studies made no mention of previous treatment history (Davies and Gray 1997a; Davies and Gray 1997b; Shin and Choi 1997).

The number of patients included in the trials varied from 19 to 101, with a mean of 47 patients. The number of patients was 20 or fewer in three studies (Appendix A). In four studies, it was not apparent from the patient selection criteria whether patients received treatment before the trial that would have confounded the results (Davies and Gray 1997a; Davies and Gray 1997b; Miyamoto et al. 1999; Shin and Choi 1997). In one study (Goudot et al. 2000), the selection criteria were vague. The remaining studies included sufficiently described selection criteria.

The average duration of treatment was 13.4 weeks (excludes certain studies because the investigation did not take place over a period of time, i.e., surgery with follow-up and pre- post-treatment studies; Fridrich et al. 1996; Goudot et al. 2000; and Miyamoto et al.; Schiffman et al. 1996; Shin and Choi 1997; Turk et al. 1996). Follow-up occurred in eight of the 15 studies, ranging from six months to four years (Appendix A). The methods used to randomize patients into treatment groups were described vaguely or not at all in all but two studies (Carlson et al. in press; Ekberg et al. 1998b). Six of the studies were double-blinded and two studies were single-blinded (Appendix A). None of the RCTs reviewed was conducted in a multi-site setting.

### *3. Therapeutic Taxonomy*

In the sections that follow, we discuss the literature in terms of the therapeutic taxonomy described above, focusing primarily on RCTs. For each of these therapeutic categories, summaries of individual RCTs are presented along with a collective summary of the non-RCTs at the end of each section. Table 6 provides a summary of the studies by therapeutic modality (Note: Table 6 includes all study types, not just RCTs). Three expert opinions did not fit into any one therapeutic modality and were therefore excluded from Table 6. Wilkinson 1997 provided an overview and commentary of treatments for TMD, Laskin 1997 draws a distinction between disorders of muscular origin and those of joint origin, and how treatment should account for this. Lastly, Greene et al. 1999 argue for treating patients in a biopsychosocial framework, by approaching treatment with conservative and scientifically validated modalities.

## Table 6: Distribution of study type by therapeutic modality*

| Study Type | Behavior Modification/ Physical Therapy | Pharmaceutical Management | Occlusal Adjustment (non-surgical) | Surgery |
|---|---|---|---|---|
| Randomized clinical trial | 4 | 4 | 4 | 3 |
| Nonrandomized trial with concurrent control | 1 | 0 | 0 | 1 |
| Nonrandomized trial with historical control | 0 | 0 | 0 | 0 |
| Case control or adjusted cohort study | 1 | 0 | 0 | 0 |
| Case series | 0 | 0 | 0 | 1 |
| Single case study or anecdote | 4 | 0 | 8 | 8 |
| Expert opinion | 1 | 0 | 1 | 1 |
| Total | 11 | 4 | 13 | 14 |

*Three studies did not fall into any one of these categories (i.e., there are only 42 studies counted in this table).

### *a) Behavior modification and physical therapy*

Four studies dealt specifically with behavior modification or physical therapy (Carlson et al. in press; Komiyama et al. 1999; Turk et al. 1996; Wright et al. 2000).

Carlson et al. (in press) studied 44 patients randomized into two groups: one received physical self-regulation training and another received standard dental care. A non-intervention control group was not established for this trial. Study duration was three weeks. Subjective patient-reported data on pain and psychological status were collected using validated measurement tools at six and 26 weeks. A statistically significant difference in outcome was found between treatment groups, and both groups improved significantly from baseline. Physical self-regulation was found to be useful in decreasing pain, increasing incisal opening without pain, and decreasing psychological dysfunction in TMD patients. Twelve of the original 56 subjects (21%) dropped out before study completion; follow-up data were not collected from these subjects and an intention-to-treat analysis was not performed. All participants were maintained on any medications they were taking prior to the study.

Komiyama et al. (1999) investigated posture correction in 60 patients randomized into three groups: one received cognitive behavioral treatment methods, one received cognitive behavioral methods with posture correction, and a non-intervention control group. Subjective data of pain intensity, mouth opening, and disturbance in daily life were collected monthly, and patients were followed for 12 months. The posture correction group showed statistically significant initial improvement over the non-intervention group, but this difference diminished over the course of the trial, and at 12 months there were no statistical differences between any of the groups. All groups improved over the course of the study, but a statistical comparison to baseline values was not reported. Nine patients dropped out of the trial before completion, although the published

report did account for them (i.e., analyses were conducted both including and not including study dropouts).

Wright et al. (2000) studied 60 TMD patients randomized into two groups: one group received posture training with TMD self-management instructions and a control group that received TMD self-management instructions only. A non-intervention control group was not established for this study. Objective and subjective data were collected using validated methods, and patients were followed for four weeks. Statistically significant improvement was found for symptom severity, maximum pain-free opening, pain threshold measurements, and patients' perceived TMD and neck symptoms. Therefore, the study indicated that posture training was a useful adjunct to self-management instructions in diminishing symptoms of TMD in patients with a primary muscle disorder.

Turk et al. (1996) evaluated the efficacy of a "tailored treatment protocol," involving the unique combination of cognitive therapy to use of stress management, biofeedback, counseling, and an intraoral appliance. Forty-eight subjects were randomized into two groups: one group received an intraoral appliance, stress management with biofeedback, and counseling ("non-tailored group") and a second group received the same treatment as the first, plus cognitive therapy ("tailored treatment group"). A non-intervention control group was not established for this study. Objective and subjective data were collected, and patients were followed-up at six months. Both groups improved significantly from baseline measurements. Additionally, a statistically significant difference in outcome was found between groups, supporting the efficacy of a tailored treatment protocol in treating TMD. The tailored treatment protocol significantly decreased pain, depression, and medication use relative to the control group. Data was collected using several standardized and validated methods, and a treatment credibility analysis was conducted to determine patient confidence in their treatment.

The studies summarized here suggest that some methods of behavior modification and physical therapy may be useful in treating the symptoms of TMD patients, though the absence of non-intervention control groups obviated the possibility of determining whether these treatments would be any better than no intervention, particularly in the long-term. Only Komiyama et al. included a control group that received no intervention. Both Komiyama et al. and Wright et al. found a significant improvement in patients treated with posture correction compared to controls in short-term measurements, but the 12-month data from Komiyama et al. showed that this difference diminished greatly over time. The Wright et al. study was not conducted over a long enough period to observe this possibility. Carlson et al. found that physical self-regulation was useful in decreasing symptoms of TMD, but this study too was of short duration. Similarly, Turk et al. showed that, for six months, a tailored treatment regimen (i.e., including cognitive therapy) was significantly more useful in treating TMD symptoms than was a non-tailored approach. Long-term studies that include non-intervention control groups are needed to show that behavioral and physical therapy are more useful than non-intervention in treating TMD symptoms, though the therapies outlined here may be useful in alleviating symptoms for short periods of time (i.e., up to six months).

### 1. Non-RCTs

Five studies were identified that used behavior modification or physical therapy and were not RCTs. One study was a non-randomized trial with concurrent control (Conti, 1997). A second study utilized the case control study design (Gramling et al., 1996). The remaining four studies were case series (see Appendix A). In addition, there was one expert opinion article that focused on behavioral and physical therapy (Dworkin, 1997). Dworkin reviewed the literature related to behavioral interventions and found that such interventions are a component of most chronic pain management programs and that such programs can be effective for TMD patients.

Conti (1997) studied 20 patients receiving either low-level laser therapy (in which a probe emitting a low energy output laser is directed over the TMJ for short durations) or a placebo treatment in which the probe is used but turned off. Though the laser therapy was hypothesized to reduce pain and increase mandibular function by affecting metabolic activation of cells and tissues in the TMJ, the investigators found no differences in pain or functioning. Gramling et al. (1996) studied 16 patients, nine of whom received habit-reversal training consisting of a seven session group training program to teach patients how to detect, interrupt, and reverse maladaptive oral habits. The comparison group constituted the six patients that met the study inclusion criteria but chose not to enroll in the study. Results after six months indicated that the therapy lowered ratings of highest weekly pain at statistically significant levels, and reduced average daily pain and increased the number of pain-free days at levels that approached but did not reach statistical significance. Friedman (1997) published a case study on one patient who was taught TMJ manipulation and exercise for a 6-week period. At the end of the treatment period the patient had reduced pain and increased functioning as indicated by maximum jaw opening. Horrell et al. (1997) studied the use of passive motion therapy in two juvenile patients, one of whom had TMJ consequent to a traumatic facial injury. Over the three-month period, both patients utilized a device to restore joint mobility resulting in increased functioning as measured by maximum jaw opening at the beginning and end of the treatment period. Martini et al. (1996) reported on the successful use of repetitive manipulation technique over a two-week period in three patients with acute and chronic jaw locking. Yokoyama reported on the short-term use of linear polarized near-infrared radiation in four patients with rheumatoid arthritis-affected TMJ pain. Pain was eliminated in each patient, and in three patients, functioning was improved as measured by maximum jaw opening.

The non-RCT literature indicated generally positive results for behavioral therapy, though most studies did not include a nontreatment group, had small samples, and followed patients over very short time periods.

### *b) Pharmaceutical management*

Pharmaceutical management of TMD was investigated in four RCTs (DeNucci et al. 1998; Ekberg et al. 1996; Schiffman et al. 1996; Shin and Choi 1997).

DeNucci et al. (1998) studied 20 patients in a randomized, two-period, within-subject, crossover study to investigate the effect of triazolam, a sedative/hypnotic, on sleep improvement and pain relief in TMD patients. Objective and subjective data were collected using validated methods, and the study was conducted over two weeks. Statistically significant improvement was found with use of triazolam versus placebo for sleep-related endpoints (e.g., sleep quality, restfulness, and time spent in stage-2 sleep), though no improvement was seen in objective or subjective pain measures. The study indicated that improvement in sleep quality does not affect pain report in TMD patients, thereby failing to support a relationship between sleep disturbances and chronic orofacial pain.

Ekberg et al. (1996) studied diclofenac sodium, a nonsteroidal anti-inflammatory drug (NSAID), as an alternative treatment for TMJ pain in 32 subjects randomized into two groups: one receiving diclofenac sodium two or three times a day and another group receiving a placebo. Objective and subjective data were collected, and patients were followed for two weeks. The treatment group showed a statistically significant improvement over the placebo group for tenderness to palpation of the masticatory muscles and frequency of TMJ pain at one of three evaluation visits. This difference diminished by the end of the two weeks, and no significant differences were found between groups for any other endpoints. At the end of the study, 38% of subjects in the treatment group and 25% of subjects in the placebo group reported an improved condition, though this difference was not statistically significant. This trial did not demonstrate that diclofenac sodium should be used as a primary treatment for TMD pain.

Schiffman et al. (1996) studied the effects of iontophoretic delivery (introduction of medication ions through tissue via electrical current) of dexamethasone phosphate, a synthetic adrenocortical steroid, on TMD symptoms in 27 subjects randomized into three groups: a treatment group (dexamethasone phosphate and lidocaine hydrochloride), a control group (lidocaine hydrochloride), and a placebo group (pH-buffered saline). Objective and subjective data were collected immediately preceding treatment and one week after treatment using standardized and validated measures. A long-term follow-up of study subjects was not conducted. The treatment group showed significant post-treatment improvement over the other two groups for only Helkimo's Anamnestic Dysfunction Index scores (a symptom checklist that assesses the subject's symptoms associated with the stomatognathic system). No statistically significant difference was found between groups for any of the other outcomes. These results suggest that dexamethasone phosphate with lidocaine hydrochloride may be effective in improving mandibular function, but not in reducing pain. It is not clear that this effect continues over time.

Shin and Choi (1997) investigated the effects of indomethacin (a nonsteroidal anti-inflammatory indole derivative) phonophoreses (introduction of medication through tissue via ultrasound massage) on pain relief in the TMJ. Twenty subjects were randomized into two groups: one group received ultrasound massage to the TMJ using 1% indomethacin cream as a conducting medium and one group received ultrasound massage using a placebo cream as a medium. Objective and subjective data were collected from subjects pre- and post- treatment, and no follow-up of study subjects was conducted. No statistically significant differences in outcome were found between the two study groups. Ultrasound massage with indomethacin cream was

found to be useful in relieving pain in the TMJ, but not significantly more so than a placebo cream.

None of the four RCTs summarized here showed that pharmaceutical management of TMD symptoms was more effective than a placebo for the majority of outcomes considered. Moreover, none of these studies followed subjects for more than 52 weeks to determine longer-term effects of treatment. DeNucci et al. (1998) found that, while triazolam improved sleep quality, this did not translate into relief of pain symptoms in TMD patients. Ekberg et al. (1996) found that diclofenac sodium does not provide a significant relief of TMD symptoms over placebo. Schiffman et al. (1996) showed that while dexamethasone phosphate and lidocaine hydrochloride provided a significant improvement in Helkimo's Dysfunction Index scores, it did not significantly improve any other outcomes investigated. Lastly, Shin and Choi (1997) found no significant post-treatment improvement using indomethacin cream over use of a placebo cream when conducting ultrasound massage. All four studies had small sample sizes and were of short duration (Appendix A).

### *c) Occlusal adjustment*

Four RCTs specifically investigated the effectiveness of non-surgical occlusal adjustment therapies in treating TMD (Davies and Gray 1997a; Davies and Gray 1997b; Ekberg et al. 1998b; Magnusson and Syren 1999).

Davies and Gray (1997a) studied 70 TMD patients using an anterior repositioning splint to address TMJ disc displacement with reduction. All patients received splints and were randomized to three different treatment groups that wore the splint only during the day, only at night, or for 24 hours a day. Data collected included self-reported subjective assessment of pain, joint sounds, and range of motion over a three-month period. All three treatment groups were reported to have improved relative to baseline in terms of pain, functioning, and the presence of disc sounds. The group wearing the splint for 24 hours a day experienced greater rates of improvement than the other two groups at levels that were statistically significant.

In their second study, Davies and Gray (1997b) studied 70 TMD patients, diagnosed with pain dysfunction syndrome, using a stabilization splint. All patients received splints and were randomized to three treatment groups that wore the splint only during the day, only at night, or for 24 hours a day. Data collected included self-reported subjective assessment of pain, joint sounds, and range of motion over a three-month period. All three treatment groups were reported to have improved relative to baseline in terms of pain, functioning and the presence of disc sounds, though there was no statistically significant difference in outcomes among the three treatment groups.

Ekberg, et al. (1998b) studied 60 treatment-naive patients who were diagnosed with TMD reported to be of arthrogenous origin, and randomized to receive either a stabilization or control appliance used at night. Both patients and the evaluating physician were blinded to the type of appliance being worn by the patients over a 10-week period. Subjective data were collected on

functioning and pain and objective data were collected on presence of TMJ sounds. Both the treatment and control groups experienced statistically significant improvements relative to baseline in all outcome measures, while the treatment group showed improvements in some measures of pain and functioning that were greater than in the control group at statistically significant levels. Almost one-third of the control group and 7% of the treatment group reported exacerbation in pain during the study period.

Magnusson and Syren (1999) studied 26 patients randomized to receive either therapeutic jaw exercises or interocclusal appliance therapy for a 24-week study. At the mid-point of the study a new "combined" treatment group was created with five patients due to persistent symptoms in this subset. Two-thirds of each treatment group and all members of the combined therapy group were also taking analgesics during the study period. Subjective outcome data were collected by mail survey from one to four years later. The authors report improvements in pain and functioning at the end of the initial study period and at follow-up one to four years later for all study groups, though no statistical analyses were presented and the treatment groups had similar outcomes.

RCTs examining the benefits of occlusal therapy found mixed results in improving TMD pain and functioning in study participants. Davies and Gray (1997a,b) conducted two studies with different types of splints, with each study examining the effectiveness of different durations or timing of splint use, with no untreated control group. In both of these short-term studies, patients in all groups improved relative to baseline. In the first study, the patients wearing the splint for 24 hours a day had significantly greater improvement compared to the other groups (Davies and Gray 1997a). Eckberg et al. (1998b) also found patients in both the stabilization appliance group and the control appliance group improved , though the treatment group experienced certain significant reductions in pain and functioning relative to the group with a control appliance. Magnusson and Syren (1999) studied patients using an interocclusal appliance, physical therapy, or combination therapy in a six-month study and found improvements in each therapy group, though statistical differences were not assessed due to small sample sizes. Overall, occlusal therapy appeared to have positive outcomes relative to baseline levels in the short term (e.g., less than six months), though splints did not emerge as being clearly superior to control groups receiving no therapy.

### 1 Non-RCTs

Nine non-RCTs dealing with non-surgical occlusal therapies for treating TMD met the inclusion criteria for this review. Eight of those studies were case reports and one was an expert opinion (Keller 1996). Keller 1996 presents a discussion of the use of orthodontics in treating TMD, making a plea that professionals involved in this area work together and maintain an atmosphere of open discussion of issues relevant to TMD and the treatment of TMD. Keller further presents a case for the use of orthodontics in treating TMD, providing an account of approximately 400 clinical results in orthodontic treatment for patients who had been diagnosed with TMD.

Of the eight case reports, five demonstrated positive outcomes for the patient or patients. Two studies reported that the treatment failed to correct the TMD, and one study did not report outcomes. Treatment duration ranged widely from 12 weeks to 10 years. The small number of studies and anecdotal nature of the reports did not allow for analysis of trends in the findings. A more detailed summary of the case reports is presented below.

DeGuchi et al. (1998) treated a patient with a chin cup to control mandibular growth and flat plane occlusal splint therapy to relieve pain and relax musculature over a period of approximately 10 years. Therapy in this case relieved the TMJ pain and helped achieve more normal movement in the mandible. Dylina (1999) treated a patient using occlusal appliance therapy for approximately three years to treat facial/joint pain and headaches. At three years, the patient was pain free. Festa et al. (1998) treated two patients with a functional distraction appliance for approximately five months in one case and two weeks in another to treat locking, reduction in mouth opening, pain, and mandibular shift. (This spring-loaded oral appliance had the intended effect of continuously and progressively stretching the muscle fibers adjacent to the TMJ, thereby reducing muscular tension, and ultimately realigning the structures of the TMJ.) No outcomes were reported because this study presented only preliminary findings. Joondeph (1999) reported on a patient treated with a mandibular anterior repositioning appliance for one year and three months to diminish TMJ pain, soft tissue noise, and myofascial discomfort. Follow-up evaluations at three and seven years showed that the patient had completely relapsed to pre-treatment condition. Keng (1996) treated a patient with a provisional occlusal acrylic resin splint for two years to relieve pain, clicking, and an over-closure of the mandible. The patient's condition was stable and asymptomatic at a two-year follow-up examination. Learreta (1999) treated a patient with an occlusal splint for nine months and with a transcutaneous electrical neurostimulator (TENS) unit to treat TMD having arisen from a streptococcus infection. An MRI one year after initial treatment showed clinical improvement in TMJ positioning. Sato et al. (1997) report on the treatment of a patient with anterior mandibular positioning for approximately two years and one month to treat disc displacement. Condylar position was corrected by anterior repositioning, but the treatment failed to correct the disc displacement. Lastly, Zuccolotto et al. (1999) treated a patient with a modified occlusal splint with a "sliding plate design" for approximately 12 weeks. The device was successful in reducing TMD pain.

### *d) Surgery*

Three published RCTs investigated the efficacy of surgical techniques to diminish symptoms resulting from TMD (Fridrich et al. 1996; Goudot et al. 2000; and Miyamoto et al. 1999).

Goudot et al. (2000) studied 62 new patients suffering from "TMJ pain and dysfunction syndrome" who had been unresponsive to noninvasive therapy for six months. The patients were randomized to receive either arthroscopy or arthrocentesis. The study measured self-reported functional status and change in pain as reported on a visual analog scale one year after surgery. Both groups improved significantly from baseline. The groups did not differ significantly from

each other in pain reduction, but arthroscopy was found to be significantly more effective in improving functional outcomes.

Fridrich et al. (1996) compared arthroscopy and arthrocentesis for the treatment of TMD. Nineteen patients were randomized into two groups: one group received arthroscopic lysis and lavage under general anesthesia, and the other group received arthrocentesis, hydraulic distention, and lavage under intravenous sedation. Objective and subjective data were collected, and patients were followed 26 months postoperatively. The overall success rates were 82% for the arthroscopy group and 75% for arthrocentesis group. However, there were no statistically significant differences in outcome between the two groups for any of the parameters evaluated. Therefore, while both modalities were associated with improved TMD symptoms, their therapeutic success rates were not significantly different. The authors did not address the possibility that the small sample size of this trial may not have provided sufficient power to detect any true difference between treatments.

Miyamoto et al. (1999) prospectively compared two techniques of arthroscopic surgery for advanced internal derangement of the TMJ. In this trial, 101 patients were randomized into two groups: one group had arthroscopic lysis and lavage (ALL) and one group received arthroscopic lysis and lavage plus arthroscopic anterolateral capsular release (ALLCR). Objective and subjective data were collected at 1, 3, 6, and 12 months postoperatively. The only statistically significant difference between groups was found at one month, when the ALLCR group had greater mouth opening than did the ALL group. Both groups had significantly less pain in the joint and better jaw opening one year postoperatively, demonstrating that both techniques were useful in the management of advanced internal derangement of the TMJ. Given their similar outcomes, the authors recommended using the less invasive method of lysis and lavage.

All three of these RCTs focused specifically on the surgical techniques of arthroscopy and/or arthrocentesis. None of these studies included a non-surgical group or a non-treatment group. For most of the endpoints in each of the studies, the authors failed to detect a statistically significant difference between the two treatment groups. Goudot et al. (2000) found a statistically significant difference between treatment groups in improving function though not in pain relief. They concluded that arthroscopy provides better results for functional treatment than does arthrocentesis. All three studies reported statistically significant improvements relative to baseline.

### 1. Non-RCTs

Ten articles reporting on surgical therapy in study designs other than RCTs met the inclusion criteria. One expert opinion report focused on the use of surgery (Barkin and Weinberg, 2000) and the lack of long-term follow-up in most studies of surgery. Only one study was cited as having long-term outcomes reported, though this study was only for arthrocentesis on acute TMJ closed lock (Nitzan 1991). The authors discussed arthroscopic and open surgical techniques as well as injection of fluids.

McNamara et al. (1996) published the only study of patients with TMD as a result of a traumatic injury (motor vehicle accident) that met the inclusion criteria. Twenty patients who received either arthroscopic surgery with midlaser therapy TMJ/occlusal stabilization post-surgery or only midlaser treatment and TMJ/occlusal stabilization were compared. Follow-up data was collected at three years. Though a statistically significant difference was not detected between groups, patients in both treatment categories had reduced pain and disc derangement following therapy. Hirota (1998) reported on 15 patients with internal derangement of the TMJ who were studied for presence of arachidonic acid metabolites or cytokines in the synovial fluid of the joint. The case series explored the impact of injecting hyaluronic acid to reduce inflammation. Pre- and post-treatment data collected over the two-week study period indicated significant reductions in pain, jaw clicking, and improvements in degree of mouth opening. There was no long-term follow-up or nontreatment comparison group included in the study. Grubbs (1999) reported a case study of a patient with a history of TMD, though no current pain, that underwent osteotomy to "align her teeth." Eight months following surgery, the patient had chronic pain and her condition had worsened. Hori et al. (1999) reported on three patients that underwent split osteotomy; all had greater pain and reduced functioning at 3, 6, and 9 months post-treatment. Israel and Scrivani (2000) reported on one patient treated with increasingly invasive therapy (from analgesics to discoplasty with distal repositioning) with poor long-term outcomes at one year following therapy. Itoh et al. (1999) published a case report on a pediatric patient treated over a five year period with increasingly invasive therapy, from occlusal splint therapy to orthodontic surgery. The patient achieved proper occlusion and was free of TMD symptoms at five years. Kondo and Aoba (1999) reported on two pediatric patients who received occlusal splints and orthopedic surgery of the neck muscles; they were followed for eight years and were found to be symptom free. Lida et al. (1998) reported a case study of a patient with partial bone necrosis in the TMJ presumed to be due to repeated injection of sodium hyaluronate. The patient underwent a sequestrectomy and was found to have increased functioning at one month post-operation. Spinazze et al.(1998) report on a patient unsuccessfully treated with increasingly invasive procedures (i.e., analgesic therapy, surgery, and gap arthroscopy). Thomas and Tucker (1999) review evidence for increasingly invasive therapy in some patients and describe the experience of a pediatric patient who ultimately received surgery for TMJ with positive long-term results.

Six of the 10 non-RCT studies of surgical intervention for TMD found that surgery was successful in reducing pain and increasing function. One of these studies (McNamara et al. 1996) was limited to patients with the specific cause of TMJ being traumatic injury to the face. Its positive findings were consistent with the assertion by multiple stakeholder interviewees that surgery can be appropriate for a narrowly defined population, i.e., those with a clear etiology who are deemed appropriate for surgical treatment by their physician). Even so, that single non-randomized study since 1996 of 20 patients constitutes limited evidence. The series of 15 patients with internal derangement of the TMJ who received hyaluronic acid showed positive outcomes, but were followed for only two weeks. Of the remaining eight reports involving surgery for one to three patients each, half showed improvement and half showed no improvement or had worsening outcomes.