PAIN and ROOT CANAL THERAPY:
Exploring their relationships within the DPBRN

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Dedication

This thesis is dedicated to:

1) My wife Lisa, who has allowed me to pursue an academic career, enabled me by providing the support and encouragement, and made numerous sacrifices along the long the challenging process, as well as

2) Future dental patients who may benefit from this work…

Chinese Proverbs:

If you want 1 year of prosperity, grow grain. If you want 10 years of prosperity, grow trees. I you want 100 years of prosperity, grow people.

Experience is a comb that nature gives to men when they are bald.

Abstract

Introduction: Root canal therapy is a commonly employed and effective dental treatment often used to treat the symptom of intraoral pain. Unfortunately some patients experience severe amounts of pain post-operatively, but it is not clear why. **Methods:** Using a prospective observational study design within the Dental Practice Based Research Network (DPBRN), we enrolled patients presenting for initial orthograde root canal therapy. The patients and dentists completed questionnaires before, immediately after and at 1-week following treatment. Descriptive statistics were used to assess study variables. **Results:** Over 6 months, 708 subjects were enrolled within the practices of 62 dentists, 46 of who were generalists and 16 endodontists, and were typical of those in the U.S. At baseline, 79% of patients were experiencing pain, with an average intensity of 5/10 (SD: 2.8), and 63% reported their pain interfered with daily activities. Necrosis was the most common pulp diagnosis (49%), while symptomatic apical periodontitis was the most common apical diagnosis (39%). Widespread pain was reported by 29% of patients. Within the 1-week post-operative period, about 16% of patients reported experiencing severe dental pain (≥7/10) and 6% reported experiencing severe pain and swelling. **Conclusions:** Patients presenting for initial orthograde root canal therapy have a significant amount of pain and pain-related interference in daily life. Severe post-operative pain was perceived in almost 1-in-6 patients treated.

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INTRODUCTION

Tooth pain is the most frequent type of orofacial pain (Lipton, Ship, & Larach-Robinson, 1993) and the most frequent reason why patients seek dental care (Armfield, Stewart, & Spencer, 2007; Maggirias & Locker, 2002). Root canal therapy is an effective treatment addressing pain-provoking dental pathosis (Pak & White, 2011; Wolcott, Rossman, & Hasselgren, 2011), and is a common treatment modality employed (American Dental Association Survey Center, 2008). Consequently pain and endodontics are related topics of great interest to both dentists and patients, as evidenced by a rich literature exploring the relationship (Keiser & Byrne, 2011; Nixdorf et al., 2010).

Patient reported outcomes are becoming increasingly expected in dental research (Hujoel, 2004) and are considered among the standard measures in pain-related research (Turk et al., 2006). The bulk of the existing endodontic pain-related research has explored this topic using self-reported instruments. Unfortunately, composite outcome measures have been used that combine subjective patient-reporting with behavioral actions and clinician-based observations, such as defining endodontic flare-up as "pain or swelling or a combination of both", occurring within "a few hours to a few days after…treatment", and "...there is disruption of the patient's lifestyle, such that the patient initiates contact with the dentist" (*e.g.* Walton & Fouad, 1992). While this approach captures important information regarding clinical burden, it does not adequately capture the patient-centered experience of pain since factors other than pain affect the outcome being counted. Furthermore, the literature on endodontic pain often involves patients from a limited type

of clinical practice, such as a single academic teaching center (*e.g.* Friedman, Abitbol, & Lawrence, 2003). Thus, generalization of these patients' characteristics and their outcomes to the average endodontic patient is questionable.

Collection of data using scientifically rigorous methods on topics of great clinical interest is the hallmark of high-impact clinical research (Cummings, Newman, & Hulley, 2007). Therefore, in dentistry, there is a need to measure pain-specific variables in a wide variety of dental practices related to endodontic care. Practice-Based Research Networks (PBRNs), which are a diverse group of clinicians in a variety of practice settings with large populations of patients presenting with common conditions, have been employed in medical research to help address the problem of recruiting representative patient populations for clinical research and translating new knowledge into practice (Tierney et al., 2007). Recently, such networks of clinical dentists have been developed to address these shortcomings that are common in published dental research (DeNucci, 2009; Tabak, 2004).

This article describes the process of implementing a large prospective study designed to measure the pain and the burden associated with initial orthograde root canal therapy. The project was conducted in the environment of a dental PBRN. During the developmental phase, multiple issues were raised and addressed under the two aims of this study:

Aim 1. Feasibility:

Since the concept of practice-based research within American dentistry is a recent development, numerous questions were raised about whether such a project was feasible, such as; is there interest in the topic by network dentists, can it practically be implemented within a community-based clinical practice, is the size and scope too large to manage, and are follow up rates and completeness of data that impairs the ability to draw conclusions. Therefore, this section of the thesis focuses on presenting data that demonstrates the ability to recruit general practicing dentists and endodontic specialists, enroll sufficient numbers of patients as participants in a timely fashion, gather patient-centered variables prior to initiation of treatment, achieve high levels of questionnaire collection, and obtain representative samples of dentists and patients receiving root canal therapy.

Aim 2. Description:

A large body of published evidence exists describing the patients presenting for root canal therapy and their pain-related variables. Several key limitations inhibit the usefulness of existing data as a whole and are the driving reasons why this research is warranted. These are; i) lack of generalizability of the patient population back to the average U.S. patient seeking endodontic care, ii) missing data, *i.e.* not obtaining pre-operatively and losses to follow up, iii) failure to obtain pain-related variables in an unbiased fashion that is patient-centered, and iv) deficiencies in study design, such as

being retrospective, and analysis, such as lack analyzing for risk factors. This is likely more a result of clinical research occurring in dentistry that is early within its evolutionary development, rather than a lack of interest or reduced significance. Therefore, this section of the thesis focuses on quantifying the pain-related variables patients experience in the pre-operative, intra-operative and 1-week post-operative time periods and describing the clinical characteristics of patients receiving initial orthograde root canal therapy. This will provide a quantification of patient-reported outcomes related to the pain they experience before, during and within the one week after treatment, so that dentists can understand the amount of pain with interference of daily life that their patient receiving endodontic care experience.

METHODS

Background

This research was conducted in the Dental Practice-Based Research Network (DPBRN), which is a consortium of participating practices and dental organizations committed to advancing knowledge about and improvement of dental practice (Gilbert et al., 2008). The DPBRN comprises five regions: Alabama/Mississippi (AL/MS), Florida/Georgia (FL/GA), Minnesota (MN), Oregon (OR), and Scandinavia (SK: Denmark, Norway, and Sweden). The dentists within the DPBRN, and their practices, have much in common with dentists at large (Makhija, Gilbert, Rindal, Benjamin et al., 2009a; Makhija, Gilbert, Rindal, Benjamin et al., 2009b), although the research presented involved no Norwegian dentists. Details about DPBRN are provided on their website <http://www.DentalPBRN.org>.

For dentists to be eligible to participate in this study, they were required to be members of the DPBRN, practicing within one of its five administrative regions, and indicating an express interest in being involved. Both general dentists and endodontists were eligible to participate. Recruitment of dentists took place by means of DPBRN communications, by notice printed in the AAE's *Communique*, through personal invitations from fellow practitioners, and by formal study invitation letters within the existing network. Enrolled practitioners represented a wide variety of practice settings including solo practitioners, private small and large group practices, large group multi-specialty dental practices within larger managed care organizations, and public health/community dental clinics.

All DPBRN practitioners recruited for these studies were considered practitioner-investigators (P-I) in that they implemented the clinical research.

All enrolled practitioners were required to complete a Memorandum of Agreement with the University of Alabama at Birmingham (UAB) and an Individual Investigator Agreement (IIA) with their regional administrative institution (Gilbert et al., 2010). The latter document signified that the P-I had undergone Human Subjects Protection training and had received regional IRB approval. Each P-I agreed to comply with all applicable federal, international, state and local laws, regulations and policies, and each signed a consent form to participate in this DPBRN study. Finally, each P-I provided financial documentation in anticipation of their reimbursement for study participation.

Overview of Study Design

The overall purpose of this clinical research was to measure the magnitude of pain and related burden that patients experience in association with initial orthograde root canal therapy. Additionally, analysis of primary outcomes explored interacting factors that influence the occurrence and frequency of severe pain in the immediate one-week period following treatment. The study was prospective in design, as defined by STROBE (von Elm et al., 2007). All data was collected using surveys that had been finalized prior to enrollment of consenting patients by the collaborating P-Is. The study protocol involved no manipulation of the treatment patients received.

IRB Oversight and Human Subjects Protection

IRB requirements in a multi-site study of this nature required the collaboration of multiple institutions (Gilbert et al., 2010), in addition to the University of Minnesota (primary investigator's home institution). Informed consent for all human subjects was obtained by each P-I prior to initiation of treatment. Individual consent forms were stored at each Regional Administrative Center according to IRB-approved procedures.

Planned Recruitment Period and Target Enrollment

Recruitment of patients was implemented over 6 months. It was anticipated that each general practitioner would recruit 1-2 patients per month and each endodontic specialist would recruit 4-5 patients per month. Therefore, the total study timeline was approximately one year, 6 months for recruitment and 6 month for follow-up, beginning in July 2010 and ending in December 2010. To accomplish these goals, recruitment was planned to include at least 36 general practitioners and 12 endodontic specialists as shown in Table 1.

Table 1: Target Enrollment for this DPBRN Study

Region	Endodontic Specialists	ES Patients	General Practitioners	GP Patients	Total DDS	Total Patients
AL/MS	1	25	5	42	6	67
FL/GA	2	50	5	42	7	92
MN	6	150	18	150	24	300
OR	1	25	4	33	5	58
SK	2	50	4	33	6	83
Totals	**12**	**300**	**36**	**300**	**48**	**600**

Sample Size Justification

The target recruitment of 600 patients was presumed that the major source of variability would be at the patient level. Still, the study team recognized the possibility of two types of clustering: 1) within endodontists and 2) within general practitioner dentists. There were no available data from which to estimate intra-class correlations (ICC) within these potential clusters, but a standard procedure would be to reduce the sample size by a factor of $D=[1+\rho(m-1)]$, where m is the number of subjects within each cluster and ρ is the ICC. We conservatively assumed an ICC of 0.05 within endodontists and 0.025 among general dentists. We assumed a higher ICC among endodontists because of the possibility that their patient populations would likely be more homogeneous with respect to their dental problems as well as their outcomes. With a total of 300 subjects for each practitioner group, the factors D are 2.20 and 1.28 for the two groups, respectively. This led to an effective sample size requirement of 136 for the endodontic specialty patients and 255 for the general practice patients, with an overall effective sample size of 391.

Sample size estimation is also based on the desired precision for study endpoint estimates and the expected prevalence of the study outcome. Previous research suggests that from 1% to 5% of people, undergoing apparently successful root canal therapy, subsequently develop severe pain in the immediate post-operative period (Keiser & Byrne, 2011). Based on an intermediate point estimate of 3%, and statistical precision expressed as no greater than +/-2% for the 95% confidence limits on either side of the point estimate,

nQuery Advisor 6.01 software indicated a sample size of 280 subjects that applies to each practice type (general practice and endodontic specialty).

Development, Field-testing and Curation of Data Collection Instruments

Questions used in previous epidemiological research (*e.g.* Grading the Severity of Chronic Pain; see von Korff et al, 1992; Women's Health Initiative; see Margolis *et al.,* 2008) were used as specific items in the study data collection forms when available. Additional questions were considered based on their usefulness having been empirically observed, and their having been used in the investigators' clinical practice, both academic (University of Minnesota) and private endodontic specialty practice (The Dental Specialists). Two general dentists and two endodontists in Minnesota field-tested the data collection forms with 2-4 patients each. After completion of this pilot testing, the primary study investigators and staff debriefed the P-Is and relevant suggestions for edits were incorporated. Following this pilot testing, data curation was conducted on all questionnaire items. Native speakers with dental expertise translated patient forms into Danish and Swedish. Practitioner forms were produced in English for all regions, as Scandinavian practitioners involved in the network were fluent in English. Forms were mailed from UAB to each Regional Administrative Center, where staff prepared individual P-I study packets and distributed them during their in-person study training sessions, which are described below.

Patient Eligibility and Recruitment

Participating P-Is enrolled eligible patients seeking dental care at their practice. Inclusion criteria were: i) patient age of 19-70 years, and ii) a permanent adult tooth requiring initial orthograde root canal therapy. Exclusion criteria were: i) evidence of treatment having been initiated for an iatrogenic pulpal exposure (although a case with a carious exposure of the pulp would not be excluded), ii) patient previously enrolled in this study (each patient could only contribute 1 tooth), iii) previous endodontic treatment that would make it unclear whether pain was associated with the current or previous attempt at treatment, iv) obvious cognitive impairments (*e.g.*, prior stroke with communication deficits, dementia, mental disability), and v) unable to provide 6 month follow-up information.

Participation was strictly voluntary. All participants were informed that they could decline or withdraw from the study at any time without consequence. A consecutive patient log tracked the reason for patient non-participation or withdrawal if the patient was willing to provide it, but there was no attempt to induce continued participation. For U.S. patients, survey completions were incentivized by means of debit cards that were mailed to them: $10 for each returned 1-week questionnaire, $10 for the 3-month questionnaire and $30 for the 6-month questionnaire. The approved incentive for the Scandinavian patients was a packet of oral self-care products of equivalent value to the debit cards.

Practitioner-Investigator Training Sessions

Before data collection began, the DPBRN project staff at each of the five Regional Administrative centers met face-to-face with each P-I and their office staff. The DPBRN staff explained the study protocol and addressed any questions. Study procedures were reviewed. The study data collection forms were explained and printed instructions for filling out the forms were provided. P-Is in private practice were remunerated $50 for each subject's completed set of baseline questionnaires returned to the regional coordinating center. It was estimated that each P-I would need 15 minutes to complete all study-related tasks for one subject. Dentists within the HealthPartners Dental Group received the same remuneration, but the money was paid to a fund managed by a committee of participating dentists. For each patient enrolled, one of the practitioner's staff members was also recognized with a $25.00 key staff incentive debit card for assisting with the management of forms for the encounter including transmission to the regional coordinator. This occurred only in settings where existing contracts allowed. In the HealthPartners Dental Group, key staff were recognized with a 'Lunch and Learn' at their clinic where food was provided in recognition of their team effort on the study. Prior union agreements precluded reimbursement to individual members.

Data Collection Forms and Procedures

All DPBRN study materials may be viewed on the DPBRN public website at: http://www.dpbrn.org/users/publications/Supplement.aspx. Specific study questionnaires

are identified in this paper by their form number. Data collection was facilitated by a laminated checklist provided to each P-I to assist in determining a patient's eligibility as well as a script for inviting participation in the study. All eligible patients were tallied on the office's consecutive patient log (Form 03). Following consent, patients completed the first 8 questions of their baseline data form (Form 04) prior to the administration of local anesthetic. All forms that were completed by patients during their clinic visit were placed in a sealed envelope, thereby maintaining the confidentiality of their responses from input by the treating P-I and staff. All patient-sealed packets from each clinical encounter were collected by the office staff, joined to the P-I's clinical encounter forms, and mailed to the Regional Administrative Center. In addition, patients were given a folder with forms to complete for the 1-week data collection along with a self-addressed and postage-paid envelope. Forms for subsequent data collection were either mailed with self-addressed and postage-paid envelope to the patients 1 week before the designated time of completion, or these data were collected by telephone call.

Source of the Data Collected

Baseline pain data reported in this paper were collected using Form 04: "Study 17-18 Patient Survey Before Treatment". This instrument contained questions pertaining to pain prior to treatment and other baseline patient characteristics. It was completed by the patient while seated in the dental chair, and prior to implementation of dental anesthesia. Graded Chronic Pain Scales (GCPS) (Von Korff, Ormel, Keefe, & Dworkin, 1992) were employed to measure pain intensity and pain interference. Study investigators assembled

additional questions to measure specific pain qualities. In the Results section, the questions employed for each variable are printed in the legends of the respective tables showing the pain outcomes.

Part of the data for this report were collected in surveys that were standardized between study regions and completed by the dental practitioners, as follows. Form 05, "Study 17-18 DDS Survey Before Treatment/Endodontic Diagnosis," included questions pertaining to tooth characteristics including type and location, and the diagnostic clinical exam observations (completed prior to instituting anesthesia). Form 07, "Study 17-18 DDS Survey After Obturation," included questions pertaining to the treatment encounter. This form also queried procedural information including the number of appointments required for obturation, and procedural difficulties. Form 09, "Study 17-18 Patient Survey Immediately After Treatment," collected information about what the patient perceived during treatment. The patient completed a questionnaire one week after the tooth obturation. Form 11, "Study 17-18 Patient Survey - 1 Week After Treatment," included questions pertaining to the tooth's status 1 week after completion of the root canal obturation. Of particular interest for this report was a description of the worst tooth pain that the patient had experienced. This survey was sent home with the patient to be completed and returned (postage paid) to the DPBRN regional coordinator. Surveys up to ten days past due date (*i.e.,* date of obturation + 17 days) were accepted and included. Other forms were collected during this study but are not reported, so they are not described here.

Conceptualization of a Diagnostic Endodontic Algorithm

A panel of investigators in Minnesota collaborated in the conceptualization and development of an endodontic diagnostic algorithm following recently published guidelines (Glickman, Bakland, Fouad, Hargreaves, & Schwartz, 2009; Gutmann, Baumgartner, Gluskin, Hartwell, & Walton, 2009; Levin, Law, Holland, Abbott, & Roda, 2009; Newton, Hoen, Goodis, Johnson, & McClanahan, 2009). This algorithm is based on a classification tree design that is composed of nodes defined by a "split condition." The choice at each node of a classification tree depends on a single clinical variable, or it may specify more than one condition that needs to be satisfied. The required examination data from an individual either satisfy or fail to satisfy each split condition, thus indicating the appropriate branch to follow as part of a data-driven pathway to a terminal node with its associated diagnosis. When a classification tree has construct validity, that is, it is constructed in accord with well-accepted medical concepts, it can be a diagnostic instrument for clinicians.

Three possible pulpal diagnoses and five apical diagnoses were selected for the terminal diagnoses, each chosen due to a hypothesized positive or negative relationship with post-treatment endodontic pain. The data submitted to this algorithm resulted in a single pulpal diagnosis and a single apical diagnosis for each patient. The three pulpal diagnoses were

mutually exclusive within their particular subgroup, as were also the five apical diagnoses within the second diagnostic group.

Seven clinical observations were required to provide data for the split conditions making up the endodontic diagnostic algorithm (Figure 1). The signs were recorded as binary data (Yes or No) in Forms 05 and 07:

Pulpal Characteristics:

Form 07_Question 1 – Bleeding present in pulp chamber?

Form 05_Question 5 – Response to cold testing?

Form 05_Question 6 – Prolonged response to cold?

Apical Characteristics:

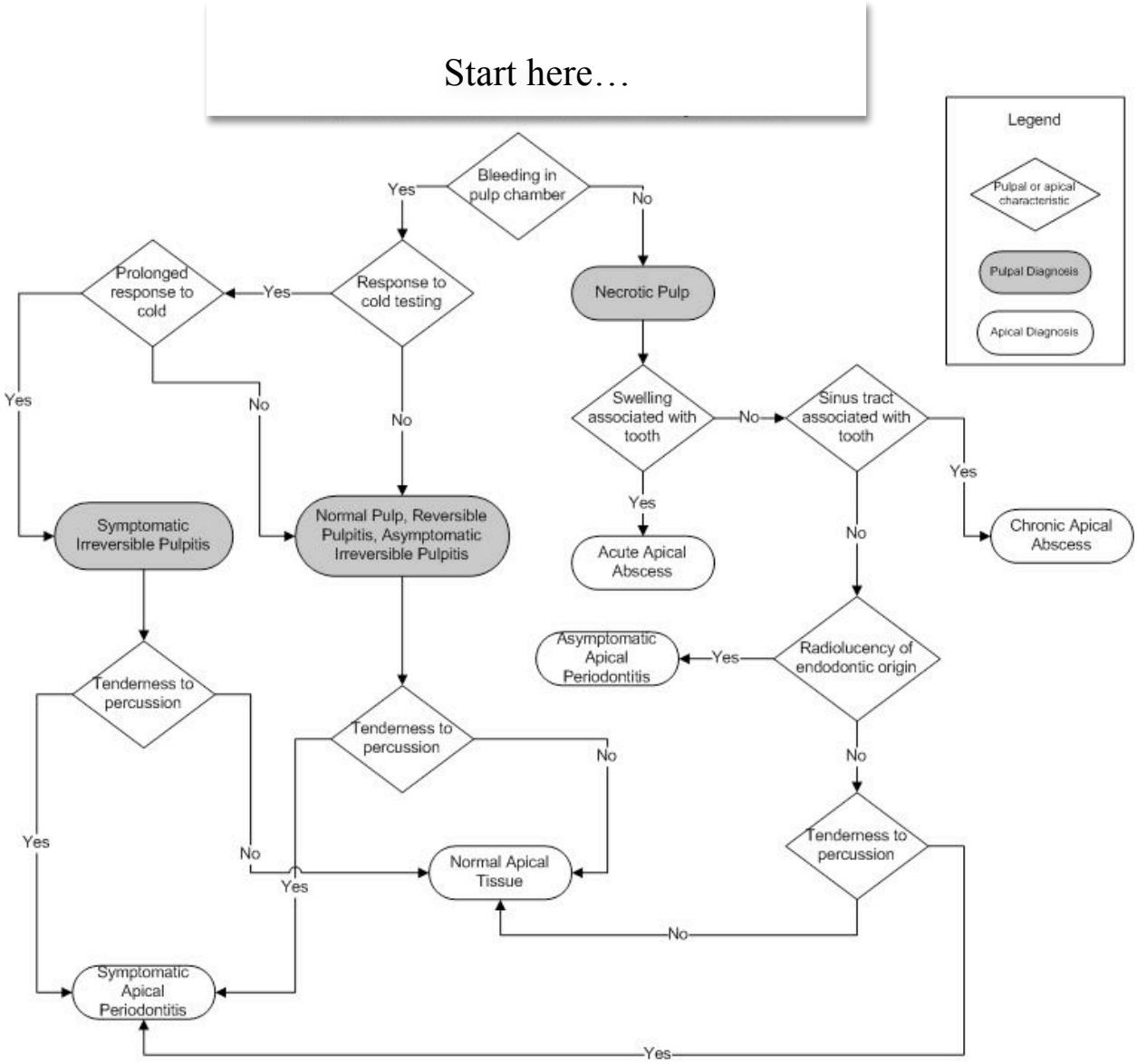
Form 05_Question 2 – Radiolucency of endodontic origin?

Form 05_Question 3 – Tooth tender to percussion?

Form 07_Question 7 – Swelling associated with tooth?

Form 07_Question 6 – Sinus tract associated with tooth?

Figure 1. Schema to Derive the Pulpal and Apical Diagnoses



Data Management Procedures and Data Quality Assurance

Regional administrative staff were asked to ensure completeness and accuracy of the data. Patient identifiable data were maintained only at the regional level. All data collection forms were labeled with a unique barcode to prevent anyone from being able to

identify Protected Health Information of any study participant, and then couriered in batches to the Coordinating Center at UAB. Date entry at the UAB Coordinating Center used standard practices. All electronic data were stored on a secure network drive with restricted access. Members of the UAB Coordinating Center statistical consulting unit were responsible to prepare the final dataset and documentation.

Statistical Procedures Employed

Frequency tables in the Results section were generated using Proc Freq (SAS® 9.2, SAS Institute, Cary, NC). Multinomial ordinal data were collapsed to binary categories for the purpose of comparing differences in subject characteristics between study regions. Statistical differences between regions were based on the chi-square statistic for binary data. Means and standard deviations were computed for the region-specific age distributions and the overall mean age distribution. When the ordinal 0 to 10 scales were treated as continuous data, Proc GLM was used to assess regional differences by specifying Region (i.e., AL/MS, FL/GA, MN, OR or SK) as the independent variable in an ANOVA model.

RESULTS

Aim 1. Feasibility:

Recruitment of Practitioner-investigators and Study Subjects

Table 2 shows that 708 subjects participated in this study. Root canal therapy for at least 1 enrolled patient was performed by 62 dentist P-Is, 46 of who were general practitioners and 16 were endodontic specialists. Six hundred subjects were projected *a priori* to be the required minimum sample size with each participant represented by one tooth requiring root canal therapy. The recruitment of 708 subjects was 18% higher than the original goal of 600, to account for participants not following up. The 62 collaborating practitioners represented a 29% increase over the 48 dentists projected to be necessary to accomplish the study goals.

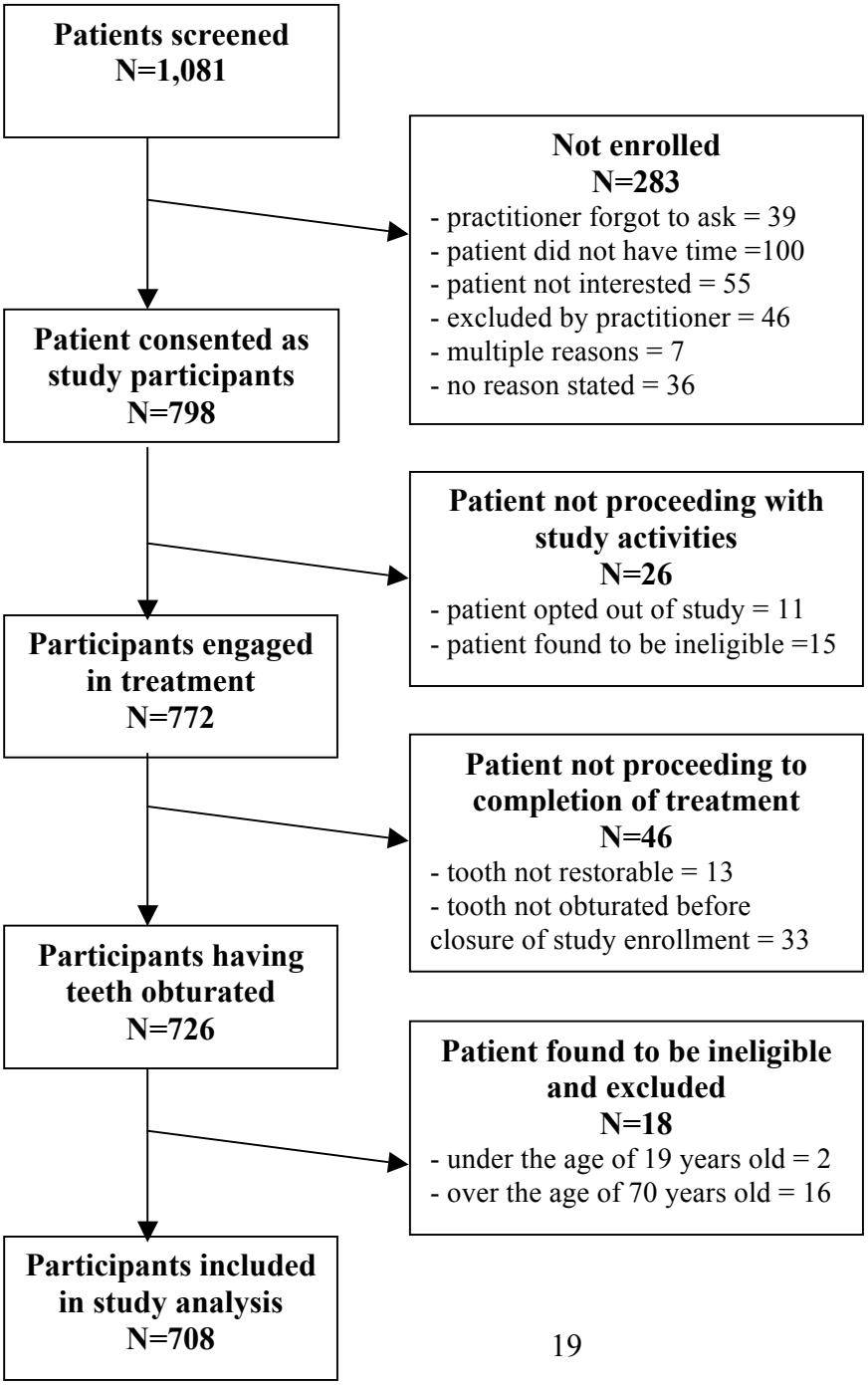
Table 2: Practitioner and Patient Enrollment Results

Region	Endodontic Specialist	Endodontist Patients	Generalist DDS	Generalist Patients	Total Practitioners	Total Patients
AL/MS	3	61	7	37	10	98
FL/GA	2	59	12	72	14	131
MN	7	260	19	130	26	390
OR	2	21	3	15	5	36
SK	2	12	5	41	7	53
Totals	**16**	**413**	**46**	**295**	**62**	**708**

Figure 2 indicates that 1,081 patients were evaluated as potential candidates for the combined cross-sectional and longitudinal arms of this study. A total of 798 patients were enrolled and 283 (26%) were not. Figure 2 shows the reasons for the non-enrollment of 283 subjects at the time of recruitment: practitioner forgot to ask (n = 39; 14%); patient had no time for participation (n = 100; 35%); patient had no interest in participation (n =

55; 19%); patient excluded from participation by the practitioner (n = 46; 16%); multiple reasons for non-participation (n = 7; 3%); and no reason was given (n = 36; 13%).

Figure 2: Patient Flow Diagram and Consecutive Eligible Log Data



Of the 798 enrolled subjects, 15 were subsequently found to be ineligible and were withdrawn, 11 returned no study questionnaires and are considered to be lost before obturation occurred, and 772 returned study questionnaires. Of these 772 participating subjects, 64 were subsequently found to be ineligible while 708 were confirmed as eligible. Of those 64 subjects found to be ineligible after their enrollment: 1) for n = 13, their root canal treatment was intentionally stopped by care provider (*e.g.* insufficient coronal tooth structure, crack identified in root, patient changed their mind), 2) for n = 33, root canal obturation was not completed prior to study closure, and 3) for n = 18, they were not in the age range of 19-70 years as specified for this study (2 under age and 16 over age). We also note that 37 eligible participating subjects (5% of the 708) were not reported in the Consecutive Eligible Log. Due to the fact that they completed the study, they are represented in the Figure 1 counts among the 1,081 potential patients, the 798 enrolled, the 772 who returned the data collection forms, and the 708 making up the final study sample.

Demographics of the Study Patient Sample

Table 3 shows the demographic characteristics of the 708 study patients. Their mean age over all study regions was 48 years (SD: 13). Differences between the site-specific age distributions tended toward statistical significance ($p = 0.06$). Females comprised 59% of the study population. They outnumbered males in just 3 regions, and these differences in gender distributions between regions reached statistical significance ($p = 0.04$).

Table 3: Demographic Characteristics of Study Subjects

	Age Distribution				Gender Distribution			Ethnicity Distribution		
Region	Mean Age in years	SD	Range in years	N	Male (%)	Female (%)	N	Hispanic or Latino (%)	Not Hispanic or Latino (%)	N
AL/MS	46	12	26 - 69	97	38 (40)	58 (60)	96	0 (0)	93 (100)	93
FL/GA	48	13	19 - 70	126	62 (49)	65 (51)	127	22 (17)	107 (83)	129
MN	47	13	19 - 70	381	143 (37)	243 (63)	386	5 (1.3)	374 (99)	379
OR	52	11	24 - 68	36	19 (53)	17 (47)	36	1 (2.7)	35 (97)	36
SK	51	14	20 – 69	53	27 (51)	26 (49)	53	1 (1.9)	52 (98)	53
Total	**48**	**13**	**19 - 70**	**693**	**289 (41)**	**409 (59)**	**698**	**29 (4.2)**	**661 (96)**	**690**
Frequency Missing				15			10			18
P-value regions				0.061			0.042			<0.0 001

Each patient is represented by his or her ethnicity (Hispanic or Latino verses Not Hispanic or Latino), and by his or her race. Ethnic distributions are shown in Table 3 and racial distributions by each study region are shown in Table 4. White patients comprised the major group in each study region. Ethnic distributions were different ($P < 0.001$) in that ≤ 1 Hispanic or Latino were mainly recruited in 2 regions. Overall, there were 600 White non-Hispanic patients making up 86% of the entire study sample and there were an additional 25 White patients with Hispanic ethnicity. Less well represented were: Black/African Americans with 5.5%, Asians with 1.9%, American Indians/Alaska Natives with 1.3%, less than 1% for Native Hawaiians/Pacific Islanders, and less than 1% for patients self-identified as “other”. The number of patients in these less represented groups totaled just 65 (9.2% of the total), among whom 4 had Hispanic or Latino ethnicity. Ethnicity data for 18 of the 708 study patients were missing.

Table 4: Racial Distribution of Study Participants by Study Region

Region	White (%)	Black/African American (%)	American Indian / Alaska Native (%)	Asian (%)	Hawaiian / Pac. Islander (%)	Other (%)	Totals
AL/MS	76 (79)	20 (21)	0 (0)	0 (0)	0 (0)	0 (0)	96
FL/GA	121 (93)	7 (5.4)	1 (0.8)	1 (0.8)	0 (0)	0 (0)	130
MN	349 (91)	11 (2.9)	8 (2.1)	8 (2.1)	1 (0.3)	5 (1.3)	382
OR	31 (89)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	35
SK	53 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	53
Total	**630 (91)**	**38 (5.5)**	**9 (1.3)**	**13 (1.9)**	**1 (0.1)**	**5 (0.7)**	**696**
Frequency Missing							12

Note: total may not equal 100% exactly due to rounding

Socio-economic Status of the Study Patient Sample

Patients were asked to respond to four possible categories of annual income: <$10,000; $10,000 to <$30,000; $30,000 to <$50,000, ≥$50,000. Study data indicate that 64% of all study participants self reported an annual income greater than $50,000 and an additional 21% were in the $30,000 to $<50,000 range. There was no statistical difference in the regional distributions of the four income categories ($p = 0.43$). Using a cutoff for annual income of $30,000, as shown in Table 5, regional differences for income tended toward statistical significance ($0.05 < p < 0.10$). In addition, Table 5 shows that significantly higher proportions of patients in 2 regions had dental insurance ($p < 0.001$) and significantly higher proportion of patients with some college education in 1 region ($p < 0.001$).

Table 5: Socio-Economic Characteristics of Study Participants

	Annual Income*			Dental Insurance			Educational Experience**		
Region	< 30,000 (%)	≥ 30,000 (%)	N	No (%)	Yes (%)	N	High School (%)	College (%)	N
AL/MS	9 (10)	84 (90)	93	21 (22)	75 (78)	96	19 (20)	76 (80)	95
FL/GA	22 (18)	99 (82)	121	46 (35)	85 (65)	131	23 (18)	108 (82)	131
MN	62 (17)	311 (83)	373	63 (16)	323 (84)	386	63 (16)	322 (84)	385
OR	1 (2.9)	34 (97)	35	0 (0)	36 (100)	36	1 (2.9)	34 (97)	35
SK	11 (21)	42 (79)	53	1 (1.9)	52 (98)	53	25 (48)	27 (52)	52
Total	**105 (16)**	**570 (84)**	**675**	**131 (19)**	**571 (81)**	**702**	**131 (19)**	**567 (81)**	**698**
Frequency Missing			33			6			10
P-value between-regions			0.067			<0.0001			<0.0001

* Annual Income was collapsed to "<30,000" (<10,000; 10,000 – 29,000) versus "≥ 30,000" (30,000 – 49,000; more than 50,000).
** Educational experience has been collapsed to "High School" (primary or secondary education) versus "College" (some college, college graduate, or advanced college degree).

Types of Teeth Receiving a Study Root Canal Obturation

Tooth types obturated in this study sample were identified using the Universal Tooth Numbering System that has been adopted by the American Dental Association. Over the five study regions, there were 77 anterior teeth obturated, 361 maxillary posterior teeth, and 268 mandibular posterior teeth for a total of 706. Information was missing on the tooth classification number for two additional obturated teeth (Table 6).

Table 6: Tooth Types Receiving a Completed Root Canal Therapy

	Maxillary Anterior Tooth (#6-11)			Maxillary Posterior Tooth (#1-5 & 12-16)			Mandibular Anterior Tooth (#22-27)			Mandibular Posterior Tooth (#17-21 & 28-32)			
Region	Right side	Left side	N (%)	Right side	Left side	N (%)	Right side	Left side	N (%)	Right side	Left side	N (%)	Total
AL/MS	5	5	10	20	32	52	3	1	4	21	11	32 ()	98
FL/GA	6	9	15	36	33	69	1	3	4	27	15	42 ()	130
MN	13	12	25	96	94	190	2	9	11	83	81	164 ()	390
OR	2	2	4	11	10	21	0	1	1	4	5	9 ()	35
SK	1	0	1	11	18	29	1	1	2	12	9	21 ()	53
Total	**27**	**28**	**55 (7.7)**	**174**	**187**	**361 (51)**	**7**	**15**	**22 (3.1)**	**147**	**121**	**268 (39)**	**706**
Frequency Missing													2

Productivity of the Study Practitioner-investigators

Table 7 shows the distribution of completed root canal treatments performed by P-Is during the six-month period of data collection. Average monthly productivity for endodontic specialists was 413 completed patients by 16 practitioners in 6 months, or 4.3 patients/specialist/month. Average productivity for general practitioners was 295 completed patients by 46 practitioners in 6 months, or 1.1 patients/generalist/month.

Table 7: Productivity of Practitioners for This Study

	General Practitioners				**Endodontic Specialists**		
Region	< 5 (%)	≥ 5 (%)	N		< 15 (%)	≥ 15 (%)	N
AL/MS	4 (57)	3 (43)	7		1 (33)	2 (67)	3
FL/GA	5 (42)	7 (58)	12		0 (0)	2 (100)	2
MN	7 (37)	12 (63)	19		0 (0)	7 (100)	7
OR	1 (33)	2 (67)	3		1 (50)	1 (50)	2
SK	1 (20)	4 (80)	5		2 (100)	0 (0)	2
Total	**18 (39)**	**28 (61)**	**46**		**4 (25)**	**12 (75)**	**16**

Frequency of Unanticipated and Adverse Events

As the care provider, the P-I was responsible for standard monitoring of patients post-operatively. In the event of an adverse event experienced by a study patient, the respective P-I was responsible for attending to the care of the patient and reporting this occurrence to the regional coordinator, who in turn was to report the occurrence to the NIDCR Office of Clinical Trial Operations and Management (OCTOM) Report. One unanticipated event occurred in the MN region where a patient included additional health-related information not solicited by the follow-up survey. No adverse events were observed.

Return Rates for Study Questionnaires & Useable Responses to Individual Questions

The return rates of usable questionnaires from the 708 eligible participating subjects were:

- Form 03: Consecutive Eligible Log properly completed was 54/62 = 87.1%
- Form 04: Patient Survey before Treatment was 704/708 = 99.4%
- Form 05: DDS Survey before Treatment was 706/708 = 99.7%
- Form 07: DDS Survey after Obturation was 708/708 = 100%
- Form 09: Patient Survey immediately after Treatment was 703/708 = 99.3%
- Form 11: Patient Survey at 1 Week after Treatment was 645/708 = 91.1%

Aim 2. Description:

Endodontic Tooth Pain Intensity during the Week Prior to Treatment

Table 8 shows region-specific Graded Chronic Pain Scale (GCPS) mean measures for the intensity of endodontic pain experienced during the week preceding recruitment. There was no statistical difference between the study regions for their mean reports of "average" pain intensity, or for their mean responses regarding "worst" pain suffered. These pain estimates are summaries of the patients' responses to questions 10 and 9 in Form 04, respectively. These questions are also printed in the legend of Table 8. Both overall means of 5.15 (SD: 2.78) for "average" pain and 6.68 (SD: 2.96) for "worst" pain indicate moderate levels of discomfort. The binary results showing the frequency of severe pain, with "severe" defined as ≥ 7 on the 0-10 scale. This level of pain was reported by 196 patients (27.7% of 708) to describe their "average" pain, and by 353 patients (49.9%) to qualify the "worst" pain that they experienced during the preceding week (Table 8).

Table 8: Pre-operative Tooth Pain Intensity during the Week Prior to Treatment

	Average Pain Intensity during past week - scale (0-10)*			Average Pain Intensity during past week - scale (0-10)*			Worst Pain Intensity during past week - scale (0-10) **			Pain Intensity at Present - scale (0-10) ***		
Region	Mean	SD	N	< 7	≥ 7	N	Mean	SD	N	Mean	SD	N
AL/MS	5.39	3.05	79	45	34	79	6.55	3.25	77	3.58	2.64	78
FL/GA	5.27	2.96	96	62	34	96	6.63	3.23	95	3.34	3.08	96
MN	5.00	2.69	330	224	106	330	6.71	2.86	328	3.20	2.77	327
OR	4.50	2.71	18	12	6	18	5.68	3.09	19	3.68	3.25	19
SK	6.08	2.38	36	20	16	36	7.31	2.27	36	5.39	3.00	36
Total	**5.15**	**2.78**	**559**	**363**	**196**	**559**	**6.68**	**2.96**	**555**	**3.55**	**2.93**	**556**
Frequency Missing			149			149			153			152
P-value between-regions			0.15			0.30			0.41			0.001

* Question 10, Form 04: In the past week, on average, how intense was your tooth pain rated on a 0 to 10 scale where 0 is "no pain" and 10 is "pain as bad as could be"? (that is, your usual pain at times you were experiencing pain)
** Question 9, Form 04: In the past week, how intense was your worst tooth pain rated on a 0 to 10 scale where 0 is "no pain" and 10 is "pain as bad as could be"?

Analgesic Medication Use and Persisting Tooth Pain Prior to Treatment

Table 9 shows region-specific frequencies of patients who self-reported taking analgesic medications, either prescribed or otherwise, for endodontic pain prior to the initiation of treatment. 60.4% (417/690) reported analgesic use prior to endodontic treatment and there was no statistical difference between the study regions for their frequencies. Assessing the persistence of pain prior to treatment, 20.2% (139/689) endorsed the statement that they had been experiencing tooth pain for at least 8 hours a day for at least 15 days per month over the previous 3 months.

Table 9: Medication Use and Presence of Persistent Tooth Pain Prior to Treatment

	Medications Taken for Pain during Past Week*			Tooth Pain Present for ≥ 8 hours/day, ≥ 15 days/month, ≥ 3 months**		
Region	No	Yes	N	No	Yes	N
AL/MS	38	59	97	76	21	97
FL/GA	55	76	131	108	19	127
MN	134	239	373	307	79	386
OR	22	14	36	25	10	35
SK	24	29	53	43	10	53
Total	**273**	**417**	**690**	**559**	**139**	**689**
Frequency Missing			18			10
P-value between-regions			0.45			0.39

* Question 4, Form 04: Have you taken anything for the pain (over-the-counter or prescription medication, herbal, other) in the last 7 days?
** Question 16, Form 04: For at least the last 3 months, have you experienced pain in more than one area of your body during at least 4 days each week?

Endodontic Tooth Pain Interference with Lifestyle Activities

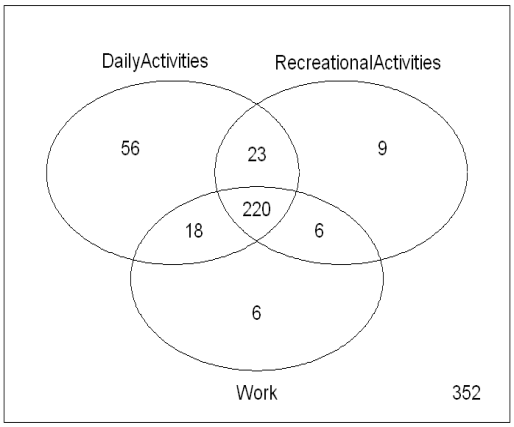
Table 10 describes the pain burden, or lifestyle interference, suffered by the study participants during the week before their recruitment. The overall mean days of pain interference affecting their usual activities during that week was 0.51 days (SD 1.22). Overall interference, as measured by the Graded Chronic Pain Scale of 0-10, showed a mean of 1.84 (SD: 2.61) for usual activities, 1.56 (SD: 2.57) for recreational activities, and 1.43 (SD: 2.45) for work (Table 9). The number of study subjects endorsing some level (> 0) of pain interference was 352 out of 708, or 49.7% of the entire study sample. This included n = 317 endorsing pain interference with their daily activities, n = 258 for interference with recreation, and n = 250 with interference with work. As shown in the Venn diagram in Figure 3, a total of 220 patients experienced some interference within all three domains.

Table 10: Pre-operative Tooth Pain Interference with Usual Activities, Daily Activities, Recreation, and Work

	Pain interference with usual activities (number of days in past week) *			Pain interference scale (0-10) with daily activities **			Pain interference scale (0-10) with recreational activities ***			Pain interference scale (0-10) with work ****		
Region	Mean days	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
AL/MS	0.57	1.30	97	1.89	2.63	97	1.79	2.70	97	1.78	2.70	97
FL/GA	0.55	1.46	128	1.67	2.62	128	1.42	2.56	126	1.22	2.27	125
MN	0.50	1.16	383	1.92	2.59	384	1.60	2.54	385	1.44	2.44	386
OR	0.40	1.26	35	1.23	2.40	35	1.11	2.52	35	0.94	2.24	35
SK	0.42	0.86	53	2.04	2.79	53	1.53	2.61	53	1.49	2.54	53
Total	**0.51**	**1.22**	**696**	**1.84**	**2.16**	**697**	**1.56**	**2.57**	**696**	**1.43**	**2.45**	**696**
Frequency Missing			13/12			11			12			12
P-value between-regions			0.92			0.54			0.68			0.35

* Question 11, Form 04: How many days in the past week have you been kept from your usual activities due to pain (e.g., school or housework)?
** Question 12, Form 04: In the past week, how much has tooth pain interfered with your daily activities (rated on a 0 to 10 scale)?
*** Question 13, Form 04: In the past week, how much has tooth pain interfered with your ability to take part in recreational activities (rated on a 0 to 10 scale)?
**** Question 14, Form 04: In the past week, how much has tooth pain interfered with your ability to work, including housework (rated on a 0 to 10 scale)?

Figure 3: Patient Burden Associated with Endodontic Pain



Pain Qualities Reported by the Study Participants

Tables 11a and 11b indicate pain qualities reported by the endodontic patients during the week prior to their treatment. Respondents to Form 04 were requested to skip question 4 that queried pain quality if they had suffered no tooth pain during the prior week. The 139 "missing" respondents for each pain quality are therefore expected. The prevalence of a given pain quality is therefore determined by dividing the number of patients

endorsing that pain quality by the total number of subjects who completed the questionnaire. Thus, we see that "ache" was the most common pain quality (286/708 = 0.404) or 40.4%. "Throbbing" was second most common with 37% endorsement. Of the 708 patients, 25%, 26.6%, and 19.6% reported the pain qualities of "dull," "sharp," and "shooting," respectively. Less common were the qualities of "electric" (5.8%) and "burning (3%). There were few between-region differences as to the report of these pain qualities: the proportion of those reporting "dull" pain was highest in the Oregon region, and the proportion of those endorsing "shooting" pain was highest in Scandinavia (both P < 0.001).

Table 11a: Quality of Pain* in Participants Experiencing Tooth Pain of Endodontic Origin

	Pain Quality = Dull			Pain Quality = Sharp			Pain Quality = Ache			Pain Quality = Throb		
Region	NA	Dull	N	NA	Sharp	N	NA	Ache	N	NA	Throb	N
AL/MS	83%	17%	84	69%	21%	84	54%	46%	84	51%	49%	84
FL/GA	65%	35%	95	65%	35%	95	53%	47%	95	55%	45%	95
MN	65%	35%	333	65%	65%	333	47%	53%	333	53%	47%	333
OR	42%	58%	19	79%	21%	19	37%	63%	19	58%	42%	19
SK	89%	11%	38	79%	21%	38	63%	37%	38	71%	29%	38
Total	**69%**	**21%**	**569**	**67%**	**33%**	**569**	**50%**	**50%**	**569**	**54%**	**46%**	**569**
Frequency Missing			139			139			139			139
P-value between-regions			<0.0001			0.32			0.15			0.26

Table 11b: Quality of Pain* in Participants Experiencing Tooth Pain of Endodontic Origin

	Pain Quality = Burning			Pain Quality = Shooting			Pain Quality = Electric		
Region	NA	Burning	N	NA	Shooting	N	NA	Electric	N
AL/MS	96%	4%	84	81%	19%	84	98%	2%	84
FL/GA	98%	2%	95	84%	16%	95	93%	7%	95
MN	97%	3%	333	75%	25%	333	92%	8%	333
OR	95%	5%	19	84%	16%	19	95%	5%	19
SK	89%	11%	38	39%	61%	38	87%	13%	38
Total	**96%**	**4%**	**569**	**76%**	**24%**	**569**	**93%**	**7%**	**569**
Frequency Missing			139			139			139
P-value between-regions			0.20			<0.0001			0.26

* Question 5, Form 04: If tooth pain was present in the past 7 days, mark all pain qualities that apply.

Spontaneous versus Provoked Pain in the Study Participants

If the patients had experienced no tooth pain during the preceding week, they were requested to skip questions 6 and 7 about spontaneity and provocation of pain. Thus, the positive endorsements to these questions in Tables 12 and 13 are, again, the primary interest. Table 12 shows that few (5.2%) were able to describe their pain as stable, that is, their pain experience was continuous rather than subject to fluctuations. Secondly, 26.6% reported that their tooth pain was spontaneous, while 47.3% described their pain as a function of a provocation. Table 13 shows three different ways in which tooth pain was reportedly provoked: for n = 336 (47.5%), pain increased during biting or chewing. For n = 310 (43.8%), pain increased as a result of thermal changes. Just 6.6% of the endodontic patients attributed their pain experience to stress. The proportion of those endorsing thermal changes as a provocation for tooth pain was highest in Minnesota (51% of respondents; P = 0.03). The other four regions showed 32% to 38% of the participants as

claiming pain provocation from thermal changes, with each regional percent estimate calculated relative to the number of study subjects within that region.

Table 12: Pain Characteristics in Participants Experiencing Tooth Pain of Endodontic Origin

	Pain is stable - never increases*			**Spontaneous pain****			**Provoked pain*****		
Region	NA	Nothing increases the pain	N	NA	Pain increases by itself"	N	NA	Pain increases when provoked	N
AL/MS	89%	11%	79	72%	28%	79	40%	60%	72
FL/GA	95%	5%	96	69%	31%	96	30%	70%	86
MN	95%	5%	333	65%	35%	333	36%	64%	318
OR	95%	5%	19	68%	32%	19	22%	78%	18
SK	89%	11%	38	68%	32%	38	56%	44%	36
Total	**93%**	**7%**	**565**	**67%**	**33%**	**565**	**37%**	**63%**	**530**
Frequency Missing			143			143			178
P-value between-regions			0.28			0.74			0.59

* Question 7, Form 04: To the question as to what makes the tooth pain worse, the response is "nothing, never gets worse."

** Question 7, Form 04: To the question as to what makes the tooth pain worse, the response is "nothing, gets worse all by itself."

*** Question 6, Form 04: Does this pain start after the tooth is used or irritated (provoked)?

Table 13: Pre-operative Provocation of Tooth Pain*

	Pain increases with biting or chewing			Pain increases from temperature changes (hot/cold)			Pain increases with stress		
Region	NA	Yes	N	NA	Yes	N	NA	Yes	N
AL/MS	41%	59%	79	53%	47%	79	94%	6%	79
FL/GA	35%	65%	95	54%	46%	95	94%	6%	95
MN	40%	60%	333	40%	60%	333	91%	9%	333
OR	47%	53%	19	32%	68%	19	89%	11%	19
SK	52%	48%	38	55%	45%	38	89%	11%	38
Total	**40%**	**60%**	**564**	**45%**	**55%**	**564**	**92%**	**8%**	**564**
Frequency Missing			144			144			144
P-value between-regions			0.40			0.026			0.83

* Question 7, Form 04: Responses to the question as to what makes the tooth pain worse.

Prevalence of Widespread Pain in Study Patients

Table 14 shows that 205/697 (29.4%) of the study subjects endorsed widespread pain. There was no statistical difference between regions as to the report of widespread pain (P = 0.12).

Table 14: Pre-operative Prevalence of Widespread Pain in Study Patients

	Bodily pain present in more than 1 area of the body, at least 4 days/week, during the last 3 months *		
Region	No	Yes	N
AL/MS	73	24	97
FL/GA	95	31	126
MN	269	117	386
OR	19	16	35
SK	36	17	53
Total	**492**	**205**	**697**
Frequency Missing			11
P-value between-regions			0.12

* Question 16, Form 04: For the last three months, have you experienced pain in more than one area of your body during at least four days each week?

Pulpal diagnoses and Their Prevalence in the Study Sample

Pulpal and apical diagnoses were established from clinical and radiographic observations. The pulpal diagnoses are shown in Table 15. These diagnoses were determined using the diagnostic algorithm, shown in Figure 1, by the research personnel. As noted above, each patient received only a single pulpal diagnosis. Pulpal diagnoses varied between: Dx1 – necrotic pulp (n = 348); Dx2 – Pain-free pulpal diagnosis that included one of the following: a normal pulp, a reversible pulpitis, or an asymptomatic irreversible pulpitis (n = 139); and Dx3 – painful symptomatic irreversible pulpitis (n = 216). Five patients

lacked a pulpal diagnosis due to the fact that at least one required data item was missing for each of them.

Table 15: Pulpal Diagnoses in Study Participants

	Dx 1			Dx 2			Dx 3		
Region	**No**	**Yes**	**N**	**No**	**Yes**	**N**	**No**	**Yes**	**N**
AL/MS	58%	42%	98	38	19	57	19	38	57
FL/GA	47%	53%	131	31	28	59	28	31	59
MN	51%	49%	390	121	75	196	75	121	196
OR	44%	56%	36	10	5	15	5	10	15
SK	53%	47%	53	16	12	28	12	16	28
Total	**51%**	**49%**	**708**	**564**	**139**	**703**	**487**	**216**	**703**
Frequency Missing			0			5			5
P-value between-regions			0.49			0.85			0.23

Dx 1: Necrotic pulp
Dx 2: Pain-free pulpal diagnosis = Normal pulp, Reversible pulpitis or Asymptomatic irreversible pulpitis
Dx 3: Symptomatic irreversible pulpitis

Apical diagnoses and Their Prevalence in Study Participants

Apical diagnoses are shown in Table 16 with, again, only one diagnosis allowed for each study patient. The apical diagnoses are represented as: Dx4 – normal apical status (n = 175); Dx5 – symptomatic apical periodontitis (n = 273); Dx6 – asymptomatic apical periodontitis (n = 156); Dx7 – acute apical abscess (n = 53); Dx8 – chronic apical abscess (n = 36). As shown in Table 2, missing data led to a failure to establish the presence or absence of specific apical diagnosis in 12 to 15 patients, depending on which diagnosis. In the end, a total of 15 participants did not have an apical diagnosis.

Table 16: Apical Diagnoses in Study Participants

	Dx 4			Dx 5			Dx 6			Dx 7			Dx 8		
Region	No	Yes	N	No	Yes	N	No	Yes	N	No	Yes	N	No	Yes	N
AL/MS	31	29	60	29	40	69	12	18	30	35	6	41	30	5	35
FL/GA	29	36	65	36	44	80	21	22	43	50	19	69	45	5	50
MN	123	90	213	90	161	251	55	85	140	165	22	187	140	25	165
OR	9	6	15	6	11	17	2	14	16	18	2	20	17	1	18
SK	15	14	29	14	17	31	3	17	20	20	4	24	20	0	20
Total	**518**	**175**	**693**	**420**	**273**	**693**	**537**	**156**	**693**	**643**	**53**	**696**	**660**	**36**	**696**
Frequency Missing			15			15			15			12			12
P-value between-regions			0.48			0.41			0.013			0.018			0.28

Dx 4: Normal apical tissue
Dx 5: Symptomatic apical periodontitis
Dx 6: Asymptomatic apical periodontitis
Dx 7: Acute apical abscess
Dx 8: Chronic apical abscess

Prevalence of Clinical Signs within the Study Participants

Three diagnostic pulpal signs are reported in Table 17: bleeding in the pulp chamber, response to the cold test, and a prolonged response to the cold test. These signs were all positive in more than 35% ($n \geq 251$) of the study sample ($n = 708$). The reported response to cold was more frequent ($P = 0.04$) in the Scandinavian patients (56.7%), and lowest in patients in the Florida region (33.6%). Prolonged response to cold testing was highest ($P = 0.002$) in the Alabama region (45.9%) and lowest, again, in the Florida patients (28.2%).

Table 17: Diagnostic Clinical Pulpal Findings

	Blood in Pulp Chamber*			Pulpal Response to Cold**			Prolonged Pulpal Response to Cold***		
Region	No	Yes	N	No	Yes	N	No	Yes	N
AL/MS	41	57	98	46	51	97	35	45	80
FL/GA	69	62	131	81	44	125	54	37	91
MN	193	197	390	208	181	389	96	137	233
OR	20	16	36	19	15	34	3	12	15
SK	25	28	53	23	30	53	31	20	51
Total	**348**	**360**	**708**	**377**	**321**	**698**	**219**	**251**	**470**
Frequency Missing			0			10			238
P-value between-regions			0.49			0.0396			0.0017

***** Question 1, Form 07: Was bleeding present in the pulp chamber?
****** Question 5, Form 05: Did the tooth respond to cold testing?
******* Question 6, Form 05: Was the response to cold testing prolonged compared to adjacent teeth?

Shown in Table 18 is the prevalence of each clinical observation that is useful for diagnosing apical status. The prevalence in the study sample of swelling being associated with the study tooth was 9.3% (n = 66 of 708). A fistula was present with 8.2% of the study teeth (n = 58 of 708). A greater prevalence was associated with apical radiolucency (42.7% of all patients) and tenderness to percussion (64.8%). Tooth-related swelling was most prevalent (P = 0.04) in the Florida region at 16.8%. The other regions varied from 7.1 to 9.4% of participants having this characteristic. There was no statistical difference between regions ($P \geq 0.24$) for frequencies of fistula, periapical radiolucency or tenderness to percussion.

Table 18: Diagnostic Clinical Apical Findings

	Swelling Associated with Tooth*			Fistula Associated with Tooth**			Apical Radiographic Lucency***			Sensitivity to Percussion****		
Region	No	Yes	N	No	Yes	N	No	Yes	N	No	Yes	N
AL/MS	93%	7%	98	94%	6%	98	62%	38%	98	35%	65%	98
FL/GA	83%	17%	131	92%	8%	131	57%	43%	129	33%	67%	130
MN	92%	8%	377	90%	10%	376	57%	43%	388	34%	66%	390
OR	92%	8%	36	92%	8%	36	39%	61%	33	29%	71%	35
SK	90%	10%	52	96%	4%	52	54%	46%	52	38%	62%	53
Total	**90%**	**10%**	**694**	**92%**	**8%**	**693**	**57%**	**43%**	**700**	**35%**	**65%**	**706**
Frequency Missing			14			15			8			2
P-value between-regions			0.04			0.60			0.24			0.88

* Question 7, Form 07: Did you identify swelling associated with this tooth?
** Question 6, Form 07: Was here a draining tract (fistula) associated with this tooth?
*** Question 2, Form 05: Does the tooth exhibit a radiolucency of endodontic origin (periradicular or apical)?
**** Question 3, Form 05: Was the tooth tender to percussion?

Procedural Variables Reported by the Study Practitioners

Table 19 shows that the proportion of tooth obturations requiring at least two patient visits was significantly greater ($P < 0.001$) in Scandinavia. The 73.6% of such cases in Scandinavia exceeded the average 17% of cases in the other study regions. The proportion of cases that were claimed by the practitioner to be more difficult than usual (Question 4, Form 07) was significantly higher ($P < 0.001$) in Oregon. Nearly 39% of cases were so described in Oregon compared to about 13% of the cases in Alabama, Florida and Minnesota. Scandinavian practitioners reported an intermediate proportion at 26%. The proportion of cases in Table 19 requiring additional attempts to obtain adequate local anesthesia ranged from 28% to 63% over the five study regions. Alabama practitioners experienced significantly more of these issues ($P < 0.001$). The proportion

of practitioners who predicted at least a slight likelihood of persistent tooth pain six months after completion of treatment was significantly greater in Scandinavia at 51% ($P < 0.001$). The comparable proportion of positive responses to this question (Question 9, Form 07) was 39% in Minnesota, and less than 26% in the remaining study regions. For each of the study binary predictors shown in Table 19, the least represented categories still included more than 15% of the total sample.

Table 19: Practitioner Reported Procedural Issues Associated with Study Tooth Obturation

	Visits Required for Completion of Treatment			Obturation Was Difficult*			Additional Procedures Required for Anesthesia**			Practitioner-predicted Pain in Six Months ***		
Region	1 visit	≥ 2 visits	N	No	Yes	N	No	Yes	N	Yes	No	N
AL/MS	69%	31%	98	85%	15%	98	37%	63%	98	74%	26%	98
FL/GA	77%	23%	131	87%	13%	131	65%	35%	131	75%	25%	131
MN	91%	9%	390	87%	13%	390	72%	28%	389	61%	39%	389
OR	58%	42%	36	61%	39%	36	64%	36%	36	78%	22%	36
SK	26%	74%	53	74%	26%	53	68%	32%	53	49%	51%	53
Total	**79%**	**21%**	**708**	**601**	**85%**	**15%**	**65%**	**35%**	**707**	**66%**	**34%**	**707**
Frequency Missing			0			0			1			1
P-value between-regions			<0.0001			<0.0001			<0.0001			0.0005

* Question 4, Form 07: In your opinion, was this procedure significantly more difficult than the typical root canal therapies you perform in your practice?
** Question 8, Form 07: Were any of the following necessary to obtain adequate anesthesia to perform the treatment? Mark all that apply: a) Second injection in same location; b) Second injection in different location; c) Block anesthesia technique different from previous injection; d) Periodontal ligament (PDL) injection; e) Intraosseous injection other than PDL (e.g., Stabident or X-tip); Intra-pulpal injection.
*** Question 9, Form 07: In your opinion, what is the likelihood that persistent pain will be present in 6 months' time? Column head (0) indicates response of "not likely." Column head (1) indicates responses of or "slightly likely" or "moderately likely" or highly likely."

Association between Pulpal and Apical Diagnoses and the Occurrence of Tooth Pain during the Week Following Obturation

Table 20 shows mean levels of the 'worst post-treatment pain' experienced by study patients during the week following their endodontic treatment. Dx3 and Dx5 were both associated with a statistically significant increase in pain (P<0.007) in comparison to the mean pain experienced in the absence of these diagnoses. The presence at baseline of the other six diagnoses appeared to be protective against post-treatment worst pain level. This protection is indicated by the negative mean differences in Table 20. Dx1 and Dx8 were associated with significantly less pain (<0.014). Dx6 tended toward a significant pain reduction (P<0.10), while the apparent protection associated with Dx2, Dx4, and Dx7 could be simply due to chance (P>0.29).

Table 20: Mean Levels of 'Worst' Post-Treatment Endodontic Pain Differentiated by the Presence or Absence of Baseline Pulpal and Apical Diagnoses *

	Diagnosis		N	Group Mean	Mean Difference	P-value for Significance
Pulpal Diagnoses	Dx1	1	318	2.1774	-0.5862	0.0136
		0	327	2.7309		
	Dx2	1	129	2.3953	-0.0558	0.8517
		0	512	2.4512		
	Dx3	1	194	2.9536	0.7366	0.0063
		0	447	2.2170		
Apical Diagnoses	Dx4	1	162	2.3272	-0.1547	0.5766
		0	469	2.4819		
	Dx5	1	248	2.9798	0.8858	0.0005
		0	383	2.0940		
	Dx6	1	138	2.0652	-0.4824	0.0991
		0	493	2.5477		
	Dx7	1	51	2.0196	-0.4658	0.2940
		0	583	2.4854		
	Dx8	1	32	1.1563	-1.3604	0.0036
		0	602	2.5166		

* These post-treatment pain data were measured using Question 4 in Form 11. This data collection instrument was completed by the patient one week after their tooth was obturated. Question 4: In the past week, how intense was your worst tooth pain rated on a 0 to 10 scale where 0 is "no pain" and 10 is "pain as bad as could be"?

Prevalence of Psychological Measures in the Study Sample

Table 21 shows the regional distributions for patient fear of this particular dental treatment. Overall, 18.5% (130/702) of the patients endorsed "much fear" in anticipation of their treatment, with statistically fewer so reporting in Oregon (P = 0.022). Only 2.3% of the patients (16/704) anticipated a poor outcome from their treatment. The greatest proportion with this response, 7.5%, was observed in Scandinavia (P = 0.038). The study patients also had the opportunity to compare their pre-treatment fears to their actual treatment experience. Of the 704 responders, 98 (13.9%) judged that the experience was as bad as they had anticipated, with the highest proportion for this response among the Scandinavian patients (P < 0.001).

Table 21: Fear of the Dental Treatment, Treatment Outcome Expectations, and Actual Treatment Experience

	Fear Over Initial Dental Appointment*			Patient's Expectations as to Treatment Outcome**			Pre-treatment Fear Compared to Treatment Experience***		
Region	Little Fear	Much Fear	N	Good	Less than Good	N	Better than Anticipated	As Bad as Anticipated	N
AL/MS	85%	15%	96	98%	2%	97	90%	10%	97
FL/GA	81%	19%	131	99%	1%	131	87%	13%	131
MN	81%	19%	386	98%	2%	387	88%	12%	387
OR	94%	6%	36	94%	6%	36	86%	14%	36
SK	68%	32%	53	92%	8%	53	66%	34%	53
Total	**81%**	**19%**	**702**	**98%**	**2%**	**704**	**85%**	**15%**	**704**
Frequency Missing			6			4			4
P-value between-regions			0.022			0.038			0.0006

* Question 1, Form 04: Are you fearful about today's appointment? The responses have been collapsed; "Little Fear" (No Fear or Little Fear) versus "Much Fear" (Quite a Lot of Fear or Very much Fear)
** Question 2, Form 04: I feel that the treatment outcome for my tooth will turn out… (mark one: Very Good, Good, Fair, Poor). The responses have been collapsed: "Good" (Very Good or Good); "Less than Good" (Fair or Poor).
*** Question 3, Form 09: Please rate your feelings of fear compared to the actual experience. a) Does not apply – I was not afraid; b) The experience was better than I feared; c) The experience was about what I feared; d) The experience was worse than what I feared. Column head "Better than Anticipated" indicates responses of (a) or (b). Column head "As Bad as Anticipated" indicates responses of (c) or (d).

Pain and Anesthesia Variables Reported by the Patients

Table 22 shows that patients' rating of their pain intensity experienced during the treatment procedure. The overall mean on a scale of 0 to 10 was 1.09 (SD: 1.90). Patients in Scandinavia reported a mean pain level of 2.51 that was statistically highest ($P < 0.001$). This latter observation is consistent with the patients' reports on the quality of their anesthesia for which 14/53 Scandinavians (26.4%) indicated some level of dissatisfaction, more than twice the rate for the other regions.

Table 22: Patient-reported Pain and Anesthesia Experienced during Treatment

	Intra-operative Pain Experience*			Patient's Perspective on the Quality of Anesthesia **		
Region	Mean	SD	N	Positive	Negative	N
AL/MS	1.11	1.96	97	89	8	97
FL/GA	1.12	2.08	129	119	12	131
MN	0.86	1.53	383	363	24	387
OR	1.33	2.24	36	33	3	36
SK	2.51	2.79	53	37	14	53
Total	**1.09**	**1.90**	**698**	**641**	**61**	**702**
Frequency Missing			10			6
P-value between-regions			0.0001			< .0001

* Question 1, Form 09: How intense was your pain during the root canal treatment on a 0 to 10 scale, where 0 is "no pain" and 10 is "pain as bad as it could be"?
** Question 2, Form 09: Please rate how your tooth felt during the root canal treatment (mark one). a) The tooth was not numb enough; b) The tooth was numb enough; c) The tooth was too numb. Column head "Positive experience" indicates a response of (b). Column head "Negative experience" indicates responses of (a) or (c).

Systemic Health Variables Reported by the Study Patients

Table 23 shows that the overall proportion of study patients reporting a diagnosis of diabetes or high blood sugar was 83 of 687 respondents, or 12.1%. There was no difference between regions (P = 0.83). Slightly over 47% of the patients reported their having smoked more than 100 cigarettes during their lifetime with, again, no difference between regions (P = 0.12).

Table 23: Systemic Health Characteristics

	Diabetes or High Blood Sugar*			100 or more Cigarettes Smoked during Lifetime**		
Region	No	Yes	N	No	Yes	N
AL/MS	85%	15%	94	62%	38%	97
FL/GA	90%	10%	125	53%	47%	125
MN	88%	12%	380	52%	48%	384
OR	89%	11%	35	58%	42%	36
SK	89%	11%	53	40%	60%	53
Total	**88%**	**12%**	**687**	**53%**	**47%**	**695**
Frequency Missing			21			13
P-value between-regions			0.83			0.12

* Question 20, Form 04: Has a doctor ever told you that you had diabetes or high blood sugar?
** Question 17, Form 04: During your entire life, have you smoked at least 100 cigarettes?

Occurrence of Severe Post-endodontic Pain and Swelling during the Week following Treatment

Table 24 indicates that 645 subjects of the 708 (91.1%) returned Form 11 one week after their root canal obturation was completed. Of these, 100 subjects (15.5%) had experienced severe pain, defined as pain ≥ 7 on a scale of 0 to 10, during the first week post-treatment. When the report of severe pain is combined with the concomitant report of "some" swelling or more, only 5.8% (41/708) subjects fit these criteria.

Table 24: Post-operative Occurrence of Swelling and the Combination of Swelling with Severe Post-operative Pain during the Week following Obturation

	Severe Pain during Week following Obturation*			**Perceived swelling during the past week****					**Perceived swelling AND ≥ 7 Worst Pain Intensity during past week - scale (0-10)**				
Region	< 7	≥ 7	N	None	A little	Some	A lot	N	None	A little	Some	A lot	N
AL/MS	84%	16%	91	46%	41%	12%	1%	95	39%	33%	22%	6%	18
FL/GA	88%	12%	127	52%	37%	6%	5%	130	30%	45%	10%	15%	20
MN	82%	18%	340	41%	42%	13%	4%	341	18%	41%	26%	15%	66
OR	79%	21%	34	34%	43%	20%	3%	35	0%	67%	33%	0%	6
SK	92%	8%	53	69%	19%	8%	4%	53	56%	22%	11%	11%	9
Total	**84%**	**16%**	**645**	**47%**	**38%**	**11%**	**4%**	**654**	**25%**	**40%**	**22%**	**13%**	**119**
Frequency Missing			63					54					1
P-value			0.22					0.009					0.29

* Question 4, Form 11: In the past week, how intense was your worst tooth pain rated on a 0 to 10 scale where 0 is "no pain" and 10 is "pain as bad as could be?
** Question 10, Form 11: How much swelling did you experience in or around the root canal treated tooth?

DISCUSSION

Aim 1. Feasibility:

Feasibility of Conducting Clinical Research Studies in the Context of the DPBRN

This report describes the feasibility of methods used to meet the study aims for a combination study, Peri-Operative Pain and Root Canal Therapy (DPBRN Study 17). The results that are reported were selected as evidence that study design and implementation were both appropriate and feasible. The minimum required sample size was estimated as 600 subjects, and this was projected to be collected over a period of 6 months. After all ineligible subjects were excluded from the data set, 708 subjects remained, 18% more than the minimum sample size that had been projected, over this 6 months of patient recruitment. Over enrollment of patients was planned to compensate for those patients who might subsequently be found to be ineligible, drop out, or be lost to follow-up. Compared to the pre-study estimate of 48 practitioners needed to accomplish the study goals, the actual recruitment of 62 practitioners represented a 29% increase. Over enrollment of P-Is was also planned to guard against some P-Is failing to meet targets for various reasons, such as unforeseen change in their personal situation, lack of patient interest, or too much difficulty performing study requirements. The study results indicate compelling confirmation for the feasibility of recruitment of both subjects and practitioners in the context of the DPBRN. We note also that the pre-study estimates of practitioner productivity were also fulfilled, with the endodontic specialists completing 4.3 patients per month and the general practitioners completing 1.1 patients per month during the six months specified for baseline data collection.

Sufficient distributions of maxillary, mandibular, anterior and posterior teeth were obtained to analyze the influence, if any, of tooth location/type on endodontic post-treatment pain occurrence. Only one adverse event was reported for patients who were recruited into this study. All data management duties performed by data entry technicians at the study Coordinating Center (UAB) were checked and found to be reliable.

A remaining question regarding study feasibility involved the return rate of questionnaires and proportion of usable responses. The return rates were excellent with a greater than 99% return for Form 04, Form 05, Form 07 and Form 09. As was noted in Results above, 37 participating subjects were not included in a Consecutive Eligible Log. These particular omissions were associated with 8 (13%) of the 62 practitioners who did not return logs. Based on this observation, it is likely that the number of ineligible patients might also have been underestimated. Also, given that 18 patients who were out of age range were enrolled, additional training with increased focus on enrollment of consecutive patients and recording pertinent information seems to be needed.

External and Internal Validity of the Research Project

Internal validity of a study pertains to the design-based minimization of potential types of bias associated with its implementation. For this observational study, internal validity issues include the absence of practitioner bias regarding subject selection, unbiased administration of the study questionnaires, and unbiased collection of study

questionnaires. The study sample was not a randomly selected representative sample, but was rather a convenience sample. However, specifying the enrollment of consecutive patients presenting for root canal therapy minimized the potential for practitioner bias in patient selection. From the Consecutive Eligible Log, practitioners had to screen 1.5 potential subjects to enroll 1 who completed all eligibility criteria. This represents a high acceptance rate of patients being seen in community dental practices to participate as a research subject. This compares well to other studies (Figini, Lodi, Gorni, & Gagliani, 2008), which further suggests the data collected represents typical patients presenting for initial root canal therapy.

The study surveys were self-reported questionnaires that were administered in a manner reasonably free from influence by persons other than the one completing the questionnaire. P-Is and their office staff were not allowed to influence their patients' responses on Forms 04 and 09. Likewise, patients were not privy to Forms 05 and 07 that were completed by the P-I. One study form, the Consecutive Eligible Log, was subject to some inattention by at least eight P-Is. However, this "failure to report" was likely non-differential, at least with respect to determining patient eligibility, in that it included eligible patients with whom a reporting incentive was associated (37 noted above) as well as ineligible patients for whom there was no reporting incentive. Collection rates of forms and missing data within questionnaires were similar across participants (subject, practitioner), type of dentist (general dentist, endodontist), and region. Taken together, it

is unlikely that there was noteworthy bias in the data collection process and this suggests a high level of internal validity.

External validity pertains to the potential for generalizing study results to similar populations elsewhere - in this case, to endodontic patients seen in a range of private dental practices within the United States. Generalizability of findings may also be inferred from the fact that study subjects were not drawn from a few practices or a single geographical area, but from 62 practices located in four widely separated regions of the United States, and in Scandinavia (Denmark and Sweden). In addition, the outcome estimates are based on a large study sample of 708 patients, which compares favorably to other prospective studies assessing outcome of orthograde root canal therapy (Ng, Mann, Rahbaran, Lewsey, & Gulabivala, 2007). In the U.S., most patients receive root canal therapy from their general dentists (American Dental Association Survey Center, 2008), while in most published research, care is provided by an endodontist (Ng et al., 2007). Thus, it seems that representation of patients treated by both types of dentists supports the external validity of the study findings.

Demographics and Socio-economic Characteristics of the Study Sample

The mean age of the study subjects was 48 years with a SD of 13 and a range of 19-70 years, which is very similar to the ages of patients seen by both general dentists and endodontists in the U.S. except for the extreme ends of the age spectrum (American Dental Association Survey Center, 2008) and slightly older than a large group of insured

patients, mean age 43 years old studied by Lazarski, Walker, Flores, Schindler, & Hargreaves (2001). Females represented 59% of the patients and males 41%, for a 1.44 ratio of female to male patients. This proportion is similar to that for U.S. patients seen by endodontists for orthograde root canal therapy, 1.40, but different from that of all general dental patients, 1.03 (American Dental Association Survey Center, 2008) and of a large group of insured patients, 1.01 (Lazarski et al., 2001). In the present study, White non-Hispanic group constituted 86% of the patients, while Hispanic ethnicity and non-White races were underrepresented in the participating clinic populations. Nearly all the study sample benefited from indicators of moderately elevated socio-economic status. The average annual income was greater than $30,000 for 84% of the participants. Dental insurance was held by 81% of the patients, and 81% had at least some college education (Table 5). U.S.-wide data on these characteristics of patients receiving dental care does not seem to be available for comparison, but such skewed statistics are consistent with prospective data describing people choosing tooth extraction over root canal therapy (Boykin, Gilbert, Tilashalski, & Litaker, 2009). Sampling differences in the five-study regions point, however, to a potential need for adjustment of the combined study endpoints to account for these differences in the final analyses for Study 17.

Adequate Frequencies of the Presence or Absence of Predictor Variables

This study was not designed to estimate, for example, outcome differences between study regions. This would have required nearly equal subject sampling in each region and this was not a study aim. Also, this study was not designed to evaluate an effect on outcome

due to Hispanic ethnicity or non-white races, and sufficient numbers were not recruited for that purpose. Only 29 of 708 (4.1%) recruits were Hispanic, and the largest non-white racial group, the Black/African Americans, was represented by only 38 of 708 individuals (5.4%). However, for the binary predictors specified in this study's design, the least represented categories included more than 10% of the total sample. These percentages pertained to: anterior teeth (11% of all teeth treated, 77/708, Table 7); annual incomes of less $30,000 (15%, Table 5); no dental insurance (19%, Table 5), education that included high school or less (19%, Table 5); and male gender (41%, Table 3). Thus, recruitment of patients and practitioners was successful in addition to collecting the quantity of data needed to answer the study questions as to the predictors of post-procedural pain.

Strengths and Weaknesses

The main strength of this research is the high levels of both internal and external validity. Given the prospective nature of the study, using accepted patient reported outcome measures leads to high levels of external validity. The representative sample of endodontic patients with a variety of symptoms and treatment needs recruited over a short period of time with high completion rates of study questionnaires suggests high levels of internal validity. Together, they suggest the finding of the study may describe with reasonable accuracy what patients having initial orthograde root canal therapy are experiencing. The primary weakness of this aim involves the documentation of patients with regards to selection. It would be ideal to have documentation of all patients that were screened, as opposed to just those eligible to be enrolled, and higher levels of

compliance completing Form 03, the Consecutive Eligible Patient Log. This also extends to properly excluding patients outside the desired age range. If this study was to be performed again, the consecutive log should be redrafted to make it easier to complete during a normal clinical day (especially for general dentists) and greater emphasis on accurately using this Form during practitioner-investigator training is needed.

Conclusions Related to Feasibility

Sufficient numbers of patients and practitioner-investigators can be recruited for a study of this type in the context of the DPBRN. Prospective observational studies of significant size can be implemented over a period of months to perform the large-scale recruitment of patients need for clinical endodontic research. The use of in-office questionnaire-based data collection forms with high levels of acceptance suggests that the burdens on patients and dentists are acceptable. High levels of patient agreement to participate in various community-based practices and high levels of data completeness, except for completion of the Consecutive Eligibility Log, suggest good internal and external validity. Taken together, we conclude that it is feasible to conduct high-quality clinical endodontic research within the Dental Practice-Based Research Network (DPBRN).

Aim 2. Description:

Endodontic Pain Intensity and Pain Burden in the Study Sample

The endodontic pain that study patients experienced during the week preceding recruitment did not vary significantly between regions (Table 8, $P \leq 0.15$). It is worth noting that severe pain, defined as 27.7% of patients to describe their "average" pain during the prior week, and 49.9% endorsed ≥ 7 on the 0-10 scale, reported that their "worst" pain attained a severe level.

The number of days of interference was a measure of pain burden, associated with the study subjects' endodontic pain, which was used to calculate loss of productivity. Table 9 shows an overall mean of 0.51 days of interference during the prior week with a SD of 1.22 days. While this average of 0.51 days may not appear to be numerically large, it does represent 7.3% of the week in the patient sample. Pain interference was also measured using the Graded Chronic Pain Scales (0-10) for interference with daily activities, recreational activities, and work. Nearly 50% of the subjects endorsed at least some level of interference related to their endodontic pain. With 15,091,860 initial orthograde root canal therapies performed a year in the U.S. (American Dental Association Survey Center, 2008), this represents about 7.5 million people experiencing interference and about 7.5 million days of lost productivity.

Endodontic Pain Qualities and Characteristics

Pain qualities, pain characteristics, and conditions that provoked endodontic pain were present frequently enough to permit assessment of their association post-endodontic treatment pain. The five pain qualities of "dull", "sharp", "ache", "throbbing" and "shooting" were present in at least 19% of the study sample ($n \geq 139$). However, "burning" and "electric" types of pain were relatively uncommon in these patients (< 6%). Spontaneous pain and provoked pain were each present in more than 26% of the sample ($n \geq 188$). Provocation of tooth pain by food mastication and thermal changes were each represented in more than 43% of the study sample ($n \geq 310$). Tooth pain that could be described as "stable or unchanging" was uncommon (5.2%), as was tooth pain provoked by stress (6.6%).

Prevalence of Widespread Bodily Pain Reported by the Study Sample

The question for Table 13 that assessed bodily pain experience showed no difference in the prevalence of this outcome across study regions ($P = 0.12$). However, 29.4% of the 697 questionnaire respondents endorsed widespread pain that could imply that they are victims to some extent of central pain sensitization. The report of pain is a subjective response, and the pain literature has demonstrated that the pain an individual feels may arise from central pain sensitization (Sarzi-Puttini, Atzeni, & Mease, 2011). A diagnosis of central sensitization to pain could not be verified in this study population, since a comprehensive rheumatological examination was not performed, yet the observed

prevalence is slightly higher than the approximate 20% population prevalence of Chronic Widespread Pain (Cimmino, Ferrone, & Cutolo, 2011; McBeth & Jones, 2007).

Usefulness of the Diagnostic Algorithm

It has been reported in the endodontic literature that the presence of symptomatic apical diagnoses or persistent apical lesions before treatment is associated with a higher frequency of post-treatment pain (Yu et al, 2011-In press in J Endodo). Given the need to inform and educate patients as to their potential outcomes, the diagnostic algorithm developed for this study may be very useful to clinicians. Table 14 confirms these earlier reports by showing that mean post-treatment pain levels are statistically greater ($P < 0.007$) when symptomatic irreversible pulpitis (Dx3) and/or symptomatic apical periodontitis (Dx5) are present at the time that the patient presents for treatment.

Procedural Issues Reported by the Study Practitioners

A primary purpose of this paper is to report the prevalence of multiple tooth-related and procedure-related issues that will later be explored for their association with post-treatment pain at one week. Table 18 shows that a proportionately higher number of Scandinavian practitioners employed at least two patient-visits to obturate a tooth ($P < 0.001$). It would be reasonable to suppose that the use of two visits might be related to the difficulty of the procedure, or a problem with achieving adequate anesthesia. Thus, it is worth noting that the proportion of cases that were claimed to be more difficult than usual (Question 4, Form 07, see Table 5) was significantly higher in Oregon. Moreover, the

proportion of cases requiring additional local anesthesia was highest among Alabama practitioners ($P < 0.001$, Table 9). Even so, the potential factors that may contribute to one verses more than one appointment are many and this study is unable to address this question.

Prevalence of Psychological Measures Reported by the Study Participants

Dental treatment in general is known to provoke a sense of fear (Armfield et al., 2007), while root canal treatment is specifically known for this and is used to study this phenomenon (Logan, Lutgendorf, Kirchner, Rivera, & Lubaroff, 2001). Eighteen percent of the participants in this study reported having "much fear", which is comparable to the 12 to 21% observed in adult population samples (Armfield et al., 2007; Milgrom, Fiset, Melnick, & Weinstein, 1988; Thomson, Locker, & Poulton, 2000). Even though catastrophizing is known to negatively affect both experimental pain (Edwards, Fillingim, Maixner, Sigurdsson, & Haythornthwaite, 2004) and immediate post-surgical pain (Pinto, McIntyre, Almeida, & Araujo-Soares, 2011), there does not seem to be reports of catastrophizing by patients, as measured by self-reported expectation of treatment outcome (Table 21) with pending endodontic therapy. Therefore it is unknown whether the observed 2.3% is representative of such patients in general.

Outcome of Severe Pain and Swelling in the Week Following Obturation

Over 15% of patients reported experiencing pain intensity at or above a rating of 7/10 is our sample, 3-5 times greater than that reported in the literature for "endo flare" (Walton

& Fouad, 1992) but in line with a recent systematic review that reported data from 17 studies that seems to cluster between 10 to 20% (Pak & White, 2011). When a second criterion of swelling is added as a required component of outcome, the frequency in the present study drops to about 6%, which is closer to the accepted rates for "endo flare-up" (Walton & Fouad, 1992). Others have observed even lower rates of "endo flare-up", under 2%, which is likely related to the addition of a third criterion, presenting to the treating clinician for an unscheduled appointment (Alves Vde, 2010; Iqbal, Kurtz, & Kohli, 2009).

Strengths and Weaknesses

The strengths of this research are that high levels of follow up data was collected from a large group of patients that seem to represent the average U.S. dental patient receiving initial orthograde root canal therapy. Furthermore, well-known data collection instruments for patient reported outcomes were used to obtain a wide variety of indicators of pain that are consistent with recommendations (Turk et al., 2006). If this research project were to be repeated, four weaknesses could be addressed with additions to the protocol. First, standard psychosocial assessment measures completed pre-operatively, would be helpful since it is well known that mood disorders, such as depression, alter the inflammatory process and pain sensory system. Second, a general assessment measure of oral health obtained pre-operatively and post-operatively, such as OHIP, would be beneficial in establishing a general measure of overall change so that a comparison with other treatments can be made, such as tooth extraction and implant placement. Third,

assessment of the diagnostic algorithm against a reference-standard, that being one derived by an expert endodontist following published guidelines (Glickman et al., 2009; Gutmann et al., 2009; Levin et al., 2009; Newton et al., 2009) using all available information. This would produce an estimate of bias produced by the algorithm, which can be adjusted after data collection. Fourth, obtaining copies of the pre-operative or diagnostic periapical radiographs and the post-obturation periapical radiographs. This will further refine the diagnostic algorithm, which was based only on signs and symptoms, and allow for radiographic indicators, specifically periapical rarefaction, to also be assessed.

Conclusions Related to Aim 2

Patients presenting for initial orthograde root canal therapy have a significant amount of tooth pain and tooth pain-related interference in daily life, as well as widespread pain. Patients presented with diagnoses of necrotic pulps and symptomatic apical periodontitis. Within the 1-week post-operative period, about 16% of patients reported experiencing severe dental pain (≥7/10) and 6% reported experiencing severe pain and swelling.

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