Title
Patient-Based Endodontic Outcomes, Systematic Reviews of Pathology and Pain Prevalences

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Patient-Based Endodontic Outcomes,

Systematic Reviews of Pathology and Pain Prevalences

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by

Jaclyn G Pak

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ABSTRACT OF THE THESIS

Patient-Based Endodontic Outcomes,

Systematic Reviews of Pathology and Pain Prevalences

By

Jaclyn G Pak

Master of Science in Oral Biology

University of California, Los Angeles, 2012

Professor Shane White, Chair

Introduction: Patient-based research can provide insight into real-world endodontics. Although highly controlled longitudinal studies have demonstrated extremely high success rates of root canal treatment; patient based studies, of communities and patient-centered outcomes, suggest very different results. Cross-sectional studies describe the health status of a population and measure the prevalence of disease or treatment. Neither the prevalence of periapical radiolucency, a surrogate for disease, nor the prevalence of root canal treatment has been subjected to systematic review, the highest level of clinical evidence. Anticipation and experience of root canal associated pain is a major source of fear for patients and a very important concern of dentists. Pretreatment, treatment, and post-treatment pain is anticipated,

experienced, remembered, and shared by patients. The aims were to address two issues of paramount importance to patients: Will this treatment reduce my pain? Will this treatment rid me of disease? This study conducted systematic review and meta-analysis of (1) prevalence of periapical radiolucency and non-surgical root canal treatment and (2) the prevalence and severity of pretreatment, treatment, and post-treatment pain in patients receiving root canal treatment.

Methods: Inclusion/exclusion criteria were used for defined searches in MEDLINE and EMBASE, Cochrane, and PsycINFO databases. 17,008 articles were identified. Title lists were scanned and abstracts read to determine utility; articles meeting inclusion/exclusion criteria were analyzed for heterogeneity. Weighted mean percentages were calculated for prevalence of overall periapical radiolucency; root canal treatment; apical radiolucency in both treated and untreated teeth; and pretreatment, treatment and posttreatment pain prevalence and severity. L'Abbe plots were used to evaluate the influence of root canal treatment on pain prevalence and severity.

Results: Defined searching produced 33 articles for analysis of prevalence of periapical radiolucency and root canal treatment, and 72 articles for prevalence and severity of pain. Most patient samples represented modern populations from countries with high or very high human development indices. Meta-analysis of prevalence of periapical radiolucency and root canal treatment was performed on 301,147 teeth; of these 5% had periapical radiolucencies, and 9% were endodontically treated. Of the 28,290 endodontically treated teeth, 37% had periapical radiolucencies; however, cross-sectional studies cannot distinguish between healing and failing cases. Of the 272,857 untreated teeth, 2% had periapical radiolucencies. The technical quality of root canal treatment was decried by most authors of the included studies. L'Abbe plots revealed that pain prevalence and severity decreased substantially after treatment. Mean pretreatment, 24-

hour posttreatment, and 1-week posttreatment pain prevalences with associated standard deviations were 81 (28%), 40 (24%), and 11 (14%), respectively. Pretreatment, 24-hour posttreatment, and 1-week posttreatment pain severities, on a 100-point scale, were 54(24%), 24 (12%), and 5 (5%), respectively. Supplemental injections were frequently required (60 [24%]).

Conclusions: The prevalence of periapical radiolucency was very high, broadly equivalent to 1 radiolucency per patient. The prevalence of teeth with root canal treatment was very high, broadly equivalent to 2 treatments per patient. Pretreatment root canal–associated pain prevalence was high but dropped moderately within 1 day and substantially to minimal levels in 7 days. Pretreatment root canal–associated pain severity was moderate, dropped substantially within 1 day of treatment, and continued to drop to minimal levels in 7 days. Supplemental anesthesia was often required.

The thesis of Jaclyn G Pak is approved.

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2012

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CHAPTER 1: INTRODUCTION

Endodontic therapy is the treatment used to retain teeth affected by pulpal or periradicular disease. Extensive caries, or sometimes trauma, allows bacteria and their toxins and waste products to enter the root canal system. This eventually results in pulpal death and periradicular inflammation or infection (Kakehashi *et al*, 1969). Because the root canal system is largely isolated from the body's immunological system, necrotic pulpal tissue and invading bacteria provide a nidus of infection and irritation to the surrounding periradicular tissues. Endodontic therapy aims to remove necrotic or inflamed pulp, the invasive bacteria, toxins and inflammatory mediators, and then to prevent re-entry of bacteria. This is achieved through chemo-mechanical cleaning, debridement, and shaping of the root canals, obturation of the root canal system, followed by placement of a leak-resistant coronal restoration.

While many aspects of endodontics; including treatment techniques, success rates, microbiology and materials; have been researched, most research has been performed in institutional settings. In contrast, patient-based research may give insight into real-world outcomes, including success in community treatment and patient perception. The differences seen between research performed in controlled institutional settings and the research articles reporting real-world situations are staggering. For example, longitudinal systematic reviews of endodontic outcomes report success rates in the high 90 percentile range (Torabinejad *et al*, 2007; Iqbal and Kim, 2007, Ng *et al*, 2007, Ng *et al*,2008, Ng *et al*, 2010); however, cross-sectional prevalence of persistent periapical pathology following root canal treatment has been reported as high as 69% (Segura-Egea *et al*, 2005). This disparity begs closer examination of patient-based research and outcomes in real-world settings. Although it has been recognized, is has not yet been studied. Possibly, future institution-based research can be tailored to address

disparities as revealed by patient-based research in a feedback-loop type mechanism. An important outcome measure that has not traditionally been the focus of research is the psychosocial component of root canal treatment. Patients anticipate, remember, and share pain related to treatment. This patient-based aspect of treatment is important to study as it can be used to reassure patients and may be a key issue in patient acceptance and treatment planning. The ultimate goal is to provide patients with treatment approaches that have the best real-world prognosis.

Patients are extremely concerned with the relief and avoidance of pain as well as the healing and avoidance of pathology. Does root canal treatment rid people (like me) of pain? Does root canal treatment rid people (like me) of disease? These questions differ from those already addressed by systematic review, largely of longitudinal studies that measured endodontic success and/or tooth survival in highly selected patient samples.

Of course, many questions relevant to the patient could not be answered by the extant literature. However, recent experience with systematic and narrative reviews guided iterative processes to identify questions relevant to general patient populations in which could be answered by systematic review of the extant literature. These patient-based questions were separately addressed within the following two chapters of this thesis.

Systematic review and meta-analysis of the existing literature identifies and analyzes all meaningfully comparable research conducted which pertains to a single research question. This type of research is useful in aiding clinicians and patients in decision making. Taking into account personal circumstances; patients, clinician, and third party providers can use the conclusions of systematic reviews to make informed decisions on which treatment option will provide the best outcome and may aid in the generation of useful health care public policy. The

concept of evidence-based dentistry has recently gained much interest as an approach to directly link research findings to clinical treatment needs and public policy.

The overall goal was to conduct systematic review and meta-analysis of (1) prevalence of periapical radiolucency and non-surgical root canal treatment and (2) the prevalence and severity of pretreatment, treatment, and posttreatment pain in patients receiving root canal treatment.

CHAPTER 2: PREVALENCE OF PERIAPICAL RADIOLUCENCY AND ROOT CANAL TREATMENT

The state of health, disease, or a treatment intervention, in a population is best measured by cross-sectional study. To date, neither the prevalence of periapical disease, as indicated by periapical radiolucency, nor the prevalence of root canal treatment have been subjected to systematic review, often considered to represent the highest level of clinical evidence.

In contrast, longitudinal studies on the success and survival of root canal treated teeth have received several excellent systematic reviews and meta-analyses. These have reported extremely high tooth survival rates, but lower and more variable success rates (Torabinejad et al, 2007; Ng *et al*, 2007; Iqbal and Kim, 2007; Ng *et al*, 2008; Ng *et al*, 2010). Definitions of endodontic treatment "success" include radiographic criteria, but radiographic methods and criteria vary among studies and are sources of substantial heterogeneity (Ng *et al*, 2007; Ng *et al*, 2008; Ng *et al*, 2010). Most longitudinal studies were performed in institutional settings, dental schools or teaching hospitals, rather than in typical general practice or community settings (Torabinejad *et al*, 2007). Most of these studies were single-center, not multi-center studies (Torabinejad *et al*, 2007). Thus, longitudinal data may not be representative of routine community general dental patient care (Wu *et al*, 2009).

Drastically different perspectives are provided by longitudinal and cross-sectional endodontic studies (Tholden van Velzen, 2005; Siquiera, 2010). Many cross-sectional studies have indicated that the overall prevalence of periradicular pathology in various patient populations is very much higher than one might expect by studying longitudinal success or survival rates (Buckley and Spangberg, 1995; De Moor *et al*, 2000; Kirkevang *et al*, 2000; Lupi-

Pergurier *et al*, 2002; Bołtacz-Rzepkowska and Pawlica, 2003; Dugas *et al*, 2003; Segura-Egea *et al*, 2004; Kabak and Abbot, 2005; Siqueira *et al*, 2005; Lynch and Burke, 2006). Apical radiolucency rates over 33% have often reported for endodontically treated teeth in cross-sectional studies (Petersson *et al*, 1989; Eriksen and Bjertness, 1991; De Cleen *et al*, 1993; Weiger *et al*, 1997; Saunders *et al*, 1997; Sidaravicius *et al*, 1999; De Moor *et al*, 2000; Kirkevang *et al*, 2000; Kirkevang *et al*, 2001; Kirkevang and Wenzel, 2003; Dugas *et al*, 2003; Segura-Egea *et al*, 2004; Kabak and Abbot, 2005; Siqueira *et al*, 2005). This apparent disparity may result from the nature of the cross-sectional study design, which measures the cumulative condition of an entire real-world population. It has also been suggested that this discrepancy may be explained by differing technical standards, inconsistencies in radiographic interpretation, different approaches to diagnosis and treatment planning, sample bias, and other confounding effects (Eriksen and Bjertness, 1991). The apparent dissonance between cross-sectional studies with the relatively high prevalence of periapical radiolucency and the excellent success and survival rates reported in systematic reviews of longitudinal studies suggests that systematic review and meta-analysis of cross-sectional studies may be revelatory.

Systematic review and meta-analysis is useful in aiding the generation of health care public policy by patient advocacy groups, providers, and third party payers. The concept of evidence-based dentistry has gained much interest as an approach to directly link research findings to clinical treatment needs and public policy.

The purpose of this study was to conduct systematic review and meta-analysis of the prevalence of periapical radiolucency and non-surgical root canal treatment.

MATERIALS AND METHODS

A systematic review was developed following established guidelines (Stroup et al, 2000). Methodology included formulating review questions, constructing a search strategy, defining inclusion and exclusion criteria, locating studies, selecting studies, assessing study quality, extracting data, and interpretation. The review questions were: (1) What is the prevalence of periapical radiolucency in adult populations? (2) What is the prevalence of conventional non-surgical root canal treatment in adult populations? (3) What is the prevalence of periapical radiolucency in teeth that have received root canal treatment in adult populations? (4) What is the prevalence of periapical radiolucency in teeth that have not received conventional non-surgical root canal treatment in adult populations?

Inclusion and Exclusion criteria

Inclusion criteria required cross-sectional data on the prevalence of both periapical radiolucency and conventional non-surgical root canal treatment in general patient populations. Inclusion criteria for paper review were articles published in English from January 1968 to December 2011; adult subjects; permanent teeth; studies with 20 or more subjects. Exclusion criteria consisted of literature that failed to meet the above inclusion criteria; treatment modalities not currently being used; studies that only sampled patients known to have or presenting for root canal treatment; and studies without radiographic measurement of periapical radiolucency or root canal treatment prevalence.

Search Methodology

Electronic searches were performed in MEDLINE and EMBASE databases. The search strategy for both MEDLINE and EMBASE was described in Table 1. The results from the

designed search strategy were supplemented by manual searches, citation mining, and expert recommendation. Manual searching involved reviewing the table of contents of every issue of the most recent 2 years of the following journal titles: American Journal of Dentistry, International Endodontic Journal, Journal of Dentistry, Journal of Endodontics, Journal of Oral Rehabilitation, Oral Surgery Oral Medicine Oral Pathology and Oral Radiology, and Endodontics, and Quintessence International. The citation mining and expert recommendation processes incorporated relevant materials that did not appear in database searches, such as book chapters or review articles. Experts were consulted to recommend additional articles or books for review. Two investigators screened the titles and abstracts of all articles identified in the electronic and manual searches. Articles that did not meet the inclusion criteria were excluded. All remaining articles were full-text reviewed in the second stage of the process.

Study Quality Rating

The quality of study methodology, design, and data analysis was assessed using the Wong Scale–Revised (Chiappelli *et al*, 2006). Studies were assessed by reviewer responses to nine questions; a score of 1 (inappropriate), 2 (mediocre), or 3 (appropriate) was assigned to each question. Out of a comprehensive total score of 9 to 27, a score under 19 indicated that the methodology, design, and analysis of the study failed to support the reliability of the authors' conclusions, necessitating exclusion from the meta-analysis.

Data Analysis

An iterative process was used to determine what data could be combined and analyzed. For each article which met validity criteria, and an acceptable quality rating, data was extracted

and compiled into a table of evidence and descriptive statistics, weighted means and associated standard deviations, calculated.

RESULTS

Description of the Existing Literature

Initial electronic and manual searches identified 11,491 titles. After title screening, 612 abstracts were reviewed and full texts for 232 papers were obtained. After full-text review and citation mining, 33 articles pertaining to prevalence of periapical radiolucency and root canal treatment were identified (Eckerbom *et al*, 1987; Petersson *et al*, 1989; Odesjo *et al*, 1990; Eriksen and Bjertness, 1991; Imfeld, 1991; De Cleen *et al*, 1993; Eriksen *et al*, 1995; Buckley and Spangberg, 1995; Soikkonen, 1995; Hugoson *et al*, 1995; Weiger *et al*, 1997; Saunders *et al*, 1997; Marques *et al*, 1998; Sidaravicius *et al*, 1999; De Moor *et al*, 2000; Narhi *et al*, 2000; Kirkevang *et al*, 2001; Lupi-Pegurier *et al*, 2002; Dugas *et al*, 2003; Jimenez-Ponzon *et al*, 2004; Hugoson *et al*, 2005; Kabak and Abbot, 2005; Loftus *et al*, 2005; Georgopoulou *et al*, 2005; Segura-Egea *et al*, 2005; Tsuneishi *et al*, 2005; Skudutyte-Rysstad and Eriksen, 2006; Sunay *et al*, 2007; Chen *et al*, 2007; Willershausen *et al*, 2009; Al- Omari 2011; Peters *et al*, 2011; Ozbas *et al*,2011). Of the 33 included papers, 29 were initially identified by electronic search, 3 by manual search and 1 by citation mining. Systematic review yielded an extremely low return rate, 0.3%, for the titles initially identified by defined searching. The 33 included studies reported 38 distinct data sets (Table 2).

The papers identified by the systematic review process were outcomes research studies, assigned a level of evidence of 2c according to the Centre for Evidence-Based Medicine, Oxford. Therefore, systematic review and meta-analysis of these articles, performed in this study, is

assigned a level of evidence of 2a, falling below systematic reviews of randomized control trials (Oxford Centre for Evidence Based Medicine, 2009).

Major sources of heterogeneity included differing outcome measures, differences in study geographic location, differences in operator type, and variations in patient selection or sample size. Interpretation criteria varied, as did radiographic methods which generally included full mouth X-ray series, but sometimes only included panoramic films.

The overall mean study quality rating of the 33 included studies was 23 (standard deviation = 2) on the 27-point Wong Scale-Revised. All studies had quality ratings of 19 or above, so none were excluded for reasons of quality.

Because systematic review is an iterative process, because it is impossible to know the results that will be found, and because of the heterogeneity of the identified studies, statistical analysis was limited to descriptive statistics.

The studies included in meta-analysis were mostly published in the 1990s and 2000s, with two exceptions (Eckerbom *et al*, 1987; Petersson *et al*, 1989). The mean year of publication was 2000. The common unit of reporting in the included literature was the tooth. Pertinently, 30 of the 33 the studies described in this article were performed in countries with very high human development indices, 2 were performed in countries with high indices, and 1 was performed in a country with a medium index. The findings of this study can be broadly generalized to modern populations in countries with high development indices.

Prevalence of Periapical Radiolucency and Root Canal Treatment

The prevalence of teeth with periapical radiolucency was very high, approximately 5% of all teeth, with a range from as low as 0.5% to as high as 12.4%, and a standard deviation of 6% (Table 2).

The prevalence of teeth with non-surgical endodontic treatment was approximately 9%, with a range from as low as 1% to as high as 22%, and a standard deviation of 7%. Substantially more teeth had endodontic treatment than radiolucency. Nonetheless, for the teeth which had endodontic treatment, approximately 37% (standard deviation = 10%) also had periapical radiolucency.

The prevalence of periapical radiolucency on teeth which had not received root canal treatment was consequential, 2% (standard deviation = 4%).

Of the 33 studies that included data on root canal treatment, 24 also contained numerical data on technical treatment quality (Eckerbom *et al*,1987; Petersson *et al*, 1989; Odesjo *et al*, 1990; Eriksen and Bjertness, 1991; Imfeld, 1991; De Cleen *et al*, 1993; Eriksen *et al*, 1995; Soikkonen, 1995; Buckley and Spangberg, 1995; Weiger *et al*, 1997; Saunders *et al*, 1997; Sidaravicius *et al*, 1999; De Moor *et al*, 2000; Lupi-Pegurier *et al*, 2002; Dugas *et al*, 2003; Loftus *et al*, 2005; Kabak and Abbot, 2005; Tsuneishi *et al*, 2005; Skudutyte-Rysstad and Eriksen, 2006; Chen *et al*, 2007; Sunay *et al*, 2007; Ozbas *et al*, 2011; Peters *et al*, 2011; Al-Omari, 2011). This data indicated that, based upon radiographic findings alone, the majority of included root canal treatments were of poor or unacceptable technical quality. Up to 78% of root canal treatments were reported as being inadequate; whereas, lower percentages, up to a maximum of 56%, of root canal treatments were reported as being acceptable (Sidaravicius *et al*, 1999; Skudutyte-Rysstad and Eriksen, 2006). Differences in criteria and reporting precluded meta-analysis of root canal treatment quality.

DISCUSSION

The prevalence of periradicular radiolucency reached epidemic proportions, 5% of all teeth. The prevalence of periapical radiolucency was broadly equivalent to 1 radiolucency per patient, given that the average number of teeth present per adult patient was 21, as reported in the most recent United States 2007-8 National Health and Nutrition Examination Survey (NHANES). Estimation of the number of radiolucencies per patient must be considered to be imprecise because some studies tended to exclude patients with few remaining teeth, only included dentate patients, or only included patients who presented and had X-rays made. Whereas other studies included entire populations including the edentulous and non-attenders, The data in this study is suggestive of a periapical radiolucency prevalence rate several times higher than that of untreated caries (NHANES). Unlike missing teeth or restorations, which are markers of past disease, periapical radiolucency is indicative of active disease. All included studies reported data on contemporary populations; however, a study of mandibles belonging to a medieval French population reported a prevalence of periapical radiolucency which approached that of the overall study mean (Lucas, 2010). The sugar trade was already well established by medieval times.

The prevalence of disease of pulpal origin may be higher than that of periapical radiolucency, as measured by the included studies. First, not all disease of pulpal origin produces radiographically evident periapical radiolucency. Second, many of the included studies used panoramic radiographs rather than periapical radiographs which are considered to be a gold-standard for endodontic diagnosis. Third, not all radiolucencies of pulpal origin are located at the root apex; some are located at other portals of exit, such as lateral or accessory canals. Fourth,

initial radiographic changes are often subtle, such as a widened periodontal ligament space or discontinuity of the lamina dura, and it is not clear that such minor changes were considered in the included studies. In contrast to prevalence studies, clinical pulpal diagnoses are generally made by considering a patient history, comprehensive endodontic evaluation, as well as periapical radiographs. However, it is possible that a very small proportion of periapical radiolucencies may not have been of pulpal origin, *e.g.*, periapical cemental dysplasia. The periapical radiolucency prevalence data in this paper should be considered as a lower limit for pathology of pulpal origin.

The prevalence of teeth with root canal treatment was very high, 9%, broadly equivalent to two treatments per patient, given NHANES data. Estimation of the number of treatments per patient must be considered to be imprecise for the reasons explained above. However, it is clear that a high proportion of root canal treated survive. The high prevalence of root canal treatment is consistent with incidence data. The American Dental Association Survey of Dental Services Rendered recorded over 15 million root canal treatments being provided in 2005-6, the most recent available data, at a time when the US population approached 300 million people, giving a crude 5% annual incidence rate. It is clear that billions of teeth are retained through root canal treatment, providing an immense oral health, functional, and psychosocial impact.

A remarkably high proportion, 37%, of the teeth that had received root canal treatment had periapical radiolucency. Even so, the majority of root canal treated teeth had healthy apical tissues, as measured radiographically. Furthermore, cases in progress to healing cannot be distinguished from those that may never heal or those that have failed by cross-sectional snapshot studies. It is possible that patients functionally and psychosocially tolerate incompletely healed endodontic treatments, as measured radiographically, without seeking additional

intervention. This possibility is supported by the presence of relatively high prevalence of apical radiolucency, 2%, in untreated teeth (Table 2). The 2% prevalence of apical radiolucency in untreated teeth indicated that there is a high probability that 1 in 2 to 3 of the individuals included in the analyzed studies had untreated periapical radiolucency, given NHANES data. The significant prevalence of apical radiolucency in untreated teeth could be attributed to absence of symptomatic awareness; lack of a comprehensive endodontic and radiographic evaluation with an accurate diagnosis; or unmet need. Radiographic failures, as distinct from functional or symptomatic failures, may not be removed from the population and may accumulate over time.

Endodontic outcomes measures, including identification and quantification of periapical radiolucency, were originally designed to enable the correlation of small differences in healing with prognostic indicators, not to describe patient-based clinical performance (Strindberg, 1956; Orstavik *et al,* 1986). Maybe, the complete absence of periradicular radiolucency along with the re-establishment of a normal periodontal ligament space and a defined lamina dura (Stringberg, 1956) is an unreasonably strict criterion for endodontic "success". Nevertheless, periradicular disease, as measured radiographically, has been shown to correlate with histologic signs of inflammation and infection, disease (Orstavik *et al*, 1986), and its treatment to greatly reduce the prevalence and severity of pain (Pak and White, 2011). Furthermore, the prognosis for successful treatment of periradicular disease decreases as the magnitude of the existing lesion increases (Chugal *et al*, 2001).

The disappointing results of this cross-sectional systematic review and meta-analysis clash with the excellent results reported in prior longitudinal systematic reviews (Torabinejad *et al*, 2007; Iqbal and Kim, 2007; Ng *et al*, 2007; Ng *et al*, 2008; Ng *et al*, 2010). The disparity

between cross-sectional and longitudinal studies may be a result of the nature of the cross-sectional study design, which measures the cumulative condition of an entire population, not just the incidence of new disease. Cross-sectional studies do not account for differences in subject experience. It is probable that the patient populations sampled in cross and longitudinal studies may differ in many ways including caries rates, clinical settings, providers, and social or economic factors. By definition, patients in longitudinal studies are receiving ongoing contact and care. Longitudinal endodontic studies tend to be performed upon self-selected patients treated in academic institutions. In contrast, patients sampled in cross-sectional studies, often performed at acute care centers, may primarily be those presenting for episodic treatment of acute conditions, not those receiving ongoing comprehensive dental care. A practice-based research network (PBRN) retrospective cohort study, and a community-based study, both suggested a lower percentage of root canal treatment success than in other institution-based longitudinal studies, and that the restorative process is a key factor for success (Tilashalski *et al*, 2004; Gilbert *et al*, 2010). Moreover, if distributions of patient variables are non-Gaussian, if relationships between dependent variables and outcomes are non-linear, or if time effects relating to healing are not understood or incorrectly accounted, discrepancies between longitudinal and cross-sectional studies may result (Louis *et al*, 1986). The limitations of longitudinal studies of root canal treatment outcomes have been discussed (Torabinejad *et al*, 2005; Wu *et al*, 2009), but cross-sectional studies have received less attention, analysis, and interpretation. It is possible that similar disparities between cross-sectional and longitudinal studies issues may be manifested by other dental treatment modalities, such as restorations or implants.

The very low search return rate suggested a need for more accurate and meaningful keyword tags, or that a more narrowly designed and efficient search strategy should have been

used. However, despite broad electronic searching, 4 of the 33 included papers were found by manual searching or citation mining. In this study the defined inclusion/exclusion criteria resulted in elimination of studies without outcomes useful for meta-analysis. Even so, the return rate observed in this study was substantially lower than for other endodontic systematic reviews (Torabinejad *et al*, 2007; Pak and White, 2011; Iqbal and Kim, 2007; Ng *et al* P1, 2011; Ng *et al* P2, 2011).

The mean year of publication of the included papers was 1999, with a range from 1987 to 2011. Therefore, the data was reasonably modern or contemporary. Most studies were performed in countries with high or very high human development indices. However, by their nature, cross-sectional studies cannot provide any assurance that the treatment methods used were contemporary, best practice, or even appropriate. An X-ray, taken after the fact, simply cannot tell us, for example, if rubber dams or appropriate irrigants were used. We were not informed as to the clinical setting or operator.

This current study focused upon prevalence data, because it was well represented in the extant literature. Unfortunately, the included prevalence studies did not allow analyses of predictive factors, but carefully designed cross-sectional studies may be an efficient way of identifying prognostic indicators in the future. Incidence data was limited. However, several studies reported serial cross-sectional samples of the same general populations over 2 to 3 decades (Eriksen *et al*, 1995; Hugoson *et al*, 1995; Skudutyte-Rysstad and Eriksen, 2006). Data from these studies did not demonstrate substantive change in the percentages of teeth with root canal treatment, teeth with apical radiolucency, untreated teeth with apical radiolucency, and root canal treated teeth with apical radiolucency over two decades.

Because the inclusion criteria demanded data on the prevalence of both periapical radiolucency and conventional non-surgical root canal treatment in general patient populations, many papers which selected samples of patients known to have had root canal treatment or patients presenting specifically for root canal treatment were excluded. However, these excluded papers contained much data on the number of treated teeth with periapical radiolucencies, albeit from biased samples. These excluded papers tended to focus upon the quality of root canal treatment; whereas, the included papers tended to examine entire communities (Table 2).

Sadly, the authors of 24 of the 33 of the included studies deplored the technical quality of the root canal treatment, based solely on radiographic assessment. These findings must reflect on the community treatment provided to samples of thousands of people in countries with high or very high human development indices. This suggests that community standards do not match institutional or best practice standards. Have teaching institutions failed to indoctrinate best practice? Have providers failed to adequately diagnose, perform and inform? Have third parties, such as insurance companies, other payers, government health services, and dental professional organizations failed to identify or address inadequate treatment? Have patients failed to inform themselves? Has society undervalued the importance of adequate technical treatment procedure or the need to provide adequate treatment resources? Likely the answers to these questions are complex and include a multiplicity of factors. Siqueira has suggested several approaches to addressing these problems: improving, providing more curriculum time for, and rethinking the way endodontic treatment is taught in dental schools; directing resources towards studying, researching, and developing treatment protocols that are less technically demanding, affordable, have a shorter learning curve, and provide better outcomes; and limiting the provision of root canal treatment to specialists (Siqueira, 2010). All of these approaches demand increased

allocation of scarce resources towards root canal treatment. It is likely that similar quality issues may affect other dental treatment modalities, such as restorations or implants. Nevertheless, the technical quality of community root canal treatment fell well below the expectations of most investigators.

CONCLUSIONS

This systematic review and meta-analysis of cross-sectional studies on the prevalence of periapical radiolucency and root canal treatment, based on data describing over 300,000 teeth from 33 studies, mostly performed in countries with high or very high human development indices, found that: the prevalence of teeth with periapical radiolucency was very high, approximately 5% of all teeth, broadly equivalent to 1 radiolucency per patient; the prevalence of teeth with root canal treatment was very high, approximately 9% of all teeth, broadly equivalent to 2 treatments per patient; the prevalence of periapical radiolucency in endodontically treated teeth was high, approximately 37%; and the prevalence of periapical radiolucency in untreated teeth was surprisingly high, approximately 2%. The technical quality of community root canal treatment was decried by most of the authors of the included cross-sectional studies. Nonetheless, billions of teeth are retained through root canal treatment.

CHAPTER 3: PAIN PREVALENCE AND SEVERITY

BEFORE, DURING, AND AFTER ROOT CANAL TREATMENT

Pain of endodontic origin is widely feared by the public (Gorduysus and Gorduysus, 2000; Udoye *et al*, 2005; Watkins *et al*, 2002). However, the provision of over 15 million root canal treatments annually in the USA, suggests that the public values root canal treatment (ADA Survey of Services Rendered 2005). Root canal procedures are commonly believed to be the most painful dental treatment, but only 17% of subjects experiencing root canal treatment described it as their most painful dental experience (Wong and Lytle, 1991). Rigorous systematic review demonstrates that root canal treatment facilitates the long-term retention of teeth with pulpal or periradicular disease that would otherwise likely be extracted (Torabinejad *et al*, 2007; Iqbal and Kim, 2007). Root canal treatment obviously alleviates pain of endodontic origin, but this important benefit has not yet been subjected to systematic review or meta-analysis.

Accurate knowledge of pain prevalence and severity associated with pulpal or periradicular disease, and its diminution by root canal treatment, has the potential to change the attitudes of the public, dentists, and other health care professionals, thus allowing more natural teeth to be retained. Dentists could be better guided by the best evidence in making anesthesia and pain management treatment decisions. In addition, more accurate evidence-based advice could be given to individual patients by individual dentists. This would improve the basis upon which individual patients make their own informed treatment decisions. Furthermore, data on expected pain could be used to reassure patients during treatment and healing, or to identify those who fall beyond the norms, so that additional care could be appropriately provided. However, the extant literature containing data on endodontic pain is rather disparate and

primarily includes papers focusing upon other topics, typically upon prognostic variables, treatment variables, or upon medications (Phillips *et al*, 2010; Stroup *et al*, 2000). Direct comparisons of pre-operative, treatment, and post-operative pain are extremely rare (Genet *et al*, 1986). Thus it is difficult for the dentist to identify, assimilate, or synthesize data on root canal treatment associated pain in a clinically meaningful manner.

Systematic review uses defined methods to search, critically appraise, and synthesize the available literature pertaining to a clinical question. Systematic review is a fundamental scientific activity which methodically digests large quantity of information to find an answer to a research question. Systematic review is an efficient and reproducible scientific technique which produces findings that may be generalized. It also allows the researcher to assess consistency of relationships and to explain inconsistencies and conflicts in data. Furthermore, it increases power and precision of estimations. Hence, systematic review and meta-analysis are widely regarded as providing the highest level of clinical evidence (Mulrow, 1994; Cook *et al* 1997; Carr, 2002; Upshur, 2003; Phillips, 2009).

The purpose of this study was to estimate and compare the prevalences and severities of pain experienced before, during, and after root canal treatment through systematic review and meta-analysis.

MATERIALS AND METHODS

A systematic review was developed following established guidelines (Stroup 2000). Methodology included: formulating review questions using a PICO (Patient Population, Intervention, Comparison, and Outcome) framework; constructing a search strategy; defining

inclusion and exclusion criteria; locating studies; selecting studies; assessing study quality; extracting data; and interpretation.

The review questions were formulated to allow estimation and comparison of pre-treatment, treatment, and post-treatment pain in patients requiring and receiving root canal treatment:

1. In patients requiring root canal treatment, what is the prevalence of pre-treatment pain?
2. In patients receiving root canal treatment, what is the prevalence of treatment pain?
3. In patients receiving root canal treatment, what is the prevalence of post-treatment pain?
4. In patients requiring root canal treatment, what is the severity of pre-treatment pain?
5. In patients receiving root canal treatment, what is the severity of treatment pain?
6. In patients receiving root canal treatment, what is the severity of post-treatment pain?

Inclusion and exclusion criteria

Inclusion criteria included comparative or non-comparative, prospective or retrospective, longitudinal data including prevalence and severity of pre-treatment and post-treatment pain; incidence of treatment pain; anesthetic efficacy; and incidence of flare-ups, swelling, and emergencies. Inclusion criteria for paper review included: articles published in English from January 1966 to December 2007; adult subjects; secondary teeth. Exclusion criteria consisted of literature that failed to meet the above inclusion criteria; treatment modalities not currently being used; grey literature (literature not listed in MEDLINE, Cochrane, PsycINFO and EMBASE databases); and studies without pain measurement outcomes.

Search methodology

Electronic searches were performed in MEDLINE, Cochrane, EMBASE, and PsycINFO databases (Table 3). The search strategies for MEDLINE, Cochrane, and EMBASE databases were as described for "endodontic studies", and for "psychosocial outcomes" in a prior investigation, but with the addition of the term "pain" (Torabinejad *et al*, 2007). The search strategy for PsycINFO was simply: keyword (periapical disease OR endodontics OR root canal). The results were supplemented by hand searches, citation mining, and expert recommendation. Hand searching involved reviewing the table of contents of every issue of the most recent 2 years of the following journal titles: American Journal of Dentistry, International Endodontic Journal, Journal of Dentistry, Journal of Endodontics, Journal of Oral Rehabilitation, Oral Surgery Oral Medicine Oral Pathology and Oral Radiology and Endodontics, Pain, and Quintessence International. The citation mining and expert recommendation processes incorporated relevant materials that did not appear in database searches, such as book chapters or review articles. Experts were consulted to recommend additional articles or books for review. Two investigators screened the titles and abstracts of all articles identified in the electronic and hand searches. Articles that did not meet the search criteria were excluded. All remaining articles were full-text reviewed in the second stage of the process.

Study Quality Rating

Quality of study methodology, design, and data analysis was assessed using the Wong Scale-Revised. Studies were assessed by reviewer responses to 9 questions; a score of 1 (inappropriate), 2 (mediocre), or 3 (appropriate) was assigned to each question. Out of a comprehensive total score of 9 to 27, a score under 19 indicated that the methodology, design,

and analysis of the study failed to support the reliability of the authors' conclusions, necessitating exclusion from meta analysis (Chiappelli *et al* 2006).

Data analysis

Where possible, data from like studies was analyzed by meta-analysis. Descriptive statistics, weighted means and standard deviations, were calculated. Pain prevalence and severity trends over the 7 days following treatment were plotted. L'Abbe plots were used to depict the effect of root canal treatment intervention on prevalence and severity of pain. Studies which reported both pre and post treatment pain were included in the L'Abbe plots. These plots are useful in assessing changes due to treatment, especially among heterogenous studies when pre-treatment values may vary widely. Pre-treatment data serves as a baseline measure to which analagous post-treatment data can be validly compared. Points plotted to the upper-left of the diagonal plot line denote an increase in pain following treatment, whereas points plotted to the lower-right of the diagonal line denote a decrease in pain following treatment.

RESULTS

Description of the Existing Literature

Initial electronic and manual searches identified 5,517 studies. Following title and abstract screening, full texts for 183 were obtained. Following full-text review, 72 articles pertaining to pretreatment, treatment, or posttreatment endodontic pain were identified (Gorduysus and Gorduysus, 2000; Genet *et al*, 1986; Alacam 1985; Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Attar *et al*, 2008; Bigby *et al*, 2007; Brennen *et al*, 2006; Claffey *et al*, 2004; Creech *et al*, 1984; DiRenzo *et al*, 2002; Dugas *et al*, 2002; Ehrmann *et al*,

2003; Eleazer and Eleazer, 1998; Elsharrawy and Elbaghdady, 2007; Fava, 1991; Fava, 1994; Fava 1995; Fava, 1998; Gallatin *et al*, 2000; Gesi *et al*, 2006; Ghoddusi *et al*, 2006; Glassman *et al*, 1989; Harrison *et al*, 1983; Henry *et al*, 2001; Ianiro *et al*, 2007; Imura and Zuolo, 1995; Iqbal *et al*, 2009; Koba *et al*, 1999; Krasner and Jackson, 1986; Kusner *et al*, 1984; Leguen 1985; Marshall and Liesinger, 1993; Martin and Cunningham, 1982; Matthews *et al*, 2009; Mattscheck *et al*, 2001; McCartney *et al*, 2007; Menhinick *et al*, 2004; Michaelson and Holland, 2002; Moorse *et al*, 1987; Morse *et al*, 1988; Mulhern *et al*, 1982; Negm, 1994; Nieburger, 1993; Nusstein *et al*, 1998; Oginni and Udoye, 2004; Oguntebi *et al*, 1992; O'Keefe, 1976; Pekruhn, 1981; Peters, 1980; Pickenpaugh *et al*, 2001; Pisano *et al*, 1985; Polycarpou *et al*, 2005; Reisman *et al*, 1997; Roane *et al*, 1983; Rosenberg *et al*, 2007; Ross *et al*, 2009; Rousseau *et al*, 2002; Rowe *et al*, 1980; Ryan *et al*, 2008; Shedletsky *et al*, 1984; Sherman *et al*, 2008; Siqueira *et al*, 2002; Soltanoff, 1987; Srinivasan *et al*, 2009; Torabinejad *et al*, 1994; Torabinejad *et al*, 2005; Walton and Fouad, 1992; Walton *et al*, 2003; Watkins *et al*, 2002; Weiger *et al*, 2000; Yesilsoy *et al*, 1988). Major sources of heterogeneity included reporting of results from differing areas of the mouth; comparison of differing materials and techniques within studies; differing follow-up times; differing outcomes measures; differing methods of measurement; differences in operator type; and variations in patient selection or sample size. The overall mean study quality rating of the 72 included studies was 23 (SD = 2) on the 27 point scale. All studies had quality ratings of 19 or above, so none were excluded from meta-analysis for reasons of quality. Evidence for the following analyses of pain prevalence, pain severity, and anesthetic efficacy are summarized in Tables 4 to 6.

Pretreatment Pain Prevalence

Pretreatment pain prevalence was high. The mean pain prevalence for all 30 studies with pre-treatment pain prevalence data was 81 % (SD 28 %) (Bigby *et al,* 2007; Brennen *et al* ,2006; Claffey *et al,* 2004; Creech *et al,* 1984; DiRenzo *et al,* 2002; Dugas *et al,* 2002; Ehrmann *et al,* 2003; Gallatin *et al,* 2000; Genet *et al,* 1986; Gesi *et al,* 2006; Henry *et al,* 2001; Krasner *et al,* 1986; Marshall and Liesinger, 1993; Mattscheck *et al,* 2001; Menhinick *et al,* 2004; Michaelson and Holland, 2002; Negm, 1994; Oginni and Udoye, 2004; O'Keefe, 1976; Polycarpou *et al,* 2005; Rosenberg *et al,* 2007, Ross *et al,* 2009; Rousseau *et al,* 2004; Rowe *et al,* 1980; Shedletsky *et al,* 1984; Torabinejad *et al,* 1994; Torabinejad *et al,* 2005; Watkins *et al,* 2002; Weiger *et al,* 2000; Yesilsoy *et al,* 1988). However, most studies using Visual Analog Scales reported 100% prevalence, because even the tiniest discomfort registered a pain score of more than zero. The mean pain prevalence for all 14 categorical studies, non-Visual Analog Scale studies, was 68% (SD 28%) (Dugas *et al,* 2002; Gallatin *et al,* 2000; Genet *et al,* 1986; Gesi *et al,* 2006; Henry *et al,* 2001; Michaelson and Holland, 2002; Oginni and Udoye, 2004; O'Keefe, 1976; Polycarpou *et al,* 2005; Ross *et al,* 2009; Rowe *et al,* 1980; Shedletsky *et al,* 1984; Weiger *et al,* 2000; Yesilsoy *et al,* 1988). Likewise, it is important to note that 3 and 4-point scales still registered pain that had substantially diminished in severity as being extant pain for prevalence calculations. Study purposes and designs likely selected for patients with pain. For all of these reasons, the pain prevalence data reported in this paper may be overestimated.

Posttreatment Pain Prevalence

Posttreatment pain prevalence was moderate. The mean pain prevalence for all 11 studies reporting prevalence results at 24 hours was 40 % (SD 24 %) (Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Genet *et al,* 1986; Glassman *et al,* 1989; Harrison *et al,* 1984;

Henry *et al,* 2001; Oginni and Udoye, 2004; Pekruhn, 1981; Pisano *et al,* 1985; Walton *et al,* 2003; Yesilsoy *et al,* 1988). The mean pain prevalence for all 12 studies reporting prevalence results at 1 week was 11% (SD 14%) (Alacam, 1985; Albashaireh and Alnegrish, 1998; Fava, 1991; Fava, 1994; Fava, 1995; Fava, 1998; Gesi *et al,* 2006; Harrison *et al,*1983; Henry *et al,* 2001; Koba *et al,* 1999; Oginni and Udoye, 2004; Pekruhn, 1981).

Posttreatment pain prevalence trends over the 7 days following treatment were described by 16 categorical studies plotted in Figure 1(Alacam, 1985; Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Fava, 1991; Fava, 1994; Fava, 1995; Fava, 1998; Genet *et al,* 1986; Glassman *et al,* 1989; Harrison *et al,* 1984; Henry *et al,* 2001; Oginni and Udoye, 2004; Pekruhn, 1981; Pisano *et al,* 1985; Walton *et al,* 2003; Yesilsoy *et al,* 1988). Prevalence decreased substantially after treatment, especially during the first two days. By 7 days, pain prevalence had generally dropped to levels of 10 % or less.

Effect of Root Canal Treatment on Pain Prevalence

An L'Abbe plot was made to include data limited to the 7 studies that included both pre and posttreatment pain prevalence data (Figure 2) (Genet *et al,* 1986; Gesi *et al,* 2006; Henry *et al,* 2001; Marshall and Liesinger, 1993; Oginni and Udoye, 2004; Torabinejad *et al,* 1994; Yesilsoy *et al,* 1988). Posttreatment pain prevalence was substantially lower than pretreatment prevalence in all cases. Pain prevalence substantially decreased over the days immediately following root canal treatment in all cases.

Pretreatment Pain Severity

Pretreatment pain severity was moderate. The mean pain severity for all 22 studies with pretreatment pain severity data was 54 % (SD 24 %) normalized to a 100 point scale (Attar *et al,* 2008; Bigby *et al,* 2007; Claffey *et al,* 2004; Creech *et al,* 1984; DiRenzo *et al,* 2002; Ehrmann *et al,* 2003; Gallatin *et al,* 2000; Genet *et al,* 1986; Gesi *et al,* 2006; Henry *et al,* 2001; Krasner *et al,* 1986; Marshall and Liesinger, 1993; Mattscheck *et al,* 2001; Menhinick *et al,* 2004; Negm, 1994; O'Keefe, 1976; Rosenberg *et al,* 2007, Rousseau *et al,* 2004; Ryan *et al¸*2008; Sherman *et al,* 2008; Srinivasan *et al,* 2009; Torabinejad *et al,* 2005). However, study designs likely selected for patients motivated to address extant pain.

Posttreatment Pain Severity

Posttreatment pain severity was moderate. Studies reported post-treatment pain severity at differing intervals. The crude mean pain severity for all 18 studies with post-treatment pain severity data at 24 hours was 24% (SD 12%) (Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Attar *et al,* 2008; Creech *et al,* 1984; DiRenzo *et al,* 2002; Ehrmann *et al,* 2003; Genet *et al,* 1986; Glassman *et al,* 1989; Harrison *et al,* 1983; Henry *et al,* 2001; Krasner *et al,* 1986; Mattscheck *et al,* 2001; Oginni and Udoye, 2004; Pisano *et al,* 1985; Rowe *et al,* 1980; Ryan *et al,* 2008; Torabinejad *et al,* 2005; Yesilsoy *et al,* 1988).

Posttreatment pain severity over the 7 days following treatment was described by 18 studies (Figure 3) (Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Attar *et al,* 2008; Creech *et al,* 1984; DiRenzo *et al,* 2002; Ehrmann *et al,* 2003; Fava, 1994; Fava, 1998; Genet *et al,* 1986; Glassman *et al,* 1989; Henry *et al,* 2001; Krasner *et al,* 1986; Mattscheck *et al,* 2001; Oginni and Udoye, 2004; Pisano *et al,* 1985; Rowe *et al,* 1980; Torabinejad *et al,* 2005; Yesilsoy *et al,* 1988). This graph showed that severity decreased substantially after treatment,

especially during the first two days. By 7 days, pain severity had generally dropped to levels of 10 % or less.

Effect of Root Canal Treatment on Pain Severity

An L'Abbe plot was made to include data limited to the 13 studies that included both pre and post-treatment pain severity data (Figure 4) (Attar *et al,* 2008; Creech *et al,* 1984; DiRenzo *et al,* 2002; Ehrmann *et al,* 2003; Genet *et al,* 1986; Gesi *et al,* 2006; Henry *et al,* 2001; Krasner *et al,*1986; Mattscheck *et al,* 2001; Menhinick *et al,* 2004; Negm, 1994; Ryan *et al,* 2008; Torabinejad *et al,* 2005). After one day posttreatment, pain severity was substantially lower than pretreatment severity. Change in pain severity over time following treatment was described by 10 of these studies. (Attar *et al,* 2008; Creech *et al,* 1984; DiRenzo *et al,* 2002; Ehrmann *et al,* 2003; Genet *et al,* 1986; Henry *et al,* 2001; Krasner *et al,* 1986; Mattscheck *et al,* 2001; Ryan *et al,* 2008; Torabinejad *et al,* 2005). In all cases, pain severity substantially decreased over the days immediately following root canal treatment.

Treatment Pain Prevalence and Severity

Data on pain prevalence and severity experienced during treatment were extremely limited, thus precluding meta-analysis. Three VAS studies showed 100% prevalence of treatment pain (Attar *et al,* 2008; Creech *et al,* 1984; Rousseau 2002). Again, any tiny discomfort registers a pain score of more than zero resulting in very high prevalence with VAS studies. Notably, these three VAS studies indicated that the severity of treatment associated pain was very low; 4, 6, and 8% respectively, on 100 point VAS scales. Three other non-VAS studies reported prevalence of treatment pain ranging from 11 to 22 % (Ghoddusi *et al,* 2006; Ianiro *et al,* 2007;

Watkins *et al,* 2002). It is important to note that the prevalence and severity of treatment pain are low in comparison to those of pre-treatment pain as described above.

Anesthetic Efficacy

Eight studies on anesthetic efficacy studies measured the need for or the effects of various types of supplemental injection (Bigby *et al,* 2007, Claffey *et al,* 2004; Elsharrawy and Elbaghdady, 2007; Ianiro *et al,* 2007; Matthews *et al,* 2009; Nusstein *et* al, 1998; Reisman *et al*, 1997; Srinivasan *et al,* 2009). These studies suggested that supplemental injections were frequently required (23 to 90%). Calculation of a crude mean indicated that supplemental anesthesia necessary 60 (24)% of the time. Supplemental anesthesia was generally successful in reducing pain and in achieving anesthesia. Two studies reported on pain experienced during injection; pain was commonly experienced during needle insertion, needle placement and during solution deposition(Matthews et al, 2009; McCartney et al, 2007). This data suggests the need for care in communication and in anesthetic injection technique.

Flare Ups and Emergencies

The mean prevalence for flare ups was 5 (4)%, as calculated from 8 papers (Eleazer and Eleazer, 1994; Imura and Zuolo, 1995; Iqbal *et al,* 2009; Morse *et al*, 1987; Morse *et al,* 1988; Oginni and Udoye, 2004; Siqueira *et al*, 2002; Walton and Fouad, 1992). The factors associated with flare ups varied; different studies sometimes reporting conflicting results. Factors associated with flare up included: severe pretreatment pain and swelling, necrotic pulps, acute periradicular abscesses, radiolucent lesions, absence of radiographic lesions, use of analgesics, operator type, instrumentation short of the apex, multiple appointments, single appointments. Emergencies

were related to the need for more pain medication, ethnicity, necrotic pulps, the initial visit, retreatment, patients with incomplete root canal treatment.

DISCUSSION

Pain research has steadily gained prominence throughout all health care disciplines. Many prior endodontic studies have attempted to relate post-treatment pain to various predictive factors: single vs. multi-visit treatment; different types of intracanal dressings; different treatment procedures; patient factors; analgesics; anesthetic; use of antibiotics; and pretreatment pain (Alacam, 1985; Albashaireh and Alnegrish, 1998; Aqrabawi and Jamani, 2006; Bigby, 2007; Brennen *et al,* 2006; Claffey *et al,*2004; Creech *et al*, 1984; DiRenzo *et al*, 2002; Dugas *et al*, 2002; Ehrmann *et al,* 2003; Elsharrawy and Elbaghdady, 2007; Fava, 1991; Fava, 1994; Fava, 1995; Fava, 1998; Gallatin *et al*, 2000; Genet *et al*, 1986; Gesi *et al*, 2006; Ghoddusi *et al*, 2006; Glassman *et al,*1989; Gorduysus and Gorduysus, 2000; Harrison *et al*, 1983; Henry *et al*, 2001; Ianiro *et al*, 2007; Koba *et al*, 1999; Krasner *et al*, 1986; Marshall and Liesinger, 1993; Martin, 1982; Mattscheck *et al*, 2001; Menhinick *et al*, 2004; Michaelson and Holland, 2002; Mulhern *et al*, 1982; Negm, 1994; Neiburger, 1993; Nusstein *et al*, 1998; Oginni and Udoye, 2004; Oguntebi *et al*, 1992; Pekruhn, 1981; O'Keefe, 1976; Pisano, 1985; Polycarpou *et al*, 2005; Roane *et al*, 1983; Rosenberg *et al*, 2007, Rousseau *et al*, 2004; Rowe *et al*, 1980; Shedletsky *et al*, 1984; Siqueira *et al*, 2002; Soltanoff, 1978; Torabinejad *et al*, 1994; Torabinejad *et al*, 2005; Udoye *et al*, 2005; Walton *et al*, 2003; Watkins *et al*, 2002; Weiger *et al*, 2000; Yesilsoy *et al*, 1988). However, relatively few papers have been directly focused upon the patient experience.

While systematic review is a useful form of research, differences in study design or patient experience can make comparison problematic. Dental procedures including third molar

extraction and root canal treatment are often used as general pain models in studies evaluating analgesic efficacy. Interestingly, a recent study investigating the use of NSAIDs for post-treatment pain pooled the results of surgical extraction of third molars, episiotomy, gynecological, urological, and other procedures (Barden *et al*, 2004). It has been suggested that post-treatment pain in different areas of the body may be pooled because similar pain mechanisms are involved (Hargreaves, 2004). In this paper, all included data was from patients experiencing pain of endodontic origin. Of course, endodontic pain may differ in severity and source, pulpal or periradicular. In this paper, data generated from different pain measurement methods, including five-point scales, four-point scales, and visual analogue scales, was normalized and pooled, wherever possible. Fortunately, endodontic pain evaluations using different types of pain scale are known to be highly correlated (Attar *et al*, 2008).

The return rate for papers which met inclusion and exclusion criteria from total hits returned through detailed searching was very low, ~1%. Endodontic pain studies may have been inadequately or improperly tagged in the databases searched. Careful selection of title words and appropriate keywords is strongly recommended to authors. The 72 studies that met the inclusion criteria had a mean score of 23 out of a possible 27 on the Wong Scale-Revised, but only 13 of the 72 studies had scores at the upper end, 25 or more.

The articles included in this meta-analysis varied in terms of experimental design and in data reporting. Some studies reported pain prevalence and pain severity for pretreatment and posttreatment conditions. Most studies provided several values at a variety of posttreatment time periods. For this reason, the number of studies included for meta-analysis of the various outcome measures differed.

Pre-treatment pain prevalence was high, likely inflated for both VAS and categorical studies. Additionally, many patients reporting to dental clinics may be episodic patients seeking treatment only because they are in pain. However, useful comparisons of pre and post treatment prevalence can still be made.

Posttreatment pain prevalence was moderate or low. All studies except for those performed by Henry *et al* (2001) and Oginni and Udoye (2004) reported 7 day pain prevalence as being less than 10% (Henry *et al*, 2001; Oginni and Udoye, 2004). The Henry *et al* study specifically selected patients with spontaneous pain from symptomatic, necrotic teeth, *i.e*. those with acute periradicular periodontitis, a notoriously painful condition. It is also important to note that all of the patients who experienced post-treatment pain in the Henry *et al* study only experienced mild pain. The high post-treatment pain prevalence in the Oginni and Udoye paper likely occurred because their scale grouped "no pain" with "mild pain". Several papers that met the inclusion criteria were not included in the meta analyses, because specific post-treatment time intervals were not reported (Ghoddusi *et al*, 2006; Kusner *et al*, 1984; Leguen, 1985; Morse *et al*, 1987; Ng *et al*, 2004).

The influence of root canal treatment on pain prevalence was clearly elucidated by plotting data from studies that reported both pre and post treatment pain in the L'Abbe Plot in Figure 2. The pretreatment pain prevalences in these studies served as baseline measures to which analagous post-treatment pain prevalences were validly compared. Although the pretreatment prevalences varied among the studies, all studies reported a steady and substantial decline in pain prevalence over time following treatment.

Pretreatment pain severity for all included studies was moderate. Some studies specifically selected subjects with moderate to severe pre-treatment pain; whereas, others were

conducted at dental clinics that likely attracted patients experiencing and presenting in pain. Thus a high variance was to be expected. Even so, few patients presented with severe pain.

Posttreatment pain severity showed a steady decrease over time, as for post-treatment pain prevalence. At 1 day, the mean pain severity had dropped in half. By 7 days, the pain severity had generally decreased to less than 10%. Again, the study by Henry *et al* reported the highest post-treatment pain severity (Henry *et al* 2001). The reasons for the higher pain severity are probably akin to the reasons for the higher prevalence level.

The effect of root canal treatment on pain severity was depicted by the L'Abbe plot in Figure 4. Three of the 11 studies included in the plot show immediate post-treatment severity levels which exceeded the pre-treatment severity levels. The increased pain severity shortly after treatment may be due to apical instrumentation, especially when pre-existing periradicular inflammation was present; injection of local anesthetic; pressure from a rubber dam clamp; or discomfort due to prolonged opening. Although pain levels fluctuated during the hours immediately following treatment in two studies, an overall decrease in severity was observed. Low levels of pain severity were generally reached within a few days. These findings underscore the need for early post-treatment pain control through non steroidal anti inflammatory drugs (NSAIDs).

Of the 67 studies which included pre-treatment or post-treatment pain data, only 5 directly reported data on pain experienced during treatment (Attar *et al*¸ 2008; Creech *et al*, 1984; Ianiro *et al*, 2007; Rousseau *et al*, 2002; Watkins *et al*, 2002). Three studies reported 100 % pain prevalence on VAS, likely for the reasons explained above. However, very low severity levels were reported, of 4 to 8 % (Attar *et al*¸ 2008; Creech *et al*, 1984; Rousseau *et al*, 2002). Two non-VAS studies reported treatment pain prevalences of 11% and 22% (Ianiro *et al*, 2007;

Watkins *et al*, 2002). These results might be somewhat alarming because complete anesthetization would be desired for patients undergoing root canal treatment. However, one of these studies measured treatment pain after a single inferior alveolar nerve block (Ianiro *et al*, 2007); whereas, in routine clinical practice a dentist would administer supplemental anesthesia as needed. The other study carefully investigated anticipated and experienced sensory and affective pain (Watkins *et al*, 2002); perhaps instruction of study subjects to pay more attention to their state of pain resulted in more felt pain during treatment.

Supplemental anesthesia was needed very frequently. However, these studies only included patients with extant pretreatment pain. The subjects were patients reporting to emergency departments, patients reporting to clinics in spontaneous or severe pain, or patients diagnosed with irreversible pulpitis. Routine anesthetic infiltrations or blocks may be insufficient to produce anesthesia with pretreatment pain. Dentists must routinely anticipate the need for supplemental anesthesia when performing root canal treatment.

The prevalence of flare ups following root canal treatment was low. Flare ups were only addressed within the overall context of this systematic review, *i.e*. pain. The definitions of flare-ups varied among studies as did the associated prognostic factors. Because the occurrence of flare ups was low and the prognostic factors are unclear, prophylactic use of antibiotics is not recommended (Keenan *et al*, 2005). However, the patient must be advised of the possibility of a flare up, the nature of a flare up, and to seek assistance should a flare up occur.

This systematic review followed guidelines appropriate for addressing our purpose (Stroup 2000). This included appropriate background and question formulation; reporting of search strategy, methods and results including graphical summaries and L'Abbe plots of study estimates and an indication of statistical uncertainty of findings; discussion of possible bias and

study quality along with consideration of alternative explanations for observed results, explanations for inconsistency and conflict in data; and the inclusion of generalizable conclusions.

CONCLUSIONS

Pretreatment root canal associated pain prevalence was high but dropped moderately within 1 day and substantially to minimal levels in 7 days. Pretreatment root canal–associated pain severity was moderate, dropped substantially within 1 day of treatment, and continued to drop to minimal levels in 7 days. Supplemental anesthesia was often required during root canal treatment.

CHAPTER 4: DISCUSSION

The systematic review process revealed that although much endodontic research has been performed and published, relatively little research exists which is directly patient-based. Most research in the dental literature is performed in institutional settings where treatment and study protocols are highly controlled. Results from these studies are then used to guide treatment protocols; however, a huge disparity exists between the results of highly controlled studies performed in institutions and results of studies which examine treatment which occurs in populations. This general finding is corroborated by results of Dental Practice Based Research Network (PBRN) studies, which are based on outcomes found in participating private practice settings. One study of root canal treatments in PBRN suggested a failure rate of approximately 27% in real world settings; root canal treatments performed on both un-insured and insured patients treated by a general dentist or endodontist. These findings indicate a need for closer examination of real world treatments.

The disparity between institutional research and real world findings begs that either further research be performed to elucidate the reason for poor success rates, as indicated by the high number of periapical radiolucencies in endodontically treated teeth, in community settings or clinical practice guidelines be reformed. Reasons for poor success rates may be multi-factorial and thus impossible to clearly identify. Poor technical quality, although not a main outcome measure of this research, was commonly reported in many articles selected for meta-analysis of prevalence of periapical radiolucency and root canal treatment (Eckerbom *et al*,1987; Petersson *et al*, 1989; Odesjo *et al*, 1990; Eriksen and Bjertness, 1991; Imfeld, 1991; De Cleen *et al*, 1993; Eriksen *et al*, 1995; Soikkonen, 1995; Buckley and Spangberg, 1995; Weiger *et al*,1997;

Saunders *et al*, 1997; Sidaravicius *et al*, 1999; De Moor *et al*, 2000; Lupi-Pegurier *et al*, 2002; Dugas *et al*, 2003; Loftus *et al*, 2005; Kabak and Abbot, 2005; Tsuneishi *et al*, 2005; Skudutyte-Rysstad and Eriksen, 2006; Chen *et al*, 2007; Sunay *et al*, 2007; Ozbas *et al*, 2011; Peters *et al*, 2011; Al-Omari, 2011). Additionally, lack of permanent restoration has been discussed as a contributing factor to non-healing endodontic lesions (Siqueira *et al*, 2005). These possible contributors to poor healing have been reported; yet, systematic review and meta-analysis of the available dental literature has not been performed to provide definitive comparisons. Patient factors, such as age, sex, health history may contribute, but are likely confounding variables and therefore difficult to study. Instead, perhaps clinical practice guidelines should be altered: possibly finding easier technical methods for community dentists to adhere to or stressing the importance of placing a permanent restoration in a more timely manner.

Root canal treatment has traditionally been anticipated and feared by the public. This attitude is corroborated by influential individuals with little scientific evidence. In President Obama's 2010 State of the Union address, he compared the bank bailout to being "as popular as a root canal." Although dental practitioners may have anecdotal beliefs about the pain relief that follows root canal treatment, pain prevalence and severity has never before been subjected to systematic review.

Results of systematic review and meta-analysis of pain prevalence and severity are very promising. Although the articles identified by systematic review were performed on disparate populations, results are trustworthy as the different pain scales have been shown to be highly correlated. Findings show that patients experience much less discomfort than they anticipate before treatment. Additionally, the diminution of pain by 7 days demonstrates its obvious benefit. Perhaps this reduction in pain is the most important outcome to patients experiencing

endodontic symptoms. Eradication of disease and infection is the obvious goal of dental practitioners; however, community endodontics as performed today, even with high levels of periradicular lesions on treated teeth, may be fulfilling the goals of patients – reduction in pain.

CHAPTER 5: CONCLUSIONS

Patient-based research is largely lacking in the endodontic literature. Systematic review of patient based studies may give a better real world picture of treatments that occur in community settings, outside of highly controlled institutional studies. The results of this study indicate that root canals are highly valuable – as indicated by the number of treatments provided to patients and their diminution of pain.

This systematic review and meta-analysis of cross-sectional studies on the prevalence of periapical radiolucency and root canal treatment, based on data describing over 300,000 teeth from 33 studies, mostly performed in countries with high or very high human development indices, found that: the prevalence of teeth with periapical radiolucency was very high, approximately 5% of all teeth, broadly equivalent to 1 radiolucency per patient; the prevalence of teeth with root canal treatment was very high, approximately 9% of all teeth, broadly equivalent to 2 treatments per patient; the prevalence of periapical radiolucency in endodontically treated teeth was high, approximately 37%; and the prevalence of periapical radiolucency in untreated teeth was surprisingly high, approximately 2%. The technical quality of community root canal treatment was decried by most of the authors of the included cross-sectional studies. Nonetheless, billions of teeth are retained through root canal treatment.

Pretreatment root canal associated pain prevalence was high but dropped moderately within 1 day and substantially to minimal levels in 7 days. Pretreatment root canal–associated pain severity was moderate, dropped substantially within 1 day of treatment, and continued to drop to minimal levels in 7 days. Supplemental anesthesia was often required during root canal treatment.

TABLE 1

I	((exp Endodontics/ or exp Dental Pulp Diseases/ or exp Periapical Diseases/ or exp "Root Canal Filling Materials"/ or Dental Pulp Test/ or Dental Pulp/ or Dental Pulp Cavity/) or (("root canal".mp. or apicectom:.mp. or apicoectom:.mp. or (dead adj3 (teeth or tooth)).mp. or (dental adj3 pulp:).mp. or endodont:.mp. or endont:.mp. or endosonic.mp. or ((lateral or vertical) adj condensation).mp. or ((non-vital or nonvital) adj3 (teeth or tooth)).mp. or obtura.mp. or obturation.mp. or obturate.mp. or (pulp adj3 (capping or therap: or extirpation:)).mp. or (pulp adj (canal$1 or chamber$1)).mp. or pulpectomy.mp. or pulpotomy.mp. or replantation.mp. or ("root" adj end adj5 fill:).mp. or ((silver or gutta) adj3 (percha or balata)).mp. or (silver adj (cone$1 or point$1)).mp. or thermafil.mp. or trans-polyisoprene.mp. or transpolyisoprene.mp. or ultrafil.mp.) or ((periradicular or radicular or periapical or apical).mp. and (exp tooth/ or exp tooth components/))) not (*Apicoectomy/ or *Dental Implantation, Endosseous, Endodontic/ or *Retrograde Obturation/ or *Tooth Replantation/)) and (Clinical Protocols/ or exp Clinical trials/ or exp Patient Care Management/ or Patient Selection/ or Practice Guidelines/ or clinic:.mp. or (recall adj3 appointment$1).mp. or ((patient or research) adj3 (recruitment or selection)).mp. or (selection adj3 (criteria or treatment or subject$1)).mp. or (treatment adj protocol$1).mp. or ra.fs. or radiograph:.mp. or ah.fs. or histolog:.mp. or (nonsurg: or non-surg:).mp.) and (exp Disease progression/ or exp Morbidity/ or exp Mortality/ or exp "Outcome assessment (health care)"/ or exp Patient satisfaction/ or exp Prognosis/ or exp Survival analysis/ or exp Time factors/ or exp Treatment outcome/ or ((beneficial or harmful) adj3 effect$).mp. or co.fs. or course.mp. or (inception adj cohort$1).mp. or (natural adj history).mp. or outcome$1.mp. or predict$.mp. or prognos$.mp. or surviv$3.mp. or fail$5.mp. or longevity.mp. or durability.mp. or succes:.mp. or random$.ti,ab. or predispos$.ti,ab. or causa$.ti,ab. or exp Case-control studies/ or (case$1 adj control$).ti,ab. or exp Cohort studies/ or exp "Comparative study"/ or exp Epidemiological Studies/ or odds ratio/ or (odds adj ratio$1).ti,ab. or exp Risk/ or risk$.ti,ab. or Meta-analysis/ or Meta-analysis.pt. or practice guideline.pt. or exp Clinical Trials/ or (randomized controlled trial or controlled clinical trial).pt. or random$.ti,ab. or (systematic adj review$1).mp. or Retreatment/ or Recurrence/ or (retreat: or revis:).mp.)
II	((Dentition, Primary/ or (immatur: adj3 (teeth or tooth)).mp. or (open adj3 (apex or apices or apexes)).mp. or blunderbuss.mp. or limit to (preschool child <2 to 5 years> or child <6 to 12 years>)) not (Dentition, Mixed/ or Dentition, Permanent/ or Adolescent/ or (mature adj3 (teeth or tooth)).mp. or (closed adj3 (apex or apices or apexes)).mp. or limit to all adult <19 plus years>)) not (Animal/ not Human/)) limit to English language

TABLE 2

Authors	Year	Study Focus	Sample size, Total # teeth	Total # of all teeth with PR	Total # teeth with RCT	# of treated teeth with PR	# of untreated teeth with PR
Al-Omari *et al.*	2011	Prevalence, Jordan	7,390	856 (11.6%)	424 (5.7%)	305 (71.9%)	551 (7.9%)
Buckley & Spangberg	1995	Prevalence, Dental School Clinic, USA	5,083	214 (4.2%)	290 (5.7%)	91 (31%)	123 (2.6%)
Chen *et al.*	2007	Prevalence, Manhattan Elderly, USA	3,533	181 (5.1%)	169 (4.8%)	60 (36%)	121 (3.6%)
De Cleen *et al.*	1993	Prevalence, Holland	4,196	189 (4.5%)	97 (2.3%)	36 (37%)	153 (3.7%)
De Moor *et al.*	2000	Quality, Dental School, Belgium	4,617	303 (6.6%)	312 (6.8%)	126 (20%)	177 (4.1%)
Dugas *et al.*	2003	Quality, Dental School,Canada	16,148	426 (2.6%)	411 (2.5%)	96 (23%)	330 (2.1%)
Eckerbom *et al.*	1987	Prevalence, Sweden	4,889	255 (5.2%)	636 (13%)	168 (26%)	87 (2.0%)
Eriksen & Bjertness	1991	Prevalence, Norway	2,940	104 (3.5%)	175 (6.0%)	64 (37%)	40 (1.4%)
Eriksen *et al.*	1995	Incidence, Norway	(1) 2,981 (2) 3,971 (3) 3,282	(1) 4 (1.4%) (2) 54 (1.4%) (3) 18 (0.5%)	(1) 100 (3.4%) (2) 133 (3.3%) (3) 42 (1.3%)	(1) 18 (18%) (2) 34 (26%) (3) 16 (38%)	(1) 25 (0.9%) (2) 20 (0.5%) (3) 2 (0.1%)
Georgopoulou *et al.*	2005	Frequency, Private Practice, Greece	7,664	1,028 (14%)	65 (8.6%)	396 (60%)	632 (8.3%)
Hugoson *et al.*	1995	Oral Health, Sweden	(1) 12,920 (2) 14,623 (3) 15,305	(1) 566 (4.4%) (2) 765 (5.2%) (3) 504 (3.3%)	(1) 1,514 (11.7%) (2) 1,708 (11.7%) (3) 1,369 (8.9%)	(1) 365 (24%) (2) 560 (32%) (3) 396 (29%)	(1) 201 (1.8%) (2) 25 (1.6%) (3) 108 (0.8%)
Hugoson *et al.*	2005	Oral Health, Sweden	14,420	305 (2.1%)	1,079 (7.5%)	189 (18%)	116 (0.9%)
Imfeld	1991	Prevalence, Quality, Elderly, Switzerland	2,004	169 (8.4%)	406 (20%)	124 (31%)	45 (2.8%)
Jimenez-Pinzon *et al.*	2004	Prevalence, Dental School, Spain	4,453	186 (4.2%)	93 (2.0%)	60 (65%)	126 (2.8%)
Kabak & Abbot	2005	Prevalence, Quality, Dental School, Belarus	31,212	3,657 (12%)	6,339 (20%)	2,867 (45%)	790 (3.2%)
Kirkevang *et al.*	2001	Prevalence, Urban Denmark	15,984	538 (3.4%)	773 (4.8%)	404 (52%)	134 (0.9%)
Loftus *et al.*	2005	Prevalence, Quality, Emergency Pts, Ireland	7,427	152 (2.0%)	152 (2.0%)	38 (25%)	114 (1.6%)
Lupi-Pegurier *et al.*	2002	Prevalence, Quality, Dental School, France	7,561	553 (7.3%)	1,429 (19%)	450 (31%)	103 (1.7%)
Marques *et al.*	1998	Prevalence, Quality, Portugal	4,446	87 (2.0%)	69 (1.6%)	15 (21.7%)	72 (1.6%)
Narhi *et al.*	2000	Oral Health, Elderly, Finland	1,016	49 (4.8%)	214 (21%)	30 (14%)	19 (2.4%)
Odesjo *et al.*	1990	Prevalence, Quality, Sweden	17,430	505 (2.9%)	1,492 (8.6%)	366 (25%)	139 (0.9%)
Ozbas *et al.*	2011	Prevalence, Turkey	9,940	172 (1.7%)	162 (1.6%)	-----	-----
Peters *et al.*	2011	Prevalence, Netherlands	4,594	118 (2.6%)	224 (4.9%)	54 (24%)	64 (1.5%)
Petersson *et al.*	1989	Prevalence, Swedish Dental Insurance system	11,497	1,001 (8.7%)	2,549 (22%)	675 (26%)	326 (3.6%)
Saunders *et al.*	1997	Quality, Dental Hospital Pts, Scotland	8,420	409 (4.9%)	472 (5.6%)	244 (52%)	165 (2.1%)
Segura-Egea *et al.*	2005	Prevalence, Type II DM + control, Spain	1,658	86 (5.2%)	32 (1.9%)	22 (69%)	64 (3.9%)
Sidaravicius *et al.*	1999	Prevalence, Lithuania	3,892	282 (7.2%)	320 (8.2%)	231 (72%)	51 (1.4%)
Skudutyte-Rysstad & Eriksen	2006	Incidence, Norway	3,971	43 (1.1%)	61 (1.5%)	26 (43%)	17 (0.4%)
Soikkonen	1995	Prevalence, Elderly, Finland	2,355	138 (5.9%)	507 (22%)	85 (17%)	83 (4.5%)
Sunay *et al.*	2007	Prevalence, Quality, Faculty Practice, Turkey	8,731	374 (4.3%)	449 (5.1%)	240 (53%)	134 (1.6%)
Tsuneishi *et al.*	2005	Prevalence, Dental School, Japan	16,232	1,522 (9.4%)	3,320 (21%)	1,329 (40%)	193 (1.5%)
Weiger *et al.*	1997	Prevalence, Private Practice, Germany	7,987	241 (3.0%)	215 (2.7%)	131 (61%)	110 (1.4%)
Willershausen *et al.*	2009	Chronic Dental Infections, Acute Myocardial Infarction pts + controls, Germany	(1) 2,825 (2) 3,550	(1) 75 (2.7%) (2) 46 (1.3%)	(1) 213 (7.5%) (2) 275 (7.7%)	(1) 34 (16%) (2) 34 (12.3%)	(1) 41 (1.6%) (2) 12 (0.4%)

Total #s	**301,147**	**16,214**	**28,290**	**10,379**	**5,693**

	% of all teeth with PR	**% of all teeth with RCT**	**% of treated teeth with PR**	**% of untreated teeth with PR**
Weighted Average (Standard Deviation) %	**5.4% (6.4%)**	**9.4% (6.6%)**	**36.7% (10.1%)**	**2.2% (3.8%)**

TABLE 3

I	((exp Endodontics/ or exp Dental Pulp Diseases/ or exp Periapical Diseases/ or exp "Root Canal Filling Materials"/ or Dental Pulp Test/ or Dental Pulp/ or Dental Pulp Cavity/) or (("root canal".mp. or apicectom:.mp. or apicoectom:.mp. or (dead adj3 (teeth or tooth)).mp. or (dental adj3 pulp:).mp. or endodont:.mp. or endont:.mp. or endosonic.mp. or ((lateral or vertical) adj condensation).mp. or ((non-vital or nonvital) adj3 (teeth or tooth)).mp. or obtura.mp. or obturation.mp. or obturate.mp. or (pulp adj3 (capping or therap: or extirpation:)).mp. or (pulp adj (canal$1 or chamber$1)).mp. or pulpectomy.mp. or pulpotomy.mp. or replantation.mp. or ("root" adj end adj5 fill:).mp. or ((silver or gutta) adj3 (percha or balata)).mp. or (silver adj (cone$1 or point$1)).mp. or thermafil.mp. or trans-polyisoprene.mp. or transpolyisoprene.mp. or ultrafil.mp.) or ((periradicular or radicular or periapical or apical).mp. and (exp tooth/ or exp tooth components/))) not (*Apicoectomy/ or *Dental Implantation, Endosseous, Endodontic/ or *Retrograde Obturation/ or *Tooth Replantation/)) and (Clinical Protocols/ or exp Clinical trials/ or exp Patient Care Management/ or Patient Selection/ or Practice Guidelines/ or clinic:.mp. or (recall adj3 appointment$1).mp. or ((patient or research) adj3 (recruitment or selection)).mp. or (selection adj3 (criteria or treatment or subject$1)).mp. or (treatment adj protocol$1).mp. or ra.fs. or radiograph:.mp. or ah.fs. or histolog:.mp. or (nonsurg: or non-surg:).mp.) and (exp Disease progression/ or exp Morbidity/ or exp Mortality/ or exp "Outcome assessment (health care)"/ or exp Patient satisfaction/ or exp Prognosis/ or exp Survival analysis/ or exp Time factors/ or exp Treatment outcome/ or ((beneficial or harmful) adj3 effect$).mp. or co.fs. or course.mp. or (inception adj cohort$1).mp. or (natural adj history).mp. or outcome$1.mp. or predict$.mp. or prognos$.mp. or surviv$3.mp. or fail$5.mp. or longevity.mp. or durability.mp. or succes:.mp. or random$.ti,ab. or predispos$.ti,ab. or causa$.ti,ab. or exp Case-control studies/ or (case$1 adj control$).ti,ab. or exp Cohort studies/ or exp "Comparative study"/ or exp Epidemiological Studies/ or odds ratio/ or (odds adj ratio$1).ti,ab. or exp Risk/ or risk$.ti,ab. or Meta-analysis/ or Meta-analysis.pt. or practice guideline.pt. or exp Clinical Trials/ or (randomized controlled trial or controlled clinical trial).pt. or random$.ti,ab. or (systematic adj review$1).mp. or Retreatment/ or Recurrence/ or (retreat: or revis:).mp.)
II	(Dental anxiety/ or odontophobia.mp. or ((dental or dentist:) adj5 (pain or anxi: or phob: or fear)).mp. or ((Pain/ or Fear/ or Anxiety/) and (exp Dentistry/ or exp Stomatognathic System/ or exp Stomatognathic diseases/)) or ("Quality of Life"/ or exp Consumer Satisfaction/ or Attitude/ or ((consumer$1 or patient$1) adj5 (satisf: or preference$1 or accept:)).mp.))
III	((Dentition, Primary/ or (immatur: adj3 (teeth or tooth)).mp. or (open adj3 (apex or apices or apexes)).mp. or blunderbuss.mp. or limit to (preschool child <2 to 5 years> or child <6 to 12 years>)) not (Dentition, Mixed/ or Dentition, Permanent/ or Adolescent/ or (mature adj3 (teeth or tooth)).mp. or (closed adj3 (apex or apices or apexes)).mp. or limit to all adult <19 plus years>)) not (Animal/ not Human/)) limit to English language

TABLE 4

Reference	Year	Study Focus	Patients (Teeth)	Pre Tx Pain	Tx Pain	Post Tx Pain	Quality Score
Alacam	1985	prognosis	(212)			3d, 14%; 7d, 1%	20
Albashaireh	1998	prognosis	300			1d, 33%; 2d, 22%; 3d, 12%; 7d, 3%	24
Aqrabawi	2006	prognosis	146			8h, 74%; 1d, 69%; 2d, 46%	23
Bigby	2007	anes eff	48	100% VAS			21
Brennan	2006	prognosis	195	100% VAS			23
Claffey	2004	anes eff	72	100% VAS			24
Creech	1984	prognosis	49	100% VAS	100% VAS	4h, 8h, 1d, 36h, 2d, all time points 100% VAS	21
Direnzo	2002	prognosis	72	100% VAS		6h, 12h, 1d, 2d, all time points, 100% VAS	24
Dugas	2002	Endo vs GP	119 (238)	98%			26
Ehrmann	2003	intracanal meds	221 (223)	100% VAS		4h, 1d, 2d, 3d, 4d, all time points, 100% VAS	21
Fava	1991	prognosis	52 (60)			2d, 5%;7d, 5%	24
Fava	1994	prognosis	52 (60)			2d, 5%;7d, 5%	24
Fava	1995	prognosis	78			2d, 100%; 7d, 6%	24
Fava	1998	prognosis	48 (60)			2d, 7%; 7d, 0%	22
Gallatin	2000	meds (abx)	40	100%		time unknown,76 %	20
Genet	1986	prognosis	803 (1204)	37%		1d, 24%; 2d, 19%; 3d, 13%; 4d, 7%	21
Gesi	2006	prognosis	256	97%		7d, 10%	23
Glassman	1989	inter-appt pain	40			8h, 83%; 1d, 55%; 2d, 11%	24
Harrison	1983	prognosis	236			1d, 30%; 7d, 8%; 30d, 2%; 60d, 1%	23
Henry	2001	medications	41	100%		1d, 93%; 2d, 68%; 3d, 59%; 5d, 41%, 6d, 27%; 7d, 32%	25
Krasner	1986	meds (abx)	50	100% VAS		8h, 1d, all time points, 100% VAS	22
Marshall	1993	medications	106	100%		81%	24
Mattscheck	2001	prognosis	30	100% VAS		4h, 8h, 12, 1d, 2d, 3d, 4d, 5d,all time points, 100 % VAS	25
Menhinick	2004	meds	57	100% VAS		time unknown, 100% VAS	25
Michaelson	2002	prognosis	497	60%			20
Negm	1994	intracanal meds	760	100% VAS		time unknown, 100% VAS	23
Oginni	2004	flare-ups	227	64%		1d, 49%; 7d, 14%	22
O'Keefe	1976	prognosis	147	81%			22
Pekruhn	1981	prognosis	102			1d, 16%; 2d, 16%; 3d, 11%; 7d, 5%	26
Pisano	1985	prognosis	74			immed, 40%; 1d, 30%; 2d, 18%	21
Polycarpou	2005	prognosis	175	62%			22
Rosenberg	2007	anes eff	48	100% VAS			22
Ross	2009	recall	7105	21%			23
Rousseau	2002	prognosis	250	100% VAS	100% VAS		26
Rowe	1980	meds	149	49%		every 2 hours (6h-36h), all time points, 100%	24
Shedletsky	1984	alternative meds	75	100%			21
Torabinejad	1994	medications	411			6%	25
Torabinejad	2005	EDTA/MTAD	73	100% VAS		12h, 1d, 2d, 7d, all time points, 100% VAS	22
Walton	2003	intracanal meds	140			74%	19
Watkins	2002	pain	333	20%	22%		24
Weiger	2000	intracanal meds	67	42%			23
Yesilsoy	1988	prognosis	186	44%		1d, 25%; 4d, 9%	26

TABLE 5

Reference	Year	Study Focus	Patients (Teeth)	Pre Tx Pain	Tx Pain	Post Tx Pain	Quality Score
Albashaireh	1998	prognosis	300			1d, 15%; 2d, 14%; 3d, 8%; 7d, 8%	24
Aqrabawi	2006	prognosis	146			8h, 49%; 1d, 43%; 2d, 24%	23
Attar	2008	meds	39	66%	4%	6h, 18%; 12h, 21%; 18h, 19%; 1d, 11%	23
Bigby	2007	anes eff	48	61%			21
Claffey	2004	anes eff	72	56%			24
Creech	1984	prognosis	49	16%	6%	4h, 14%; 8h, 18%; 1d, 16%; 36h, 10%; 2d, 2%	21
DiRenzo	2002	prognosis	72	41%		6h, 26%; 12h, 19%; 1d, 17%; 2d, 11%	24
Ehrmann	2003	intracanal meds	221 (223)	43%		4h, 37%; 1d, 23%; 2d, 38%; 3d, 11%; 4d, 9%	21
Fava	1994	prognosis	52 (60)			2d, 4%; 7d, 0%	24
Fava	1998	prognosis	48 (60)			2d, 2%; 7d, 0%	22
Gallatin	2000	meds (abx)	40	86%		7d, 34%	20
Genet	1986	prognosis	803 (1204)	26%		1d, 15%; 2d, 12%; 3d, 9%; 4d, 5%	21
Gesi	2006	prognosis	256	28%		2%	23
Glassman	1989	inter-appt pain	40			8h, 44%; 1d, 24%; 2d, 6%	24
Harrison	1983	prognosis	236			1d, 19%; 7d, 5%; 30d, 1%; 60d, 0.5%	23
Henry	2001	medications	41	69%		1d, 56%; 2d, 33%; 3d, 27%; 4d, 27%; 5d, 16%; 6d, 10%; 7d, 11%	25
Krasner	1986	medications	50	33%		8h, 39%; 1d, 28%	22
Marshall	1993	meds	106	86%			24
Mattscheck	2001	prognosis	84 (30)	9%		4h, 12%; 8h, 11%; 12h, 10%; 1d, 11%; 2d, 8%; 3d, 6%; 4d, 3%; 5d, 4%	25
Menhinick	2004	meds	57	76%		14%	25
Negm	1994	meds	760	71%		62%	23
Oginni	2004	flare-ups	227			1d, 33%; 7d, 7%	22
O'Keefe	1976	prognosis	147	64%			22
Pisano	1985	prognosis	74			immed, 21%; 1d, 14%; 2d, 8%	21
Rosenberg	2007	anes eff	48	69%			22
Rousseau	2002	prognosis	250		8%		26
Rowe	1980	meds	149			6h, 38%; 8h, 47%; 12h, 46%; 18h, 38%; 1d, 40%; 36h, 34%	24
Ryan	2008	anes eff	43	70%		immed, 11%; 6h, 50%; 12h, 49%; 18h, 32%; 1d, 28%	25
Sherman	2008	anes eff	40	91%			23
Srinivasan	2009	anes eff	40	66%			22
Torabinejad	2005	prognosis	73	24%		12h, 16%; 1d, 15%; 2d, 15%; 7d, 6%	22
Yesilsoy	1988	prognosis	186			1d, 16%; 4d, 6%	26

TABLE 6

Reference	Year	Study Focus	Patients (Teeth)	% requiring supp. injection	Quality Score
Bigby	2007	anes eff	48	74	21
Claffey	2004	anes eff	72	77%	24
Elsharrawy	2007	anes eff	40	90%	20
Ianiro	2007	anes eff	40	29%	23
Matthews	2009	anes eff	82	67%	22
Nusstein	1998	anes eff	51	51%	26
Reisman	1997	anes eff	48	75%	22
Srinivasan	2009	anes eff	40	22%	22

FIGURE 1

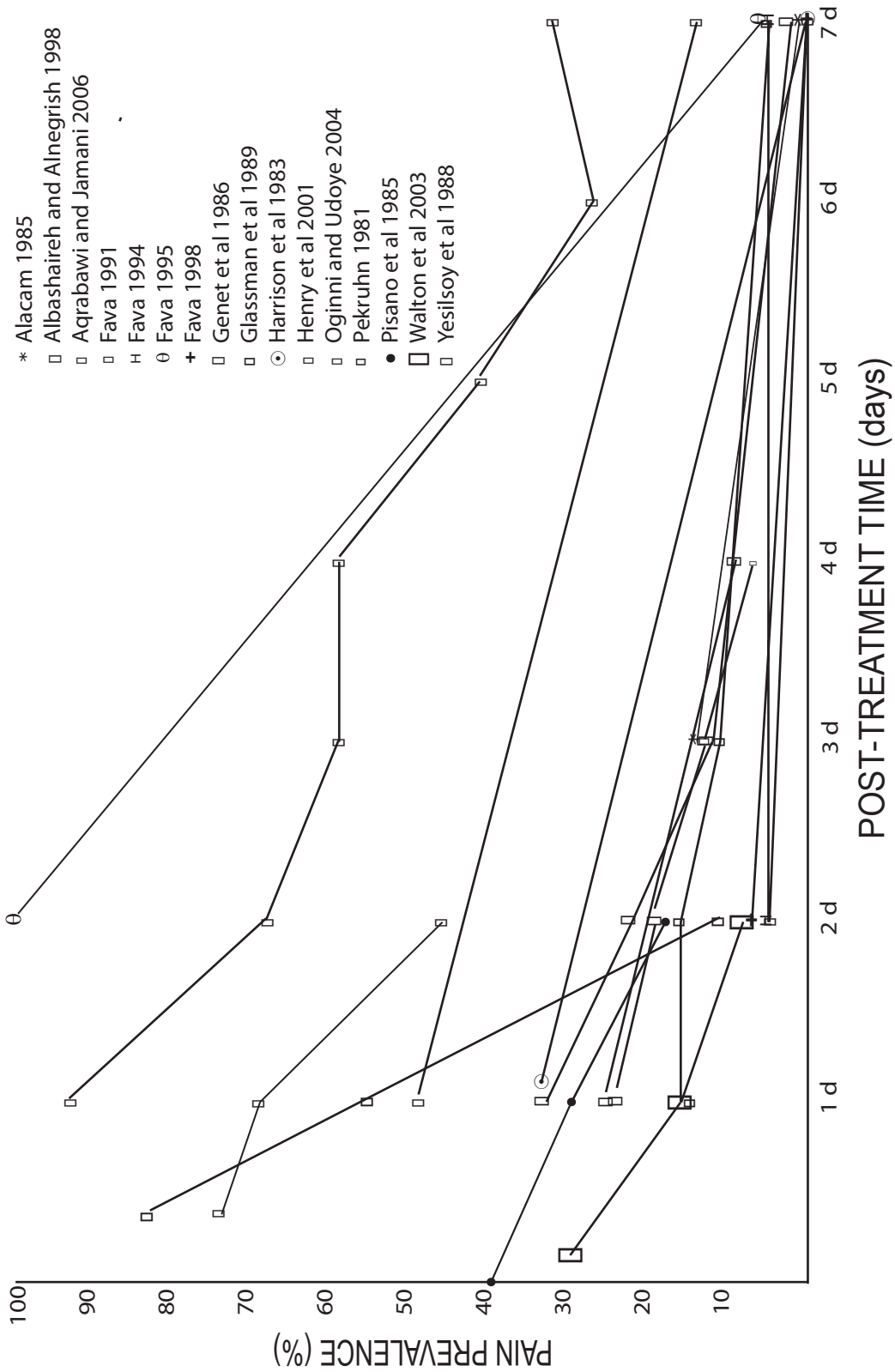

* Alacam 1985
Albashaireh and Alnegrish 1998
Aqrabawi and Jamani 2006
Fava 1991
Fava 1994
Fava 1995
Fava 1998
Genet et al 1986
Glassman et al 1989
Harrison et al 1983
Henry et al 2001
Oginni and Udoye 2004
Pekruhn 1981
Pisano et al 1985
Walton et al 2003
Yesilsoy et al 1988
PAIN PREVALENCE (%)
100
90
80
70
60
50
40
30
20
10
1 d
2 d
3 d
4 d
5 d
6 d
7 d
POST-TREATMENT TIME (days)

FIGURE 2

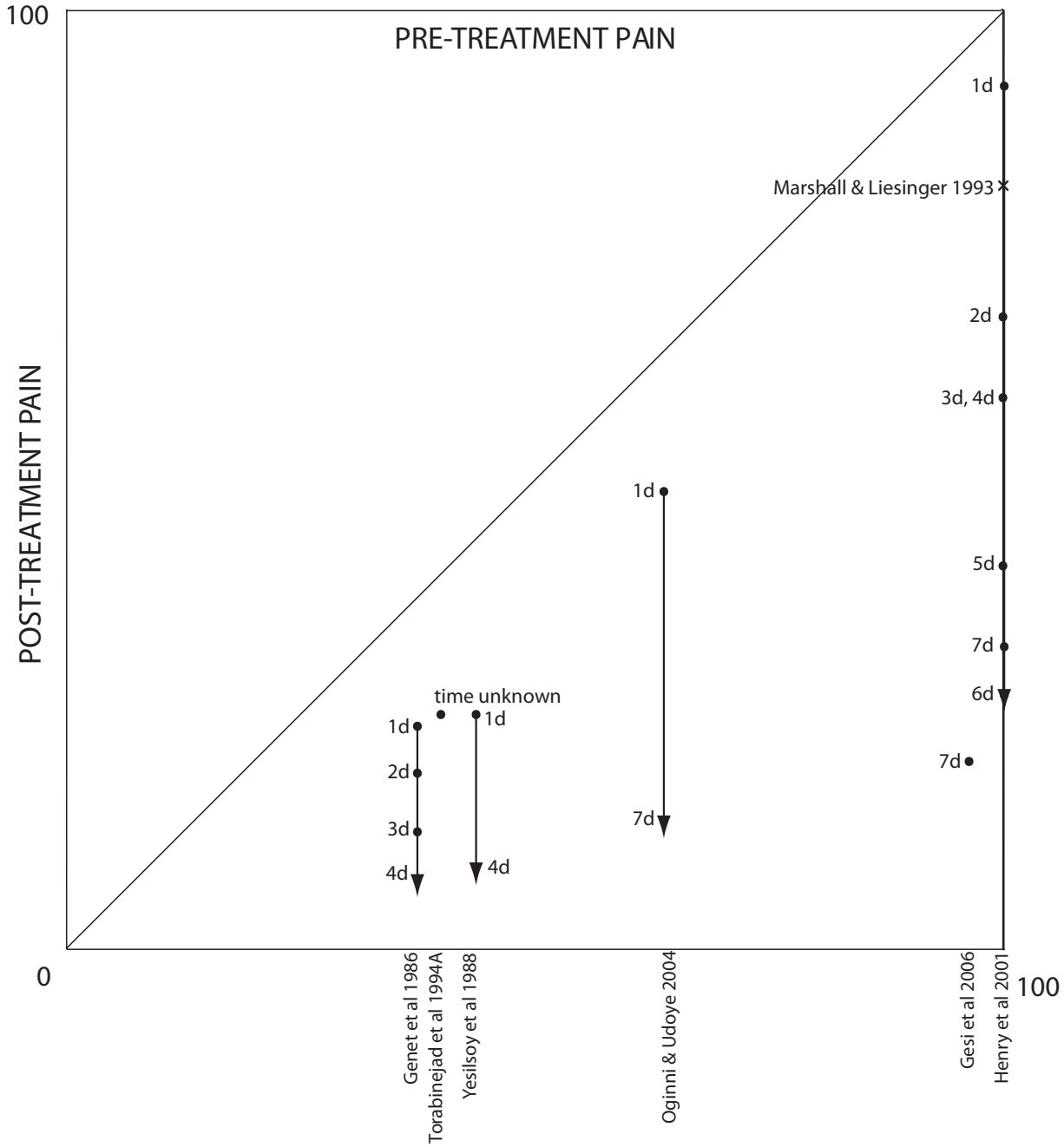

100
PRE-TREATMENT PAIN
POST-TREATMENT PAIN
0
100
1d
Marshall & Liesinger 1993
2d
3d, 4d
5d
7d
6d
7d
1d
7d
time unknown
1d
2d
3d
4d
1d
4d
Genet et al 1986
Torabinejad et al 1994A
Yesilsoy et al 1988
Oginni & Udoye 2004
Gesi et al 2006
Henry et al 2001

FIGURE 3

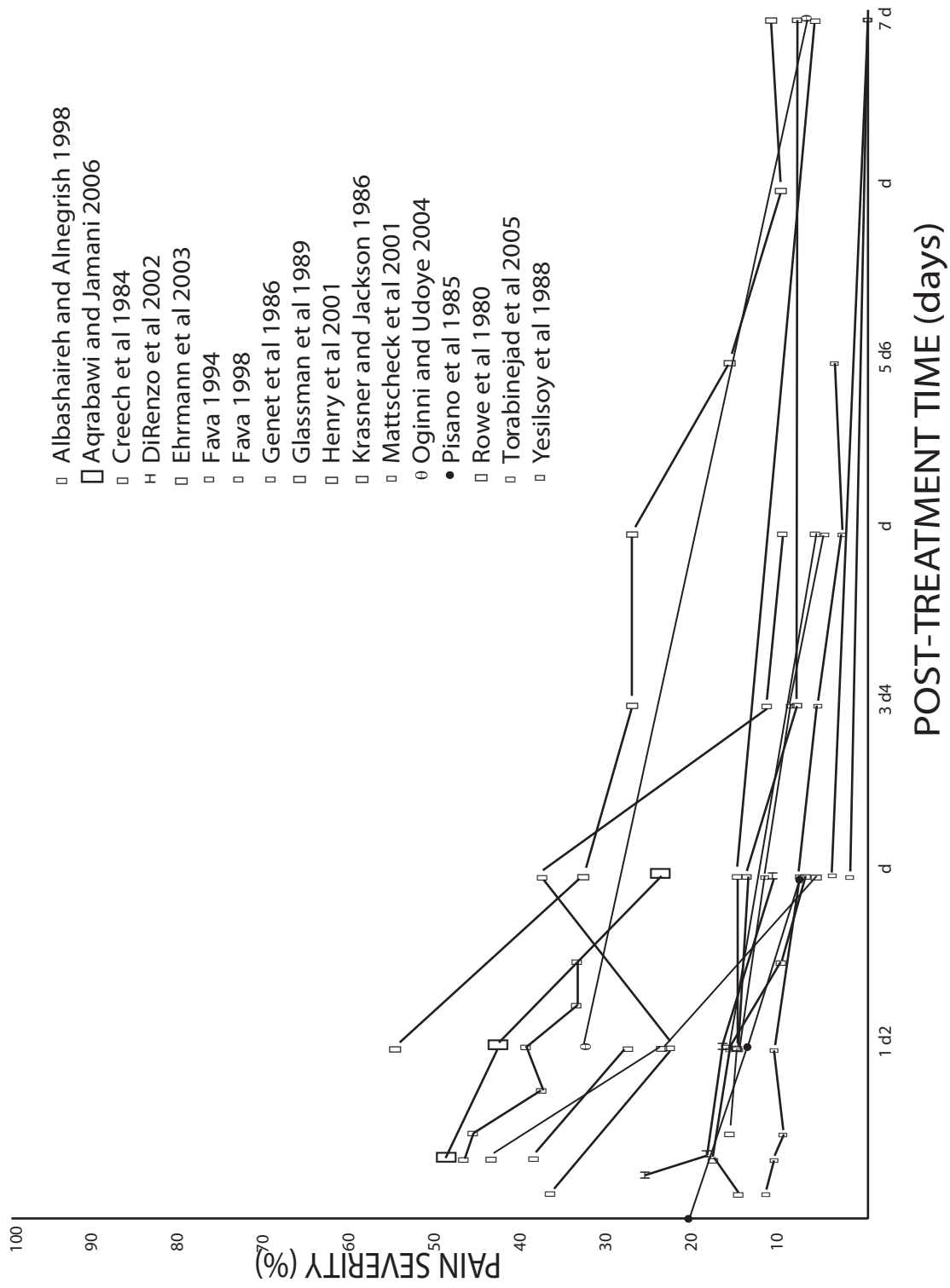
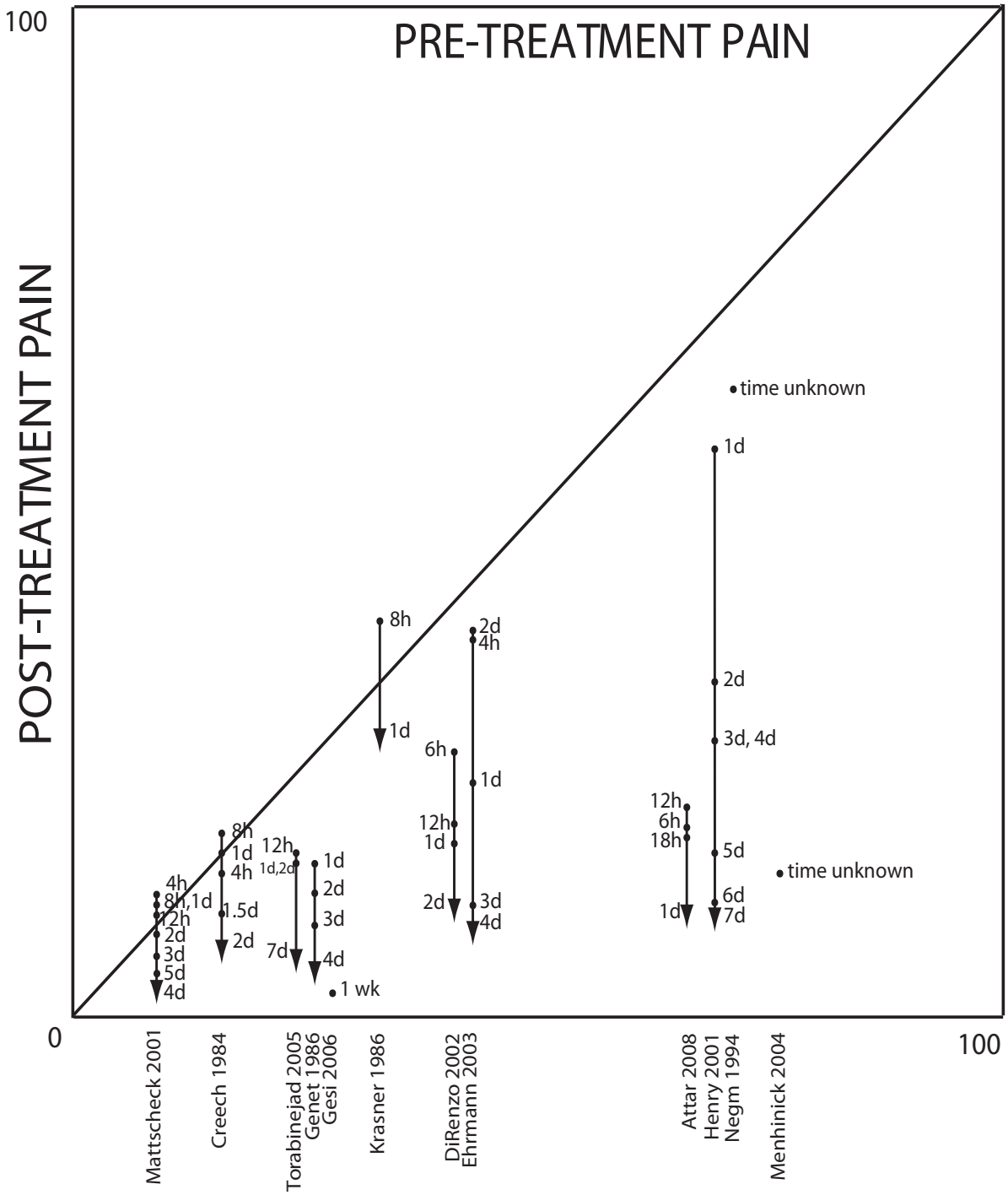

Albashaireh and Alnegrish 1998
Aqrabawi and Jamani 2006
Creech et al 1984
DiRenzo et al 2002
Ehrmann et al 2003
Fava 1994
Fava 1998
Genet et al 1986
Glassman et al 1989
Henry et al 2001
Krasner and Jackson 1986
Mattscheck et al 2001
Oginni and Udoye 2004
Pisano et al 1985
Rowe et al 1980
Torabinejad et al 2005
Yesilsoy et al 1988
PAIN SEVERITY (%)
100
90
80
70
60
50
40
30
20
10
1 d2
d
3 d4
d
5 d6
d
7 d
POST-TREATMENT TIME (days)

FIGURE 4


100
PRE-TREATMENT PAIN
POST-TREATMENT PAIN
0
100
time unknown
1d
2d
3d, 4d
5d
6d
7d
time unknown
8h
1d
2d
4h
6h
1d
12h
1d
2d
3d
4d
12h
6h
18h
1d
8h
1d
4h
2d
12h
1d,2d
7d
1d
2d
3d
4d
1 wk
4h
8h,1d
12h
2d
3d
5d
4d
1.5d
2d
Mattscheck 2001
Creech 1984
Torabinejad 2005
Genet 1986
Gesi 2006
Krasner 1986
DiRenzo 2002
Ehrmann 2003
Attar 2008
Henry 2001
Negm 1994
Menhinick 2004

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