Non-CTIMP Study Protocol

Study title: Pain following root canal treatment

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CONTENTS

LIST OF ABBREVIATIONS

Insert abbreviations as required

This is not an exhaustive list.
Any additional abbreviations used within the protocol must also be added here.

ACCORD	Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
PI	Principal Investigator
QA	Quality Assurance
REC	Research Ethics Committee
SOP	Standard Operating Procedure

1.0 INTRODUCTION

1.1 BACKGROUND

Pain is a very subjective sensation that has be defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Rosenberg, 1998). Root canal treatment is the process of eliminating pain by removing inflamed or dead pulpal tissues, cleaning and shaping the root canal system, to allow for the placement of a restoration that prevents microleakage. Pain following root canal treatment (RCT) is an unpleasant outcome for both dentists and patients. It is multifactorial, which could be mediated by cognitive, emotional as well as motivational factors, that may also be related to personal characteristics (Weich et al., 2008). The causes of pain following RCT include mechanical, chemical and/ or microbial injury to the pulpal or the tissues surrounding the roots. Other factors may include inadequate cleaning and shaping, over-instrumentation and extrusion of debris, irrigant, intracanal medication, tooth type and position, gender as well as age (ElMubarak et al., 2010; Watkins et al., 2002; Ali et al., 2012; Torabinejad et al., 1988; Morse et al., 1986; Imura and Zuolo, 1995; Siqueira, 2003; Walton et al., 2003; Mattscheck et al., 2001). Patient's bite (occlusion) may also play an important role in triggering pain following RCT. Occlusal adjustment has been reported to prevent post-operative pain in teeth which underwent RCT (Rosenberg et al., 1998).

Pain can either be tooth-related (odontogenic) or not tooth-related (non-odontogenic). The tooth-related pain following RCT can be further subdivided into intra-appointment flare-up, immediate post-operative pain, intermediate post-operative pain (within the first three months after treatment) and long-term post-operative pain (persistent pain lasting longer than 6 months to years after treatment) (Nixdorf et al., 2010). Intra-

appointment flare-up is the presence of severe pain and swelling of the soft tissues and the oral mucosa with regards to the root-treated tooth, occurring within a few hours to a few days after treatment, which usually would result in patients coming in for an unscheduled emergency appointment (Udoye & Aguwa, 2010; Iqbal et al., 2009; Yu et al., 2012; Gotler et al., 2012; Mattscheck et al., 2001; Walton & Fouad; 1992; Shah et al., 2011; Pasqualini et al., 2012; Ehrmann et al., 2003 and Thesis et al., 2008).

The objective of RCT has always been to eradicate as much microorganisms as possible from the root canal system, creating an environment that is favourable for healing to take place (Orstavik et al., 1991; Sjogren et al., 1997; Siqueira et al., 2000). It also facilitates retention of teeth, to remain in function (Gilheany et al. 1994, Ørstavik & Pitt Ford, 1998). Nonetheless, pain following root canal treatment has been reported to be within 3% to 69.3%, mainly experienced within the first 24 to 48 hours (Ince et al., 2009; Gomes et al., 2017; Bourreau et al., 2015; Sing and Garg, 2012; Oginni and Udoye, 2004; Albashaireh and Alnegrish, 1998; Risso et al., 2008; Ng et al., 2004; Glennon et al., 2004; ElMubarak et al., 2010; Siqueira et al., 2002; Bhagwat and Mehta, 2013; Fava 1995). On the other hand, studies reported 5% - 25% incidence of persistent pain, lasting for 6 months or longer (Nixdorf et al., 2010; Nixdorf et al., 2015, Nixdorf et al., 2016, Philpott et al., 2019). Regardless of the mild to moderate possibility of pain occurring following root canal treatment, it is a poor indicator of a successful outcome of root canal treatment.

1.2 RATIONALE FOR STUDY

Although numerous studies have been conducted regarding pain following root canal treatment, there still appears to be contradicting results in the outcome as well as pain management, mainly due to the differences in the study protocols and small sample size.

Findings from this study is aimed at evaluating incidence of immediate post-operative pain, be it for primary RCT or re-treatment cases. Additionally, it is also aimed for clinicians to understand the possible factors of root canal treatment that may be related to immediate post-operative pain. As a result, clinicians will be able to accurately diagnose the pain and appropriate treatment planning can be carried out. Patients will also be better educated in managing their symptoms, which includes the consumption of appropriate pain medication. It is also hoped that the validation of the pain assessment tool used in this study will help dental practitioners to record pain more easily.

2.0 STUDY OBJECTIVES

2.1 OBJECTIVES

2.1.1 The primary objectives of this study are:

(i) to evaluate the incidence of post-operative pain after RCT at 24H, 48H and 7 days

(ii) to evaluate the factors affecting post-operative pain

(iii) to evaluate the quality of life (QoL) following RCT at 24H, 48H and 7 days

2.1.2 The secondary objective include:

(i) to evaluate the duration of post-operative pain

(ii) to evaluate the severity of post-operative pain

2.2 Endpoints

2.2.1 Primary endpoints

(i) Patient decided to extract the tooth undergoing root canal treatment

(ii) Patient does not want to continue with root canal treatment in Edinburgh Dental Institute

2.2.2 Secondary endpoints

(i) Tooth had procedural errors (such as perforation or ledge) that would affect the accuracy of the results of this study

(ii) The tooth was filled (obturated) to an unsatisfactory level; extremely short (> 2mm) or extruded (> 2mm)

3.0 STUDY DESIGN

This study is a prospective clinical study, which evaluates pain following the completion of non-surgical root canal treatment and re-treatment cases. The study is planned to take place from July 2021 until June 2022. Patient cohort would be patients referred to Edinburgh Dental Institute for root canal treatment. Root canal treatment and re-treatment cases will be performed by Postgraduate Trainees (Years 1,2 and 3) in Endodontology and Prosthodontics, core trainees, specialist registrars in the Restorative Departments and staff members of the Restorative Department, Edinburgh Dental Institute. (Please refer to Appendix 1)

Patients who are deemed suitable for this study, screened by clinicians on duty during Restorative New Patient Clinic, will be invited to participate in this study. They will be given the Patient Information Sheet (PIS) at the beginning of the session and will be given time to decide on whether to participate in the study or not. If a suitable patient happens to not have the PIS and consent form during the 1st treatment visit, the patient will be provided with the PIS and consent form during the 1st treatment visit and will be given up to 24H to decide on participating the study or not. The pre-operative assessment, which will include pain assessment will be conducted as per normal routine prior to the commencement of RCT. At 24H (+/- 2H) the Principal Investigator will call the patient to follow-up. If the patient has agreed to participate in the study, the 24H post-operative pain and quality of life assessment will be conducted at the same time. Once patients have agreed to participate, they will be required to provide written consent which will be attached together with the PIS. On the first treatment day, patients will be required to answer a pre-operative Pain Assessment Questionnaire (Appendix 3), which will be answered in the presence of the clinician treating the patient, before the commencement of RCT. The Pain Questionnaire is the combination of Numeric Rating Scale (NRS) and Modified Verbal Rating Scale (VRS) adapted from previous published studies, with the addition of question on the presence of pre-operative pain duration. The pre-operative questionnaire will incorporate questions on pain intensity, the need, name and dosage of painkillers used by the patient on that day, and the last dose taken (in hours) as well as the duration of pain felt, as the longer the duration of pre-operative pain felt has been associated with

higher incidence of post-operative pain (Polycarpou et al., 2005). Also, pre-operative pain felt within the last 24 hours prior to root canal treatment has been associated with higher probability of post-operative pain (Arias et al., 2013).

Following the completion of treatment, patients will be provided with post-operative Pain Assessment Questionnaire (Appendix 4), for the evaluation of post-operative pain. A copy of the pain questionnaire will be given to the patients which will be used as a guide when the pain history is obtained. This will be carried out verbally via phone by the main investigator of the study (NAF). Patients will not be required to return the forms to the institute.

In addition to pain evaluation, this Pain Questionnaire also incorporates the intake of painkillers taken. In the event that painkillers are taken by patients for pain control, patients are required to record the pain intensity before the consumption of painkillers, apart from recording the dosage and frequency of painkillers taken. Patients will be advised on the standard painkiller regimen as a post-operative instruction after the completion of RCT. Painkiller consumption is also an indirect measure of post-operative pain intensity, hence, that is why this has been added to the Pain Assessment Questionnaire. Apart from pain assessment, post-operative quality of life (POQoL) post-treatment will also be assessed, based on questionnaire adapted from Pasqualini et al., 2016. (Appendix 5).

Patients will be given the liberty to pull out from the study at any time, throughout the duration of the study. Similarly, the investigator will also be able to remove patients from the study, throughout the duration of the study, in the event that the teeth being root-treated were faced with complications that may alter the accuracy of the study. Withdrawal or removal will be recorded in the ‘Withdrawal/ Removal Form’.

In terms of clinical notes required, a clinical template of the most important information required will be provided for all clinicians performing root canal treatment/ retreatment, in order for a standardized record to be obtained (Appendix 6). The clinical notes should include:

1. Any additional special tests done/ repeated

2. Assessment of soft tissues for signs of infection

3. Assessment of the tooth of concern:
(i) Type and quality of pre- existing restoration
(ii) Tenderness to palpation
(iii) Tenderness to percussion
(iv) Mobility
(v) Periodontal pocket depth

4. Additional sensibility tests conducted
(i) EPT
(ii) Cold test

5. Diagnosis on the first treatment visit

6. Whether any treatment has been carried out prior to having treatment initiated at Edinburgh Dental Institute (EDI)

* At the end of the treatment notes template, a sentence on providing patients with pre-operative and post-operative questionnaires will be added as a reminder to the clinicians. This will also be re-emphasized verbally to the nurses and clinicians in charge.

4.0 Study Population

4.1 Number of participants:
150 participants

Participant population:
All patients referred to Restorative Department, Edinburgh Dental Institute for root canal treatment treated by postgraduate trainees in Endodontology and Prosthodontics (Years 1,2,3), Core Trainees and Specialist Registrars in the Restorative Department as well as staff members of Edinburgh Dental Institute.

Number of sites involved:
Only patients seen in the Restorative department of EDI will be included.

Length of recruitment period:
September 2021 until March 2022

4.2 Criteria

Inclusion Criteria	Exclusion Criteria
All teeth requiring primary root canal treatment	Surgical root canal treatment
All teeth requiring root canal re-treatment	Patients on long term analgesics and steroids
Age 18 – 100 years old (completely formed apex)	Primary teeth
Permanent teeth	Teeth with procedural errors either being referred for the management or created during the procedure
Periodontal pocket depth < 4mm and with mobility within normal limits	Traumatized teeth
	Teeth with open apices
	Periodontally involved teeth
	Cases with hypochlorite accident
	Short or extruded root canal obturation
	Cases whereby patency was not achieved
Patients with the ability to give informed consent	

5.0 PARTICIPANT SELECTION AND ENROLMENT

5.1 Identifying participants

1. Who will identify the participants?

Clinicians working on the Restorative New Patient Clinic

2. Details of the first approach:

- Patients referred to Edinburgh Dental Institute requiring root canal treatment or retreatment within the inclusion criteria will be invited to join the research

- Patients will be given the Patient Information Sheet (PIS), by the clinicians seeing them during the New Patient clinic and will be given time to consider their participation

- Patients can either decide on the same day before the end of their appointment during the New Patient clinic and provide with written consent or to bring back the PIS during the first treatment visit

5.2 Consenting Participants

1. The consent process

- Patients will be given the Patient Information Sheet (PIS), by the clinicians seeing them during the New Patient clinic and will be given time to consider their participation

  Patients will be informed on the procedure of the research study, which will include routine root canal treatment, that patient requires. The only additions to the procedure would be the inclusion of pre-operative pain questionnaire prior to the commencement of the treatment as well as the post-operative pain and immediate post-operative quality of life (QoL) assessment at 24H, 48H and 7 days.

- Patients can either decide on the same day before the end of their appointment during the New Patient Clinic and provide with written consent or to bring back the PIS during the first treatment visit. The written consent will be attached together with the PIS. If the patient decides to participate in the study during the New Patient Clinic, the clinician attending to the patient on that day will be taking the consent. If the patient takes a longer time to decide and brings back the consent form during the first treatment visit, the clinician in-charge in providing the treatment will be taking the consent.

2. Possible limitations

- Participants will be informed in the PIS and consent form that phone calls will be made at 24 hours, 48 hours and 7 days (+/- 2 hours) post-operative to assess pain experience after root canal treatment as well as the quality of life after treatment

5.2.1 Withdrawal of Study Participants

Participants are free to withdraw from the study at any point or a participant can be withdrawn by the Investigator. If withdrawal occurs, the primary reason for withdrawal will be documented in the participant's case report form, if possible. The participant will have the option of withdrawal from:

(i) All aspects of the trial but continued use of data collected up to that point . To safeguard rights, the minimum personally-identifiable information possible will be collected.

(ii) Details required for withdrawal from study include:

(a) Reason for withdrawing
(b) Treatment level at which patient withdraw or has been withdrawn by the Principal Investigator

6.0 STUDY ASSESSMENTS

6.1 Study assessments

This study will begin with:
1. Assessment of the eligibility criteria during Restorative New Patient Clinic, seen by clinicians on duty during the New Patient clinical sessions

2. If patient is found suitable for the study, the patient will be invited to participate in this study and will be given the Patient Information Sheet (PIS) and consent form on the same day of the New Patient clinic

3. The patients will be given time to consider their participation and can either return the consent form on the same day of their New Patient clinic appointment, whereby they will be given time during the gap between before going to Radiology Department for pre-operative radiograph(s) and return the consent form once they come back from the Radiology Department or during the first treatment visit. Written consent will be obtained upon returning the consent form and the patients will be given a study number based on numerical order (1,2,3 etc…)

4. On the first treatment day, patients will be given the pre-operative Pain Assessment Questionnaire (a modified version adapted from VRS and NRS)

5. After the completion of treatment, the patients will be given post-operative Pain Assessment Questionnaire (a modified version adapted from VRS and NRS) and post-operative quality of life (QoL) questionnaire. Patients will be called at 24 hours, 48 hours and 7 days after treatment for the assessment.

Assessment	Screening	Treatment Day	24H	48H	1 week
Assessment of eligibility criteria & PIS	X				
Written informed consent	X*	X*			
Pre-operative pain assessment		X			
Post-operative pain assessment			X	X	X
Post-operative quality of life (POQoL)			X	X	X

Table 1: Research study plan in table form

***Written consent can either be obtained on the screening day or 1st treatment visit.**

7.0 DATA COLLECTION

Detailed data to be collected:

1. The Principal Investigator (NAF) will go through TRAK diaries to check for Restorative New Patient Clinic Sessions
- The Principal Investigator will provide the clinicians on New Patient Clinic with PIS and consent forms
- The Principal Investigator will follow-up with these clinicians at the end of the day to collect all returned consent forms as well as to keep track of patients who have brought back the consent forms and are due to return them during the first treatment appointment

2. Since most patients will be placed in the waiting list after the New Patient Clinic appointment, before being assigned a clinician for the root canal treatment, the Principal Investigator will use the 'watch' feature on TRAK to keep track of the suitable patients that have been recruited during the New Patient Clinic to take note of the clinician that will be assigned to the patient

3. Once the patients have been assigned a clinician, the Principal Investigator will go through the TRAK diaries of the clinicians involved in providing RCT, for the collection of the consent forms and distribution of pre-operative, post-operative pain assessment questionnaires and PoQOL questionnaires.

4. The main investigator will create a document containing details of patients who have agreed to participate in the study, which will be securely saved on K-drive

5. The main investigator will call patients to assess post-operative pain at 24H, 48H and 7 days, as well as the assessment of post-operative quality of life (QoL) at the same time frame

6. The main investigator will also need to record any withdrawals from the study

Time points for collection:
- Pre-operative pain on treatment day before commencement of treatment
- Post-operative pain and quality of life (QoL) at 24H, 48H, 7 days

Data collector:
- Principal Investigator (NAF)

Details of standardized tools used:

1. Pre-operative pain assessment questionnaire
2. Post-operative pain assessment questionnaire
3. Post-operative quality of life (POQoL) assessment

Method to maximize completeness of data:

1. Patients will be contacted via phone to assess post-operative pain and quality of life
- Questionnaires used have been validated for verbal/ phone call assessment

7.1 Source of data documentation

The source of data will be from:

i) Pre-operative pain assessment questionnaire

ii) Post-operative pain assessment at 24H, 48H and 7 days

iii) Post-operative quality of life (POQoL) assessment at 24H, 48H and 7 days

7.2 Case report forms

The pain assessment questionnaires will be paper-based which will be stored securely in a pin-locked locker in the Postgraduate room on Level 4 of Edinburgh Dental Institute

8.0 DATA MANAGEMENT

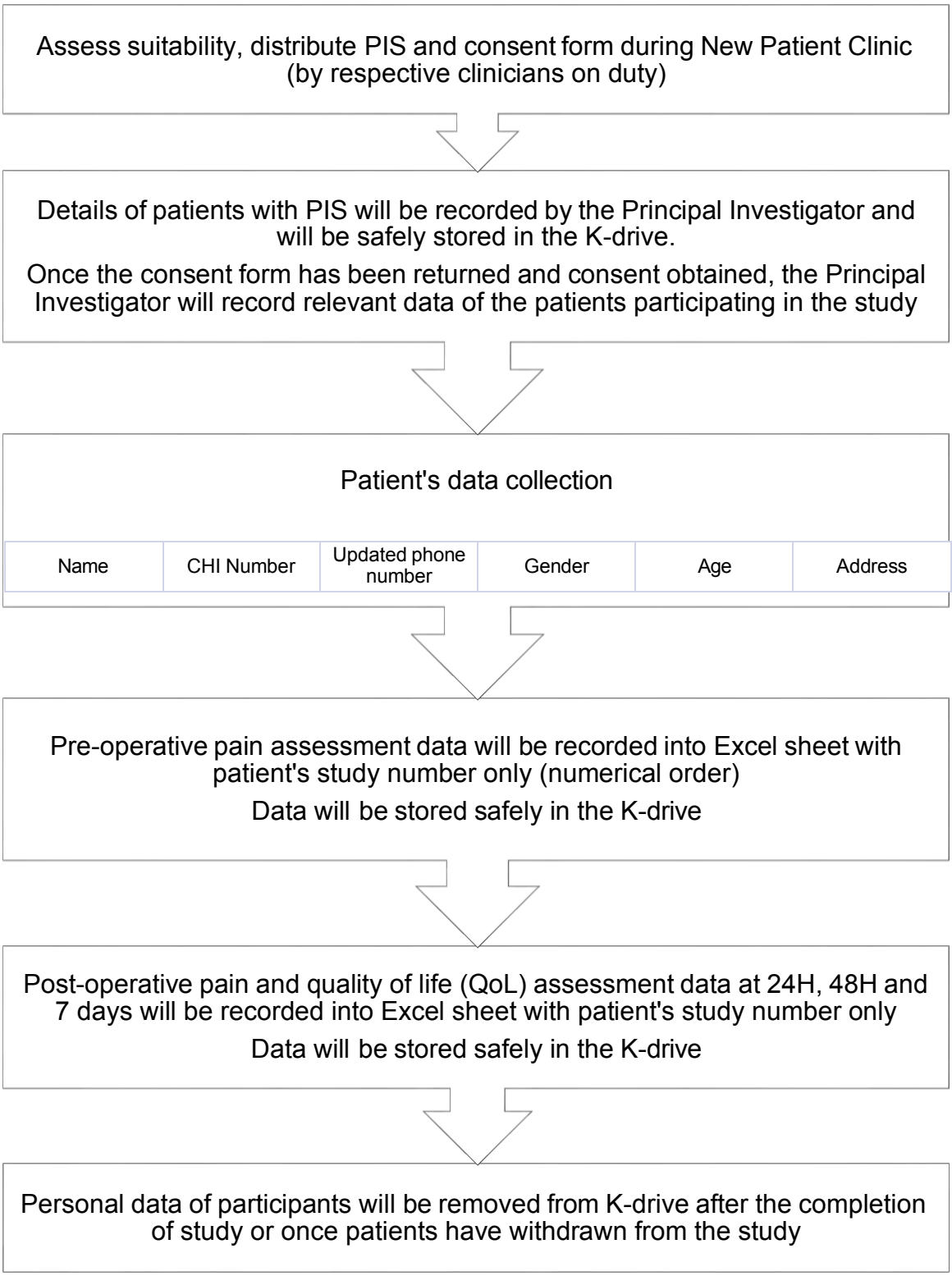
8.1.1 Personal data collection

The following personal data will be collected as part of the research:

1. Name
2. CHI number
3. Gender
4. Age
5. Address
6. Updated phone number

- All data will be stored on a password protected document saved on NHSL computers under the K drive. Patient identifiable information will not be copied or transferred from these computers. All the analysis of the data will be carried out on NHSL computers.

8.1.2 Data Information Flow



8.1.3 Transfer of Data

Data collected or generated by the study (including personal data) will not be transferred to any external individuals or organisations outside of the Sponsoring organisation(s).

8.1.4 Data Controller

The University of Edinburgh and NHS Lothian.

8.1.5 Data Breaches

Any data breaches will be reported to the University of Edinburgh and NHS Lothian Data Protection Officers who will onward report to the relevant authority according to the appropriate timelines if required.

9.0 STATISTICS AND DATA ANALYSIS

9.1 Sample Size Calculation

Power analysis – NA
Sample size – 150
Effect size – NA
Dropout rates – 20%

9.2 Proposed Analyses

Detail the variables to be used for assessment and how these will be reported (e.g. means, standard deviations, medians etc.) Write detailed plans for analyses of primary and secondary outcome measures including:

Summary measures to be reported

The data will be analysed via logistic regression analysis. Each factor will first be analysed via the single-logistic regression analysis. The multiple-logistic regression analysis will then be conducted to compare the factors with each other

Method of analysis

Logistic regression analysis

Plans for handling missing, unused and spurious data, non-compliers and withdrawals

NA as the data will most likely not be used then

Plans for pre-defined subgroup analyses

Logistic regression analysis

Statement regarding use of intention to treat analysis

The intention to treat analysis will not be utilized as the study involves routine root canal treatment/ retreatment. Regardless of the case suitability, the patients will still be treated

Details of any interim analysis

NA

10 ADVERSE EVENTS

This study is a low-risk study, a normal clinical procedure of routine root canal treatment for patients requiring the treatment. It does not involve intervention with new materials or technology.

However, this study does evaluate the incidence of pain following root canal treatment. Therefore, patients will receive standardized post-operative instructions after the completion of root canal treatment. This post-operative instruction follows the SDCEP guidelines as well as adapted from Menhinick et al., 2004. If ever required, this will be re-emphasized during the follow-up phone calls.

11 OVERSIGHT ARRANGEMENTS

11.1 INSPECTION OF RECORDS

Investigators and institutions involved in the study will permit trial related monitoring and audits on behalf of the sponsor, REC review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

11.2 STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study and, if so, at what frequency.

Risk assessment, if required, will determine if audit by the ACCORD QA group is required. Should audit be required, details will be captured in an audit plan. Audit of Investigator sites, study management activities and study collaborative units, facilities and 3rd parties may be performed.

12.1 ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonization Tripartite Guideline for Good Clinical Practice (ICH GCP). **Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met.**

12.2 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

12.2.1 Informed Consent

The Investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of what is involved.

Participants must receive adequate oral and written information – appropriate Participant Information and Informed Consent Forms will be provided. The oral explanation to the participant will be performed by the Investigator or qualified delegated person, and must cover all the elements specified in the Participant Information Sheet and Consent Form.

The participant must be given every opportunity to clarify any points they do not understand and, if necessary, ask for more information. The participant must be given sufficient time to consider the information provided. It should be emphasized that the participant may withdraw their consent to participate at any time without loss of benefits to which they otherwise would be entitled.

The participant will be informed and agree to their medical records being inspected by regulatory authorities and representatives of the sponsor(s).

The Investigator or delegated member of the trial team and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained. The participant will receive a copy of this document and a copy filed in the Investigator Site File (ISF) and participant's medical notes (if applicable).

12.2.2 Study Site Staff

The Investigator must be familiar with the protocol and the study requirements. It is the Investigator's responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their trial related duties.

12.2.3 Data Recording

The Principal Investigator is responsible for the quality of the data recorded in the CRF at each Investigator Site.

12.2.4 Investigator Documentation

The Principal Investigator will ensure that the required documentation is available in local Investigator Site files ISFs.

12.2.5 GCP Training

- The Principal Investigator has attended a GCP training on 18/5/2021

For non-CTIMP (i.e. non-drug) studies all researchers are encouraged to undertake GCP training in order to understand the principles of GCP. However, this is not a mandatory requirement unless deemed so by the sponsor. GCP training status for all investigators should be indicated in their respective CVs.

12.2.6 Confidentiality

All laboratory specimens, evaluation forms, reports, and other records must be identified in a manner designed to maintain participant confidentiality. All records must be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant. The Investigator and study site staff involved with this study may not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished information, which is confidential or identifiable, and has been disclosed to those individuals for the purpose of the study.. Prior written agreement from the sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

12.2.7 Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the General Data Protection Regulation and Data Protection Act) with regard to the collection, storage, processing and disclosure of personal information.

Computers used to collate the data will have limited access measures via usernames and passwords.

Published results will not contain any personal data and be of a form where individuals are not identified and re-identification is not likely to take place

STUDY CONDUCT RESPONSIBILITIES

12.3 PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, must be reviewed and approved by the Chief Investigator.

Amendments will be submitted to a sponsor representative for review and authorisation before being submitted in writing to the appropriate REC, and local R&D for approval prior to participants being enrolled into an amended protocol.

12.4 MANAGEMENT OF PROTOCOL NON-COMPLIANCE

Prospective protocol deviations, i.e. protocol waivers, will not be approved by the sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC, and local R&D for review and approval if appropriate.

Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the sponsors every 3 months. Each protocol violation will be reported to the sponsor within 3 days of becoming aware of the violation. All protocol deviation logs and violation forms should be emailed to QA@accord.scot

Deviations and violations are non-compliance events discovered after the event has occurred. Deviation logs will be maintained for each site in multi-centre studies. An alternative frequency of deviation log submission to the sponsors may be agreed in writing with the sponsors.

12.5 SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

If a potential serious breach is identified by the Chief investigator, Principal Investigator or delegates, the co-sponsors (seriousbreach@accord.scot) must be notified within 24 hours. It is the responsibility of the co-sponsors to assess the impact of the breach on the scientific value of the trial, to determine whether the incident constitutes a serious breach and report to research ethics committees as necessary.

12.6 STUDY RECORD RETENTION

All study documentation will be kept for a minimum of 3 years from the protocol defined end of study point. When the minimum retention period has elapsed, study documentation will not be destroyed without permission from the sponsor.

12.7 END OF STUDY

The end of study is defined as the last participant's last visit.

The Investigators or the co-sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the REC, and R+D Office(s) and co-sponsors within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved. End of study notification will be reported to the co-sponsors via email to resgov@accord.scot

A summary report of the study will be provided to the REC within 1 year of the end of the study.

The patients will continue to receive all planned treatment even after the completiong of the study. They will also be routinely reviewed at 6 months after the completion of the root canal treatment, as this is the practice in the Restorative Department, Edinburgh Dental Institute.

12.8 INSURANCE AND INDEMNITY

The co-sponsors are responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Chief Investigator and staff.

The following arrangements are in place to fulfil the co-sponsors' responsibilities:

- The Protocol has been designed by the Chief Investigator and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused by poor protocol design by the Chief Investigator and researchers employed by the University.
- Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The co-sponsors require individual sites participating in the study to arrange for their own insurance or indemnity in respect of these liabilities.
- Sites which are part of the United Kingdom's National Health Service will have the benefit of NHS Indemnity.
- Sites out with the United Kingdom will be responsible for arranging their own indemnity or insurance for their participation in the study, as well as for compliance with local law applicable to their participation in the study.

13.0 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

13.1 Authorship Policy

Ownership of the data arising from this study resides with the study team.

14.0 REFERENCES

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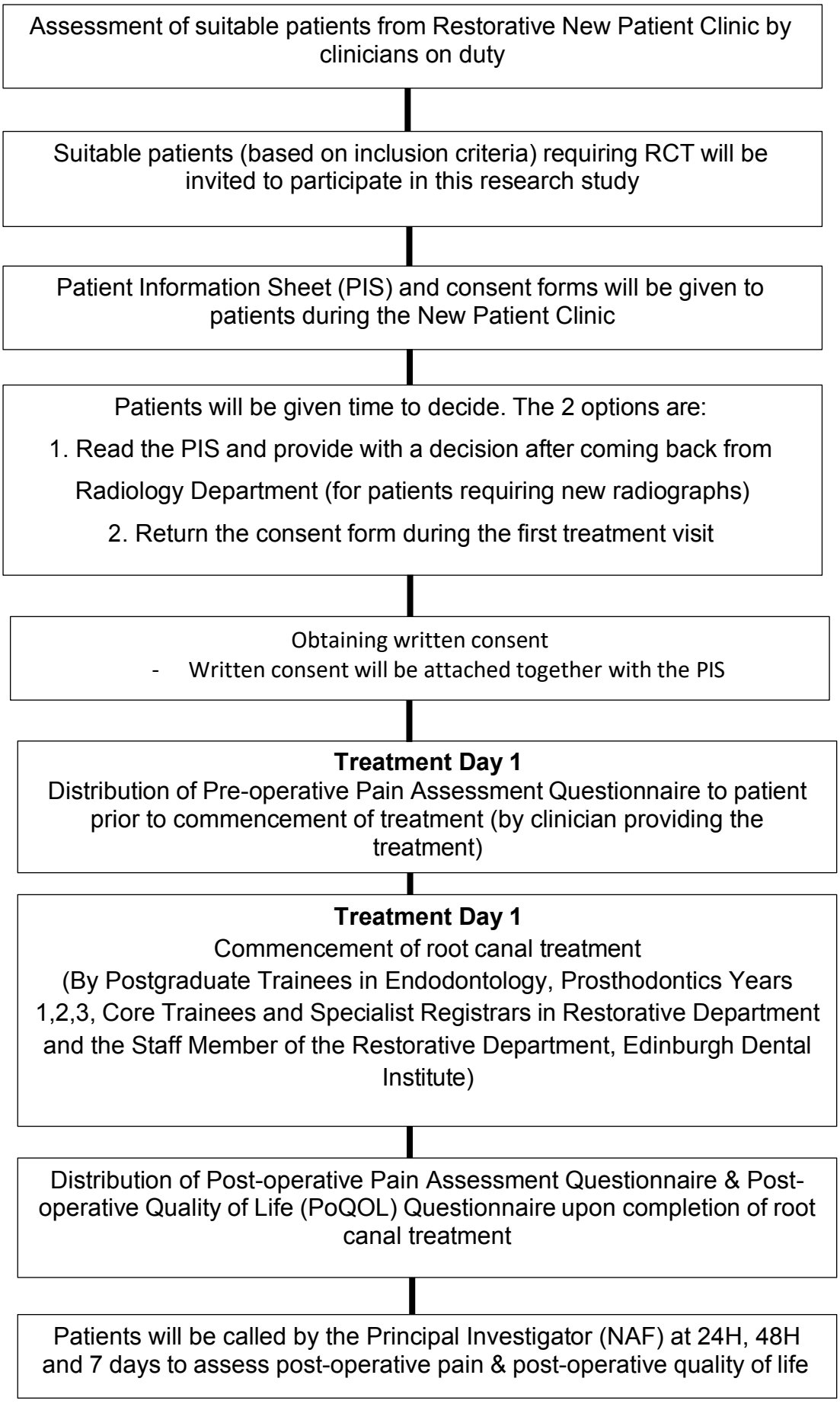
APPENDIX 1 - Study design



APPENDIX 2 – Treatment Notes Template

Management for today:

1. Any additional special tests done/ repeated

2. Assessment of soft tissues for signs of infection

3. Assessment of the tooth of concern:

(i) Type and quality of pre- existing restoration

(ii) Tenderness to palpation

(iii) Tenderness to percussion

(iv) Mobility

(v) Periodontal pocket depth

4. Additional sensibility tests conducted

(i) EPT

(ii) Cold test

5. Diagnosis on the first treatment visit

6. A not on whether any treatment has been carried out prior to having treatment initiated at EDI

7. Treatment sequence

8. Radiographic outcome

Note: Please distribute post-operative pain assessment & post-operative quality of life assessment questionnaires to patients. Thank you

Pain following root canal treatment <PfRCT>
<Version 2.0 17August2021>
<IRAS ID - 295316>

Name:

Participant ID:

Fine to be called after 5 pm and on weekends: ☐

CONSENT FORM

	Pain following root canal treatment	Please **initial each** box
1	I confirm that I have read and understood the Participant Information Sheet (v4.0_29September2021) for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my dental care and/ or legal rights being affected.	
3	I understand that relevant sections of my dental notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and/ or NHS Lothian), from regulatory authorities or from the NHS organisation where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data and/ or dental records.	
4	I understand that data collected about me during the study may be converted to anonymised data.	
5	I agree to take part in the above study.	

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

Name of Person Giving Consent	Date	Signature
Name of Person Receiving Consent	Date	Signature