

EVIDENCE-BASED DENTISTRY SERIES

Evidence-based dentistry: Prognosis

James D. Anderson, BSc, DDS, MScD,^a and George A. Zarb, BChD, DDS, MSc, MS, FRCD(C)^b

CLINICAL SCENARIO

A 58-year-old man is a new patient to your practice seeking general dental care. His present complaints include occasional facial pain and clicking in the region of his left temporomandibular joint (TMJ). His medical history and recent general medical examination are unremarkable. His dental history and available records from his previous dentist include nonsurgical treatment for TMJ pain 2 years ago. On examination, he has a reasonably complete, well cared for dentition, with bilateral stable occlusion.

Although his joint pain is less than it was 2 years ago, he still has some pain on movement and asks if he can expect any relief. His previous records, which include TMJ tomographs, support a diagnosis of internal joint derangement characterized by disk displacement with reduction. To answer his question, you are unsure about the association, if any, between disk displacement and the relief of joint pain. After your initial examination, you offer him a return appointment to discuss his question and to plan the details of his other dental treatment. In the meantime, you resolve to find evidence for the association between disk displacement and joint pain.

THE SEARCH

Using your office computer, you do a Medline search using the search engine Ovid (Ovid Technologies, Inc, New York, N.Y.). In the 1996-2000 database, you enter the term “temporomandibular joint disorders,” which returns 726 hits—far too many to review individually. Using the Index feature, you view the MeSH subheadings associated with temporomandibular joint disorders and decide that “/physiopathology” most closely describes what you seek. Entering this subheading with temporomandibular disorders reduces the number of hits to 186—still too many to review. Because disk displacement is a feature of interest, you enter “disk displacement.” Ovid maps that term to sev-

eral subject headings of which “Dislocations” is the best descriptor. A refinement of this term, again using “/physiopathology”, yields 29 hits. Combining this statement with the previous statement reduces the number of hits to 8—a number that can be reviewed. However, after reviewing these titles, none seem to be relevant to the patient’s problem. Changing databases to 1991-1995 and rerunning the search brings up 12 titles. A review of these titles and their abstracts reveals an article in the *Journal of Orofacial Pain* by de Leeuw et al² that appears to address the patient’s concerns.

The title of this article focuses on internal derangement seen in your patient, and the abstract suggests that the report includes information gathered by following affected patients for a long time. You suspect this article may contain the answer you wish to provide for your patient, but you are concerned that there may be biases in the study that may distort the conclusions. You decide to do a critical appraisal of the article before allowing yourself and the patient to be convinced by the conclusions, because the information may affect your treatment recommendations to the patient.

INTRODUCTION

Research study designs used to qualify prognostic factors

Every day we inform patients of the prognosis for a particular tooth or other clinical problems. But what are we really saying? We are attempting to give the patient an idea of the possible outcomes of the present condition, and the frequency with which these outcomes are likely to occur. For example, in offering an opinion about a tooth with reduced periodontal attachment, we (almost reflexively) consider various characteristics of the patient, such as age, oral hygiene status, bruxing habits, and occlusal loading. These characteristics serve as “prognostic factors.” They need not actually cause the expected outcome, but rather merely be associated with it strongly enough that the factors tend to predict the outcomes—good or bad. There are various kinds of prognostic factors: demographic (such as age, sex), disease specific (such as bleeding on probing), or comorbid (for example, radiated tissue, poorly controlled diabetes). Prognostic factors are usually distinguished from “risk factors” that are the characteristics associated with the development of the problem in the first place. For example, poor oral hygiene is accepted as a risk factor in the initiation of periodontal disease leading to attachment loss, whereas bleeding on probing is thought to be a prognostic factor predicting

Modified from Laupacis A, Wells G, Richardson S, Tugwell P, and the Evidence-Based Medicine Working Group. Users’ guides to the medical literature. V. How to use an article about prognosis. *JAMA* 1994;272:234-7.

^aMedical Director, Craniofacial Prosthetic Unit, Toronto-Sunnybrook Regional Cancer Centre; and Professor, Department of Prosthodontics, Faculty of Dentistry, University of Toronto, Toronto, Ontario, Canada.

^bAssociate Dean, Head of Prosthodontics; and Professor, Faculty of Dentistry, University of Toronto, Toronto, Ontario, Canada.

attachment loss. Treatment can be regarded as a prognostic factor, because it can affect the outcome of a condition. Articles on prognosis then, look not only at the natural history of a given condition, but also at the clinical history.

The ideal way to test the effect of different prognostic factors would be to randomize patients to different factors. However, this may not be possible, or is unethical. Some prognostic factors are inherent patient characteristics, such as gender or comorbid conditions. These are not under the control of the investigator, and as such could not be randomized among subjects. For instance, with our current understanding of the association of oral hygiene and gingival health, we would be reluctant to randomize patients to a group who performs no oral hygiene measures over a 5-year period, and observe the incidence or progression of periodontal disease.

As a good alternative, the cohort study is a strong design to reveal the increased risk of a particular outcome being associated with a particular prognostic factor. Here, patients who have not yet had any of the potential outcomes are assigned into cohorts on the basis of the existing prognostic factors of interest. The investigators then follow the cohorts forward for a specified period, observing the subjects to determine whether the outcome of interest occurs. The frequency and/or timing of these outcome events for each cohort, yields information on each of the prognostic factors. The magnitude of the association is determined between each cohort's outcomes and each cohort's prognostic factors. We then have measured information on the prognosis of a disease process.

Cohort studies must conform to certain design rules if they are to be methodologically sound. The patients in each cohort must be representative of the full range of patients in the underlying population of interest (for example, all adults over 15 years), and must be clearly defined (such as bilateral molar Class I occlusion with all teeth present distal to the canines). The outcome criteria must be objective and as easily measured in one cohort as another.

There is a potential problem with cohort designs. If the outcome of interest takes a long time to be revealed, or if the incidence of the outcome is low, the follow-up times in a cohort design can become very long. The result is that the project becomes expensive, maintaining calibrated observers becomes difficult, there is a greater risk that comorbidities and nonstandardized cointerventions may occur for some of the subjects, and the risk of subject dropout increases. These difficulties have a negative impact on the validity of the results. Such may be the case in studies of temporomandibular disorders (TMDs). Further, in studies of many conditions such as the TMDs, care must be given to the definition of the outcome of interest or the

"outcome event": Is it restoration of comfort (a pain scale), or freedom of movement beyond a certain threshold? The difficulties of defining an objective outcome measure become apparent.

Another possible methodological design is the case-control study. In this design, the investigator gathers up "cases" (patients who have already had the outcome of interest) and "controls" (those who have not). The investigator selects patients for these groups that have characteristics as similar as possible, except for the possible prognostic/risk factors. A count is made of the number of patients in each group who have (or have had) the prognostic factor of interest. Contrary to the cohort design, this design looks backward in time to find the prognostic factors associated with the outcome. This design requires less time and is likely less expensive, but it is open to several biases that can significantly weaken the evidence it produces. For example, because these studies only examine the patient at one point in time, a positive outcome event is scored if the subject currently has the outcome, or if he or she remembers having the outcome. Recalling the existence of the prognostic factor or the outcome event may depend on the patient's memory or earlier records, both of which are often incomplete. This is particularly true for transient events or disease processes that "wax and wane." Pain is an outcome/prognostic factor that can be transient in TMDs. Subjects may not remember having pain or understand how the observer wants them to assess their past pain, whereas subjects who currently have pain will be more likely to report it and the observer can consistently measure it. Because of the transient nature of the outcome, the subjects may be assigned to the wrong study group, and this will affect the scoring of the prognostic factor.

Another problem with case-control designs, not encountered in cohort designs, is that they cannot tell the absolute risk of an outcome (eg, 10% over 5 years), because the subjects are not followed over time. These designs can only tell the relative risk (RR) of an outcome occurring if a particular prognostic factor is present (eg, 3.5 times as likely compared with a subject that does not have the prognostic factor). However, case-control studies may be the only practical alternative in which outcomes are rare, or in which follow-up times must be long.

In the article by de Leeuw et al,² the patients who had nonsurgical treatment for osteoarthritis and internal derangement 30 years ago were divided into 2 groups according to whether they had reducing disk displacement or permanent disk displacement. They were reexamined for the 1994 report. Although the assignment of patients into cohorts, and the establishment of outcome criteria were not performed at the start of the period, the study appears to be a cohort design and the prognostic factor of interest is the

reducing disk displacement, a salient feature of our patient. The control group for comparison is the permanent disk displacement group. A separate control group was chosen at the end of the period. This group was not followed over the 30 years, and thus is not part of the cohort design.

ARE THE RESULTS OF THE STUDY VALID?

Primary guides

Was there a representative and well-defined sample of patients at a similar point in the course of the disease? In any article about the prognosis of a condition, the reader must be assured that the patients in the study really do have the condition of interest, and not some other process that could be confused with the condition of interest. The authors therefore should be very explicit in detailing the criteria by which patients were chosen for the study.³ de Leeuw et al² applied modern diagnostic criteria to the 30-year-old records. They excluded patients if they believed the subjects had craniomandibular disorders other than osteoarthritis and internal derangement, or when full agreement between 2 observers on the diagnosis could not be reached. Very explicit criteria were given in a companion article.⁴

Because the chosen patients are only a sample of all patients with the condition of interest, it is important that they be representative of the full range of people who have that condition. To establish this, the manner of recruiting the patients must be clearly reported. This description addresses possible biases that may cause the composition of the selected groups to favor 1 segment of the population. For example, patients chosen from faculty clinics, specialty offices, general practice, or by public advertising, may have different demographic characteristics, or different disease severity. Patients chosen from specialty offices may have more severe problems, thereby making unfavorable outcomes more likely compared with patients recruited through public advertising; a problem called "referral filter bias." The patients in the study by de Leeuw et al⁴ were referred to the department of oral and maxillofacial surgery at a university hospital, suggesting that they may have been more severely affected than other members of the population. Less favorable outcomes might be expected in this sample than in the general population of people who have osteoarthritis and derangement.

Outcome events may not occur at the same rate over time. For example, the classic article by Tallgren⁵ clearly showed the differences in rate of residual ridge resorption, between the first and subsequent years after extraction. Therefore, any study of this phenomenon would have to ensure that the inclusion criteria contained a statement indicating the acceptable time since extraction to qualify a patient for the study. The start-

ing point of the study need not be the starting point of the condition, but it is important that all patients enter the study at the same point in their clinical course of the condition of interest. This should be clearly described and is referred to as the inception cohort. If subjects enter the study at different points in the clinical course of their disease, the recorded incidence of outcome events may be inaccurate. de Leeuw et al² do not comment on the duration of the condition before treatment.

Was follow-up sufficiently long and complete? As noted previously, prognostic factors may precede an outcome by a long time, so it is necessary to follow the study patients for long enough for the outcome event to happen and be recorded. Similarly, if the outcome of interest is reversible or is more than a single event, the follow-up must be frequent enough to catch the event. The classic example of the importance of this point can be found in the work of Goodson and coworkers at Forsyth.⁶ It took frequent, repeated observations of periodontal attachment levels to reveal the sporadic, discontinuous progression of periodontal disease. This differed from the previously presumed prognosis of periodontal disease defined as a slow steady advance. The length of follow-up therefore needs to be clearly outlined, in terms more specific than just the average length of observation for the group. The reader needs to know how many patients were actually followed for the full term of the study.

The completeness of follow-up impacts the conclusions in various ways. Where the follow-up time for some of the patients is shorter, it simply may be that they were recruited later. But when the follow-up time is short for subjects because they were lost to follow-up, the reasons for attrition need to be identified and reported. These reasons for patients being lost to follow-up may include an exacerbation of the outcome of interest, and thus have an impact on the interpretation of the results. For example, it would not be possible to follow the pattern of attachment loss on a tooth (the outcome of interest) if the tooth has been extracted for periodontal reasons (a relevant outcome that would shorten the follow-up time for that tooth). Conversely, patients may decline to return for follow-up, believing themselves to no longer be affected by the condition of interest. Patients whose TMD pain subsides without treatment might contribute much to our understanding of the natural history of TMDs. However, if these subjects were lost to follow-up, their change in pain status would not be recorded. The incomplete data would create a false conclusion.

The extent to which the patients lost to follow-up erode the validity of the report, depends on the relationship between the proportion of patients lost, and the proportion of patients who have the outcome of interest. For example, if 10% of the patients are lost

from a group that had an outcome rate of 30%, the real outcome rate could be as high as 40%. The difference between 30% and 40% is unlikely to significantly change the interpretation of the findings. However, if the outcome rate is only 1% and 10% are lost, a potential 11% rate is different from that reported, and could greatly change the reader's interpretation. For example, in the second review of the original Swedish (Brånemark) implants,⁷ 143 patients did not appear for the final follow-up visit. This was greater than 20% of the patient sample. But the article reports a 10-year rate of continuous prosthesis stability of 98% for the maxilla and 100% for the mandible (failure rates of 2% and 0%, respectively). It would take only a very few failures among the 20% of the patients lost to follow-up to radically change the success rates, and our interpretation of them. It is important to report the reasons for the loss to follow-up and show that these reasons are unrelated to the outcome, and that the "lost to follow-up" numbers are equally distributed in the 2 groups. Failure to report this information reduces the reader's confidence in the final study analyses.

Because de Leeuw and coworkers² chose the patients at the end of the 30-year period, there is no way to know how many of the original participants were lost to follow-up. The patients were chosen for the study only if their current addresses could be traced. Undoubtedly, there are patients who qualified for inclusion 30 years ago who were not reexamined because of address changes—a factor that may have, but was unlikely to have changed the conclusions.

Secondary Guides

Were objective and unbiased outcome criteria used? It is necessary to establish a clear definition of outcome events before the study starts to allow consistent recording of the study results. The definition may be simple: the presence or absence of a tooth. Alternatively, the outcome may be more equivocal, such as the decision to remove a tooth. One dentist may declare a tooth salvageable where another would not. The important element is that, where any judgment is required to determine an outcome, the observer must be trained in the outcomes assessment and blind to the presence of the prognostic factors—or even the purpose of the study—wherever possible.

Similarly, where such judgments are made over more than 1 group of patients or more than one point in time, the measurement methods should be the same at each examination or observation. For example, if one is attempting to show changes in vertical dimension of occlusion over time, one could not compare a clinical measure of vertical dimension taken today with a measure of vertical dimension on a cephalograph that was taken years ago.

Because of the long time interval, de Leeuw et al² concede that the current examinations and exploration of symptoms by interview could only be compared with the 30-year-old records that were sometimes incomplete. Further, the same person who did the original examination did not do the current examination. The current examiner "...will have systematically adapted his methods of examination during these years according to increasing knowledge about temporomandibular disorders as well as changes in opinions and methods in general." No definition of the outcome events was established 30 years ago, and no mention is made of blinding the examiners to the prognostic groups. There are therefore several significant systematic and design weaknesses in the handling of the outcome criteria in this article, which diminish confidence in the conclusions. Some of these factors were inevitable because of the passage of time.

Was there adjustment for important prognostic factors?

A useful way to learn more about a suspected prognostic factor is to follow a cohort of patients who exhibit that factor. The incidence of outcomes in those people compared with the incidence in a control group will yield the relative risk (RR) of the outcome for that prognostic factor, compared with the control group. Indeed, several such groups can be followed, each with distinctive prognostic factors. However, for this arrangement to be valid, the group with the distinctive prognostic factor must be the same in all other respects (that could have an effect on the outcome) as the control (or other comparison) groups. This is not always easy to achieve, and where it cannot be done, there may be unintended differences between the groups. Where it is possible to do, the randomized controlled trial offers an opportunity to properly control for these known and unknown variables that may cause spurious differences.

Articles on prognosis look not only at the natural history of a given condition, but also at the clinical history. Treatment, then, can be regarded as a prognostic factor, because it can affect the outcome of a condition, although it is not an intrinsic characteristic of the patient. For example, in a group of 59 male patients with myofascial pain, the patients' rating of their pain decreased significantly over a period of 7 weeks after treatment with an occlusal stabilization splint. However, the pain score was not significantly different from the score in patients who received only a palatal splint with no occlusal surface.⁸ In this respect, articles that include treatment as a prognostic factor become similar to articles on therapy. The main interest in prognosis, however, is on the incidence of the outcomes for the given condition, rather than a comparison between alternative treatments. Therapy articles, on the other hand, use the incidence of outcomes as a tool to make inferences about the value of one treatment compared with another.

Table I. Reconstruction of data abstracted from Table I of de Leeuw et al²

	Pain on movement	No pain on movement	Total
Reducing disk displacement	1 (a)	40 (b)	41
Permanent disk displacement	2 (c)	52 (d)	54
Total	3	92	95

Applying formula for relative risk $[a/(a+b)]/[c/(c+d)]$ yields $[1/(1+40)]/[2/(2+52)] = 0.024/0.037 = 0.649$.

WHAT ARE THE RESULTS?

How large is the risk of the outcome event(s) in a specified period?

This is a key question that patients often want answered. The reply can be expressed in 3 forms:

1. In absolute terms: For example, in Table I of de Leeuw et al,² the prevalence of pain on movement in joints with internal derangement dropped from 0.439 to 0.171, 2 to 4 years after nonsurgical treatment. Thus, it appears that there is a 26.8% drop in the risk that joint pain will still be present 4 years later. There was a further drop of nearly 15% to a prevalence of 0.024, 30 years after treatment.

2. In relative terms: In Table I of de Leeuw et al,² only 1 of the 41 temporomandibular joints that originally had reducing disk displacement still had pain on movement 30 years after treatment (proportion of 2.4%). Among the 54 joints with permanent disk displacement, only 2 still had pain on movement 30 years later (a proportion of 3.7%). These figures from the de Leeuw et al² article are set out in the 2x2 table (Table I) of our article. Applying the formula for the relative risk to a cohort study reveals that joints with reducing disk displacement are only 0.65 times as likely to still have pain on movement 30 years after treatment, as joints with permanent disk displacement.

3. Over time: The rate at which outcome events take place may not be constant over time, and neither of the above expressions reflect this. The survival curve provides a graphical representation of the incidence of outcome events over time. Starting at 100% (all subjects are free of events), the graph declines as each event occurs. Therefore, this requires that outcomes be clearly defined events, and the time of their occurrence must be recorded precisely. (The curves can also account for subjects lost to follow-up, and can be used in calculations of comparisons between curves.) The annual success rate for individual implants in the mandible was reported by Adell,⁶ and shown graphically using a survival curve (Fig. 1). The curve for the "Development group" shows a continuing mild deterioration of the "success rate," which is somewhat steeper during the first year after implant placement. The curves for

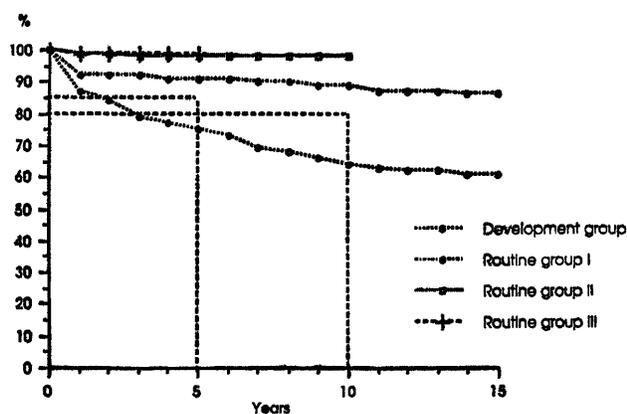


Fig. 1. Annual success rates for individual implants in mandibles calculated from time of implant placement. Five-year 85% and 10-year 80% levels are indicated. (Reproduced with permission from: Adell R, Eriksson B, Lekholm U, Brånemark P-I, Jemt T. A long-term follow-up study of osseointegrated implants in the treatment of totally edentulous jaws. *Int J Oral Maxillofac Implants* 1990;5:347-59.)

the "Routine groups" show some early deterioration, but the later groups show almost no deterioration after that. Comparison of these 2 curves suggests that, with increased clinical experience in implant therapy, implant losses in the mandible can be limited to the first year after placement. This is an important prognostic point.

How precise are the estimates of risk?

Because the 3 kinds of answers above are derived from samples of the population, they are necessarily estimates of the true risk of outcome for the population as a whole. How precise the estimates are will depend of course on the number of patients followed. Confidence intervals are an expression of that precision. The estimates can be quite precise for the shorter periods of follow-up, but will often decline as the periods grow longer. The length of time it takes to enroll subjects, and the loss of some to follow-up will erode the number of subjects and thus the precision of the estimates of risk of the outcomes of interest will decrease. In the article by de Leeuw et al,² the joints with reducing disk displacement were 0.65 times as likely to have persistent pain on movement as the joints with permanent disk displacement. This difference does not sound like much, but how accurate is it? Applying the statistics for the confidence interval on a relative risk,⁹ it turns out that the 95% confidence interval for the relative risk is between 0.061 and 6.94. In other words, in the population as a whole, 95% of the time, those joints with reducing disk displacement are between 0.061 and 6.94 times as likely to have pain on movement 30 years after treatment as those with permanent disk displacement. This is quite a wide range, suggesting that the

relative risk estimate of 0.694 is not very precise. Note that the range includes the number 1 (implying a ratio of 1:1 or no difference in the rate of pain on movement between the reducing and permanent disk displacement groups). Therefore, given the limitations of this study, one cannot conclude that there is a relationship between disk displacement and persistent pain on movement.

WILL THE RESULTS HELP ME IN CARING FOR MY PATIENTS?

Were the study patients similar to my own?

To answer this question, the reader needs a clear, detailed description of the study patients. The range of the demographic and clinical characteristics of the patients, and possibly the treatment setting, will have to be fully described to allow the reader to make a judgment. As noted earlier, the referral pattern can alter the composition of the study population, and thus potentially affect the rate of outcome events. If a clear description reveals that the study patients are very similar to our own, we can then apply the results with confidence.

The subjects in the article by de Leeuw et al² were limited to patients with osteoarthritis and internal derangement selected from a tertiary care center. The patient in the scenario is seen in a private practice setting and his records make no mention of osteoarthritis. The reader then must decide whether the patient may in fact have an undiagnosed osteoarthritis with a derangement similar to patients that would be seen in a university hospital. If not, does that make the patient sufficiently different from the subjects described in the article that the conclusions of the article could not be applied to the patient?

Will the results lead directly to selecting or avoiding therapy?

The TMD literature is an area in which an evolving knowledge of the natural and clinical course of these conditions is having an impact on the choice of treatment. Historically, we have come through a period of aggressive treatment with occlusal rehabilitation and TM joint surgery, with little understanding of the natural history of these conditions.¹⁰ However, efforts have been made to provide research diagnostic criteria for the heterogeneous group of TM disorders.^{3,11} In addition, other prognostic data are being collected to further define the natural and clinical course of the conditions,⁸ and these are having an impact on our choice of treatment.

Are the results useful for reassuring or counseling patients?

In conditions such as the TMDs, where reassurance of the patient is often treatment enough, that reassurance stems from knowledge of the natural history of the condition. "Treatment" per se may not be needed. The prognostic results, then, are very valuable in sparing the patient unnecessary intervention. The information provided by de Leeuw et al² suggests that the patient may expect further reduction in the pain on movement without further treatment. The minimal pain at the end of 30 years is unlikely to be different from the pain experienced by a patient with permanent disk displacement.

REFERENCES

1. Laupacis A, Wells G, Richardson S, Tugwell P. Users' guides to the medical literature. V. How to use an article about prognosis. *JAMA* 1994; 272:234-7.
2. de Leeuw R, Boering G, Stegenga B, de Bont LG. Clinical signs of TMJ osteoarthritis and internal derangement 30 years after nonsurgical treatment. *J Orofac Pain* 1994;8:18-24.
3. Truelove EL, Sommers EE, LeResche L, Dworkin SF, Von Korff M. Clinical diagnostic criteria for TMD: new classification permits multiple diagnoses. *J Am Dent Assoc* 1992;123:47-54.
4. de Leeuw R, Boering G, Stegenga B, de Bont LG. Symptoms of temporomandibular joint osteoarthritis and internal derangement 30 years after nonsurgical treatment. *J Craniomand Pract* 1995;13:81-8.
5. Tallgren A. The continuing reduction of the residual alveolar ridges in complete denture wearers: a mixed-longitudinal study covering 25 years. *J Prosthet Dent* 1972;27:120-32.
6. Goodson JM, Tanner AC, Haffajee AD, Sornberger GC, Socransky SS. Patterns of progression and regression of advanced destructive periodontal disease. *J Clin Periodontol* 1982;9:472-81.
7. Adell R, Eriksson B, Lekholm U, Brånemark PI, Jemt T. A long-term follow-up study of osseointegrated implants in the treatment of totally edentulous jaws. *Int J Oral Maxillofac Implants* 1990;5:347-59.
8. Dao TT, Lavigne GJ, Charbonneau A, Feine JS, Lund JP. The efficacy of oral splints in the treatment of myofascial pain of the jaw muscles: a controlled clinical trial. *Pain* 1994;56:85-94.
9. Sackett DL, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine. How to practice and teach EBM. New York: Churchill Livingstone; 1997.
10. Dolwick MF, Sanders B. TMJ internal derangements and arthrosis. St Louis: Mosby; 1985.
11. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: review, criteria, examinations and specifications, critique. Special reprint. *J Craniomandib Disord Facial Oral Pain* 1992; 6:302-55.

Copyright © 2000 by The Editorial Council of *The Journal of Prosthetic Dentistry*.

0022-3913/2000/\$12.00 + 0. 10/1/107085

doi:10.1067/mp.2000.107085