

# **Understanding Pain after Dental Procedures**

**NIDCR Protocol Number: 19-073-E**

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**Principal Investigator: Muhammad Walji, PhD**

**NIDCR Program Official: Dena Fischer, DDS, MSD, MS**

**NIDCR Medical Monitor: Kevin McBryde, MD**

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**3 June, 2022**

## **Revision History:**

Dr. Kalenderian controls version number and date, which appear on the title page and header/footer of each protocol page. We will use 0.1, 0.2, 0.3, etc., for early drafts of the protocol. Once all NIDCR and study team comments have been resolved, we will re-label the last draft version 0.x as final version 1.0 for UH3 submission.

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<b>Draft/Version Number</b>	<b>Version Date</b>	<b>Summary of Revisions Made:</b>
0.1	5Dec2019	Original first draft Protocol
0.2	27Febr2020	Full Revision
0.3	4Mar2020	Draft for team input in preparation for F2F meeting
0.4	12Mar20F20	Draft for F2F meeting review
0.5	23Mar2020	Draft for Dr. Fischer's input
0.6	05May2020	Draft for team discussion and review
0.7	13June2020	Draft for team review
0.8	19June2020	Draft for team review
0.9	29Jun2020	Draft for Dr. Fischer's input
0.10	23July2020	Draft addressing Dr. Fischer's comments
0.11	04Aug2020	Draft in preparation for Node Coordinators' Cascading review
0.12	05Aug2020	Draft for Node Coordinators' Cascading review
0.13	08Oct2020	Revision based on Node Coordinators' Cascading Review
0.14	15Oct2020	Finalized Revision with track changes for Dr. Fischer's review
0.15	02Nov2020	Draft addressing Dr. Fischer's comments
0.16	05Nov2020	Draft incorporating RC Comments
0.17	01Dec2020	Draft incorporating PEC feedback

0.18	18Dec2020	Draft incorporating study team feedback
0.19	27Jan2021	Draft incorporating updated statistical power analysis
0.20	01Feb2021	Updated team members contact information
0.21	29Mar2021	Incorporated feedback NIDCR for initial team review
0.22	02Apr2021	Final team review
0.23	05Apr2021	Incorporated Feedback from Dr. McBryde (section 2.3.1)
1.0	16Aug2021	First final version Protocol for Transition Packet
2.0	08Feb2022	Amended Protocol after CIRB Approval with. minor changes and correction of errors

## **STATEMENT OF COMPLIANCE**

The study will be conducted in accordance with the International Conference on Harmonisation guidelines for the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), and the NIDCR Clinical Terms of Award. All personnel involved in the conduct of this study have completed human subjects' protection training.

## SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

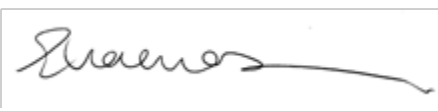
Principal Investigators:

Signed: 

Date: 06142021

Name: Muhammad F. Walji, PhD

Title: Principal Investigator UG3 and UH3 phases

Signed: 

Date: 06142021

Name: Elsbeth Kalenderian, DDS, MPH, PhD

Title: Consultant UH3 phase and Principal Investigator UG3 phase

## TABLE OF CONTENTS

	PAGE
LIST OF ABBREVIATIONS	6
PROTOCOL SUMMARY	9
Schedule of Events	12
Schematic of Study Design for Ramp-up	14
Schematic of Study Design for Full Study	16
1	192
	232.1
	232.2
	242.3
	252.3.1
	252.3.2
	263
	263.1
	263.2
	274
	295
	315.1
	335.1.1
	335.1.2
	345.2
	345.2.1
	355.2.2
	355.3
	356
	356.1
	366.2
	366.3
	376.4
	376.5
	387
	387.1
	387.2
	397.2.1 mHealth Questionnaires
	38
7.2.2 System Usability Scale (SUS)	39
7.2.3 Unified Theory of Acceptance and Use of Technology (UTAUT)	39
7.3.4 Overview of the Instruments	39

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8	418.1
	418.2
	428.2.1
	428.2.1.1
	428.2.1.2
	428.3
	439
	4410
	4411
	4411.1
	4411.2
	4611.3
	4712
	5013
	5013.1
	5113.2
	5214
	5214.1
	5214.2
	5214.3
	5214.4
	5214.5
	5214.6
	5315
	5315.1
	5415.2
	5415.3
	5515.3.1 Schedule
	54
15.3.2	5515.3.3
	5615.4
	5615.5
	5616
	5717
	58

### LIST OF ABBREVIATIONS

AE	Adverse Event/Adverse Experience
APS-POQ-R	American Pain Society Patient Outcome Questionnaire
CAD/CAM	Computer Aided Design/Computer Aided Manufacture
CDT	Code on Dental Procedures and Nomenclature
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CSOC	Clinical Study Oversight Committee
CT	Computerized Tomography
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
DSMP	Data Safety Monitoring Plan
EHR	Electronic Health Record
EQ	Enrollment Questionnaire
FFR	Federal Financial Report
FWA	Federalwide Assurance
HIPAA	Health Insurance Portability and Accountability Act
HIT	Health Information Technologies



ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
RR	Relative Risk
ISM	Independent Safety Monitor
mHealth	Mobile Health
MOP	Manual of Procedures
mPOWER	mobile Post-Operative Wound Evaluator
N	Number (typically refers to participants)
NIDCR	National Institute of Dental and Craniofacial Research, NIH, DHHS
NIH	National Institutes of Health
OCTOM	Office of Clinical Trials Operations and Management, NIDCR, NIH
OHRP	Office for Human Research Protections
OHSR	Office of Human Subjects Research
PI	Principal Investigator
QC	Quality Control
QI	Quality Improvement
QM	Quality Management
PEARL	Practice Based Research Networks Impacting Periodontal Care
PROs	Patient-reported Outcomes
SAE	Serious Adverse Event/Serious Adverse Experience

SES	Socioeconomic Status
SOP	Standard Operating Procedure
SUS	System Usability Scale
UK	United Kingdom
US	United States
UTAUT	Unified Theory of Acceptance and Use of Technology

## PROTOCOL SUMMARY

<b>Title:</b>	Understanding Pain after Dental Procedures
<b>Précis:</b>	<p>This is a longitudinal, prospective cohort study seeking to provide insight on pain experienced by patients caused by dental procedures. For the observational study, approximately 170 National Dental PBRN practitioners (which may or may not include the practitioners from the ramp up study) from all geographic regions will be recruited and made study ready for an expected/active participation of approximately 150 practitioners who will enroll a targeted maximum of 3147 total patients who will undergo a surgical dental procedure. Up to 215 practitioners may be recruited if necessary. These patients will receive push notifications through text messages via the FollowApp.Care platform on their mobile devices at designated time intervals on days 1, 3, 5, 7, 14, 21 and 23 following the dental procedure. The observational study will be preceded by a ramp up study for which we will recruit up to 15 practitioners who will enroll 30-75 total patients. By obtaining patient data via their mobile devices, we expect to promptly and precisely identify specific pain experiences for surgical dental procedures. We will also collect pain management strategies and medications implemented by the patient and practitioner. We will perform a generalized mixed model to determine variation in pain intensity and pain interference by dental procedure.</p>
<b>Objectives:</b>	<p><b>Our primary objective is:</b></p> <ol style="list-style-type: none"> <li>1. <b>Assess post-operative pain experiences by dental procedure type through 21 days post-procedure as reported by patients following dental procedures; and assess patients' satisfaction with pain management following dental surgical procedures.</b></li> </ol> <p><b>Primary outcomes:</b></p> <ol style="list-style-type: none"> <li>a. Pain Experience (Pain intensity, Pain interferences)</li> <li>b. Satisfaction with pain management</li> </ol> <p><b>Our secondary objectives are:</b></p> <ol style="list-style-type: none"> <li>2. <b>Assess post-operative pain management strategies at one week following dental surgical procedures, as recommended by practitioners and reported by patients.</b></li> </ol>

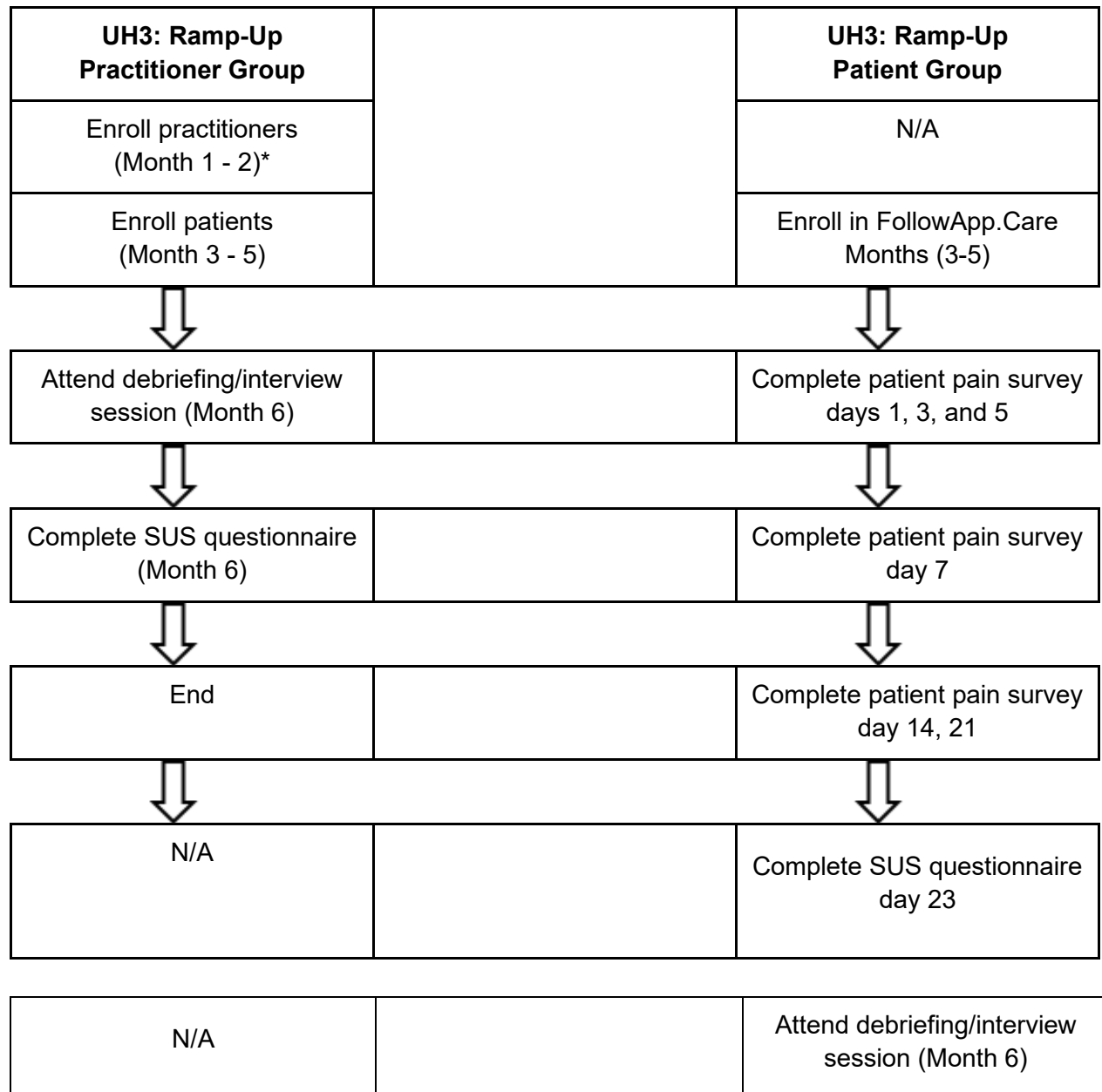
	<p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>a. Analgesic medications used by patients</li> <li>b. Concordance with pain management strategy as recommended by the practitioner and reported by the patient</li> <li>c. Other pain management strategies used by patients, including non-medicine methods for pain relief</li> </ul> <p>3. <b>Evaluate practitioner and patient acceptance of FollowApp.Care.</b> We will evaluate FollowApp.Care usage, perceived usefulness, ease of use and impact on clinical workload</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>a. Practitioner FollowApp.Care acceptance</li> <li>b. Patient FollowApp.Care acceptance</li> </ul>
<p><b>Population:</b></p>	<p>Ramp up study: up to 15 National Dental Practice-Based Research Network (PBRN) practitioners and 30-75 patients.</p> <p>Full-scale observational study: approximately 170 National Dental PBRN practitioners (which may or may not include the practitioners from the ramp up study) from all geographic regions will be recruited and made study ready for an expected/active participation of approximately 150 practitioners who will enroll a targeted maximum of 3147 total patients. Up to 215 practitioners may be recruited if necessary, to end up with at least 150 who enroll the desired number of patients.</p> <p>Gender: Males, Females</p> <p>Age range: 18-No limit</p> <p>Demographic group: National Dental PBRN practitioners and their patients who are physically and cognitively able to consent and complete study procedures.</p>
<p><b>Number of Sites:</b></p>	<p>Across the six Network regions in the United States</p>
<p><b>Study Duration:</b></p>	<p>Approximately 4 years, includes ramp-up period (6 months), full-scale observational study (3 years), debriefing/interviews following</p>

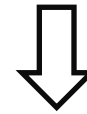
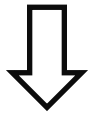
	<p>observational study participation, data synthesis and manuscript preparation.</p>
<p><b>Subject Participation Duration:</b></p>	<p><i>Patients:</i> The participation duration for each patient (either in the ramp up or the observational study) is 23 days from the specific procedure. The patients will receive text notifications at predetermined time intervals (e.g., 9 am) on Day 1, 3, 5, 7, 14, 21 and 23 following their procedure and will be prompted to complete a brief assessment of their pain experiences using the mHealth questionnaire covering the preceding 24-hour timeframe. The patient will have 48 hours to complete each survey; this will be made clear in the welcome message received through the FollowApp.Care platform. On Day 23, the enrolled patients will also be invited to complete a usability questionnaire (SUS) once they have completed all questionnaires (day 1,3,5,7,14,21). Upon completion of the patient recruitment phase of the ramp-up study, a random subset of patients will be asked to participate in a debriefing/interview session.</p> <p><i>Practitioners:</i> The ramp up study will be approximately 6 months, from the beginning of practitioner recruitment (2 months) to the end of the ramp-up study. Practitioner participation for the ramp-up study will be approximately 4 months, including 3 months for participation in the ramp-up study itself, followed by one month for debriefing/interview sessions and completion of a usability questionnaire. These practitioners may enroll in the full observational study and thus extend their participation time. The observational study is approximately three years, allowing for staggered enrollment for the participating practitioners (9 months), 18 months for actual patient enrollment per practitioner, and time for practitioner debriefing/interview participation and completion of a usability questionnaire (6 months) after all patient data have been collected. Practitioner participation for the full observational study will be approximately 21 months.</p>
<p><b>Estimated Time to Complete Enrollment:</b></p>	<p>Full Study: Approximately 9 months for practitioner enrollment; overlapping with 18 months for patient enrollment; concluding with 6 months for having participating providers complete the individual debriefing/interviews and the Unified Theory of Acceptance and Use of Technology (UTAUT) questionnaire at the end of the study.</p>

**SCHEDULE OF EVENTS**

Below we provide a schematic of the protocol-specified schedule of events for all individual study participant groups. It captures each study visit/assessment time point and planned activity for each time point as part of the ramp-up and full observational study.

Ramp-up study:



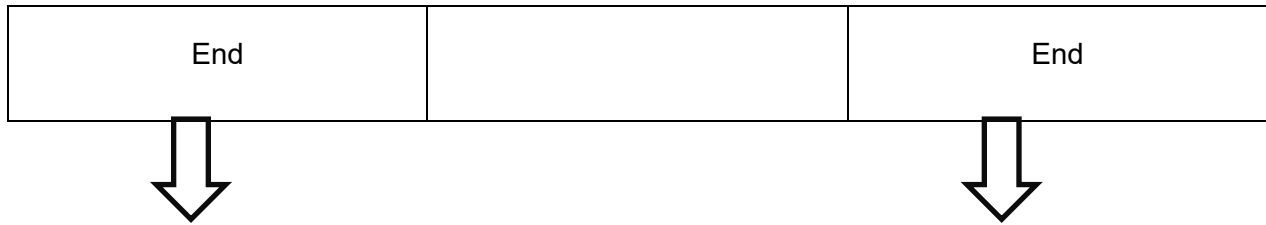


End		End
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\*The months relate to the months of the ramp-up study.

Full Study:

<b>UH3: Study Practitioner Group</b>		<b>UH3: Study Patient Group</b>
Enroll practitioners (Month 13 - 21)*		N/A
Enroll patients (Month 13-30)		Enroll in FollowApp.Care Months (13-30)
Attend debriefing/interview session (Months 32-36)		Complete patient pain survey days 1, 3, and 5
Complete UTAUT questionnaire (Months 32-36)		Complete patient pain survey day 7
End		Complete patient pain survey day 14, 21
N/A		Complete SUS questionnaire (Day 23)



\*The months relate to the months of the full study.

**SCHEMATIC OF STUDY DESIGN FOR RAMP-UP**

Prior to Enrollment	Total N: Enroll up to 15 practitioners from all 6 regions combined who will recruit 30-75 total patients
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Day 0 (day of procedure)	<ul style="list-style-type: none"> <li>- Office staff may provide an information/ Health Information Portability and Accountability Act (HIPAA) sheet to patients and instruct the patient to discuss the study with the practitioner</li> <li>- For patients interested in study participation, the practitioner or other appropriately trained office staff will verify inclusion/exclusion criteria</li> <li>- For patients interested in study participation, the practitioner or other appropriately trained office staff will ask the patient prior to the dental procedure if s/he wants to enroll in the study, provide the patient with an information sheet if the patient does not already have one and will obtain the verbal authorization to put their information on the HUB and into FollowApp.Care.</li> <li>- Patients will be sent a 'welcome' text after enrollment in FollowApp.Care.</li> <li>- Neither the office staff nor the appropriately trained individual will obtain consent from the patient. The patient will provide consent by clicking on the link when receiving the welcome message.</li> <li>- Dental office team will assure the patient received welcome text before leaving the office.</li> <li>- Office staff can enter PHI into the HUB and screening logs</li> <li>- Practitioners will complete the day 0 eCRF</li> </ul>
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Days 1, 3, and 5	<ul style="list-style-type: none"><li>- At 9:00 am on Days 1, 3, 5 following their procedure, patient participants will receive a text notification prompting them to respond to a series of questions about pain intensity, medications used, and other complications, within 48 hours. (mHealth survey 1)</li><li>- Patient participant responses will be available only to the Practitioner through the FollowApp.Care system. Practitioners may respond to the information using their normal practices or via FollowApp.Care</li></ul>
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Day 7	<ul style="list-style-type: none"><li>- At 9:00 am on Day 7 after the procedure, patient participants will receive a text notification prompting them to respond, within 48 hours, to mHealth survey 1 (a series of questions about their pain intensity, medications used, and other complications), as well as a few additional questions about their pain management experience (participation in decision making, satisfaction with pain treatment, usage of other pain management strategies) and pain interference (mHealth survey2).</li><li>- Patient participant responses will be available to the practitioner through the FollowApp.Care system. Practitioners may respond to the information using their normal practices or via FollowApp.Care</li></ul>
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Days 14 and 21 (lingering pain)	<ul style="list-style-type: none"><li>- At 9:00 am on Days 14 and 21 following their procedure, patient participants will receive a text notification prompting them to respond, within 48 hours, to a series of questions about their pain intensity, medications used, and other complications to monitor potential lingering pain.</li></ul>
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	<ul style="list-style-type: none"> <li>- Patient participant responses will be available to the practitioner through the FollowApp.Care system. Practitioners may respond to the information using their normal practices or via FollowApp.Care</li> </ul>
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Day 23	<ul style="list-style-type: none"> <li>- At 9:00 AM on Day 23 following their procedure, patient participants will receive a text notification prompting them to respond, within 48 hours, to a series of questions about the usability of the platform.</li> </ul>
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Patient Acceptance Assessment	<ul style="list-style-type: none"> <li>- On completion of the patient recruitment phase of the ramp-up study, a subset of up to 25 patients will be asked to participate in a debriefing/interview session. Additionally, all participating patients (up to 75) will be asked to complete a usability survey to assess their satisfaction with the platform.</li> </ul>
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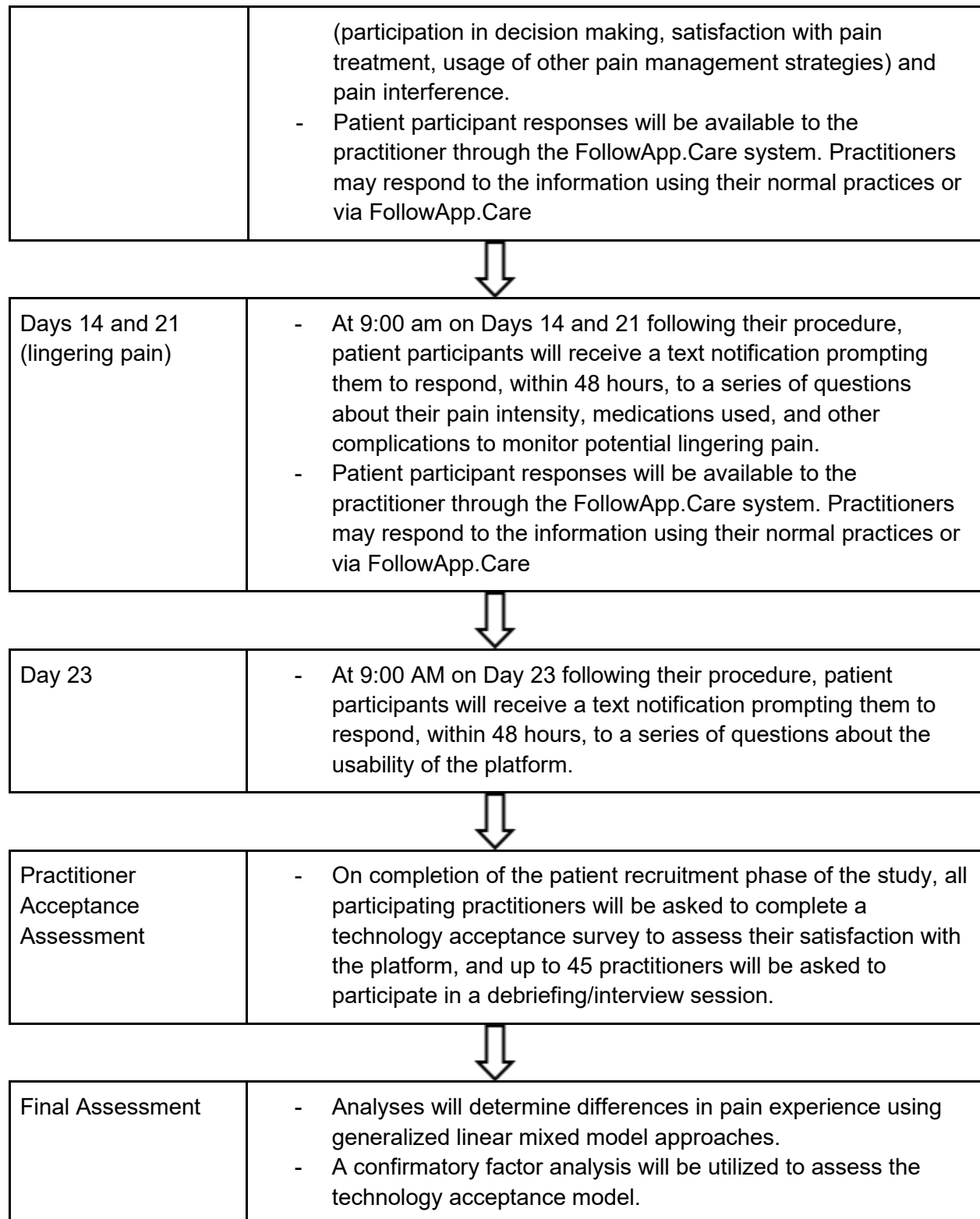
Practitioner Acceptance Assessment	<ul style="list-style-type: none"> <li>- On completion of the patient recruitment phase of the ramp-up study, all participating practitioners (15) will be asked to participate in a debriefing/interview session and complete a usability survey to assess their satisfaction with the platform</li> </ul>
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**SCHEMATIC OF STUDY DESIGN FOR FULL STUDY**

Prior to Enrollment	<ul style="list-style-type: none"> <li>• Total N: Enroll a minimum of 150 (starting with approximately 170 study ready practitioners and up to 215) practitioners from all 6 regions who will recruit a targeted maximum of 3147 patients</li> </ul>
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Day 0 (day of procedure)	<ul style="list-style-type: none"><li>- Office staff may provide an information sheet to patients and instruct the patient to discuss the study with the practitioner</li><li>- For patients interested in study participation, the practitioner or other appropriately trained office staff will verify inclusion/exclusion criteria</li><li>- For patients interested in study participation, the practitioner or other appropriately trained office staff will ask the patient prior to the dental procedure if s/he wants to enroll in the study, provide the patient with an information sheet if the patient does not already have one and will obtain the verbal authorization to put their information on the HUB and into FollowApp.Care.</li><li>- Patients will be sent a 'welcome' text after enrollment in FollowApp.Care.</li><li>- Neither the office staff nor the appropriately trained individual will obtain consent from the patient. The patient will provide consent by clicking on the link when receiving the welcome message. This will send an alert to the practitioner that the patient is now enrolled.</li><li>- Dental office team will assure the patient received welcome text before leaving the office.</li><li>- Office staff can enter PHI into the HUB and screening logs</li><li>- Practitioners will complete the day 0 eCRF</li></ul>
	
Days 1, 3, and 5	<ul style="list-style-type: none"><li>- At 9:00 am on Days 1, 3, 5 following their procedure, patient participants will receive a text notification prompting them to respond to a series of questions about pain intensity, medications used, and other complications, within 48 hours.</li><li>- Patient participant responses will be available to the practitioner through the FollowApp.Care system. Practitioners may respond to the information using their normal practices or via FollowApp.Care</li></ul>
	
Day 7	<ul style="list-style-type: none"><li>- At 9:00 am on Day 7 after the procedure, patient participants will receive a text notification prompting them to respond, within 48 hours, to a series of questions about their pain intensity, medications used, and other complications, as well as a few questions about their pain management experience</li></ul>



## 1 KEY ROLES AND CONTACT INFORMATION

<b>Principal Investigator:</b>	Muhammad F. Walji, MS, PhD Associate Dean for Technology Services and Informatics And Professor for Diagnostic and Biomedical Science Department of Diagnostic and Biomedical Sciences School of Dentistry, University of Texas Health Science Center at Houston 7500 Cambridge Street. Suite 4184 Houston, TX 77054 Phone: (713) 486-4275 Email address: <a href="mailto:muhammad.f.walji@uth.tmc.edu">muhammad.f.walji@uth.tmc.edu</a>
<b>Medical Monitor:</b>	Kevin McBryde, MD 6701 Democracy Boulevard, Room 638 Bethesda, MD 20892-4878 Phone: 301 594 0170 Email address: <a href="mailto:mcbrydekd@mail.nih.gov">mcbrydekd@mail.nih.gov</a>
<b>NIDCR Program Official:</b>	Dena Fischer, DDS, MSD, MS Director, Center for Clinical Research Program Director, Clinical Trials and Practice-Based Research National Institute of Dental and Craniofacial Research 6701 Democracy Boulevard, MSC 4878 Bethesda, MD 20892-4878 Phone: 301 594 4876 Email address: <a href="mailto:dena.fischer@nih.gov">dena.fischer@nih.gov</a>
<b>NIDCR Project Scientist</b>	Margaret Grisius, DDS 6701 Democracy Boulevard, MSC 4878 Bethesda, MD 20892-4878 Phone: 301 451-5096 Email address: <a href="mailto:margaret.grisius@nih.gov">margaret.grisius@nih.gov</a>
<b>The National Dental Practice-Based Research Network Admin &amp; Resource Center (ARC) Network Director</b>	Gregg Gilbert, DDS, MBA, FAAHD, FACD, FICD Distinguished Professor and Chair, <a href="#">Department of Clinical &amp; Community Sciences</a> School of Dentistry, University of Alabama at Birmingham 1720 Second Avenue South Birmingham, AL 35294 Phone: 205-934-5123

	Email address: <a href="mailto:ghg@uab.edu">ghg@uab.edu</a>
<b>Principal Node Director:</b>	D. Brad Rindal, DDS HealthPartners Institute for Education and Research 8170 33rd Avenue South P.O. Box 1524, MS 23301A Minneapolis MN 55440-1524 Phone: 952-967-5026 Email address: <a href="mailto:Donald.B.Rindal@HealthPartners.Com">Donald.B.Rindal@HealthPartners.Com</a>
<b>Principal Node Director:</b>	Rahma Mungia, BDS, MSc, DDPHRCS UT Health San Antonio Phone: (210) 562-5685 Email address: <a href="mailto:mungia@uthscsa.edu">mungia@uthscsa.edu</a>
<b>Network Coordinating Center Director:</b>	Mary Ann McBurnie, PhD Senior Investigator Kaiser Permanente Center for Health Research 3800 N Interstate Ave Portland, OR 97227 Phone: (503) 528-3952 Email address: <a href="mailto:MaryAnn.McBurnie@kpchr.org">MaryAnn.McBurnie@kpchr.org</a>
<b>NCC Data Manager</b>	Kimberly Funkhouser, PhD Kaiser Permanente Center for Health Research 3800 N Interstate Ave Portland, OR 97227 Phone: (503) 335-6340 Email address: <a href="mailto:kimberly.funkhouser@kpchr.org">kimberly.funkhouser@kpchr.org</a>
<b>Statistician</b>	Alfa-Ibrahim Yansane, PhD University of California, San Francisco School of Dentistry 3333 California Street, 495C San Francisco, CA 94118 Phone: 415-502-6506 Email: <a href="mailto:Alfa-Ibrahim.Yansane@ucsf.edu">Alfa-Ibrahim.Yansane@ucsf.edu</a>
<b>Institutions:</b>	The National Dental Practice-Based Research Network (the Network), which is a consortium of participating dental practitioners who conduct

	<p>practice-based oral health research in their practices and dental organizations. It encompasses six regional Nodes, each with an administrator, or Node Director. The National Administrative and Resource Center is located at the University of Alabama at Birmingham, and the National Coordinating Center is located at the Kaiser Permanente Center for Health Research in Portland, OR.</p> <p>The National Dental Practice-Based Research Network Admin &amp; Resource Center                  Gregg H. Gilbert, DDS, MBA, FAAHD, FACD, FICD                  Distinguished Professor and Chair, <a href="#">Department of Clinical &amp; Community Sciences</a>                  School of Dentistry, University of Alabama at Birmingham                  1720 Second Avenue South                  Birmingham, AL 35294                  Phone: 205-934-5123                  E-mail address: <a href="mailto:ghg@uab.edu">ghg@uab.edu</a></p> <p>The National Dental Practice-Based Research Network National Coordinating Center                  Mary Ann McBurnie, PhD                  Senior Investigator                  3800 Interstate Ave                  Portland, OR 97227                  Kaiser Permanente                  Center for Health Research                  3800 N Interstate Ave                  Portland, OR 97227                  Phone: 503.528.3952                  Email address: <a href="mailto:maryann.mcburnie@kpchr.org">maryann.mcburnie@kpchr.org</a></p>
<b>Other Key Personnel:</b>	<p>Dr. Joel White, DDS, MS - Clinical expert                  University of California at San Francisco                  School of Dentistry                  707 Parnassus Ave., D-3248                  Box 0758   San Francisco, CA 94143                  Phone: 415.476-0918                  Email address: <a href="mailto:Joel.White@ucsf.edu">Joel.White@ucsf.edu</a></p>
<b>Consultant</b>	<p>Elsbeth Kalenderian, DDS, MPH, PhD</p>

	<p>Academic Center for Dentistry Amsterdam (ACTA)                  Gustav Mahlerlaan 3004, Room 6N-09                  1081 LA Amsterdam, The Netherlands                  Phone: +1 31 20 598 0676                  Email address: <a href="mailto:e.kalenderian@acta.nl">e.kalenderian@acta.nl</a></p>
<p><b>Node Coordinators</b></p> <ul style="list-style-type: none"> <li>● Midwest Node Coordinator</li> <li>● Southwest Node Coordinator</li> <li>● South Central Node Coordinator</li> <li>● South Atlantic Node Coordinator</li> <li>● Western Node Coordinator</li> </ul>	<p>Donald B. Rindal, DDS                  Health Partners                  2500 Como Ave                  Saint Paul, MN 55108-1460                  Phone: 952-967-5026                  Email: <a href="mailto:donald.b.rindal@healthpartners.com">donald.b.rindal@healthpartners.com</a></p> <p>David Cochran, DDS, PhD                  University of Texas Health San Antonio Dentistry                  8210 Floyd Curl Drive                  San Antonio, TX 78229                  Phone: 210-562-3604                  Email: <a href="mailto:cochran@uthscsa.edu">cochran@uthscsa.edu</a></p> <p>Muna Anabtawi, DDS, MS, CCRP                  University of Alabama at Birmingham                  School of Dentistry                  1919 7<sup>th</sup> Avenue. S.                  SDB                  Birmingham, AL 35233                  Phone: (205) 934-2578                  Email address: <a href="mailto:munaanab@uab.edu">munaanab@uab.edu</a></p> <p>Valeria Gordan, DDS, MS, MS-CI                  University of Florida College of Dentistry                  PO Box 100415                  Gainesville, FL 32610-0415                  Phone: (352) 273-5846                  Email address: <a href="mailto:vgordan@dental.ufl.edu">vgordan@dental.ufl.edu</a></p> <p>Jeff Fellows, PhD                  Kaiser Permanente Northwest Center for Health Research</p>



<ul style="list-style-type: none"><li>• Northeast Node Coordinator</li></ul>	<p>3800 N Interstate Ave Portland, OR 97227 Phone: 503-335-6784 Email: <a href="mailto:jeffrey.fellows@kpchr.org">jeffrey.fellows@kpchr.org</a></p> <p>Cyril Meyerowitz, DDS, MS Eastman Institute for Oral Health 625 Elmwood Avenue, Box 683 Rochester, NY 14620 Phone: 585-275-4935 Email: <a href="mailto:Cyril.Meyerowitz@urmc.rochester.edu">Cyril.Meyerowitz@urmc.rochester.edu</a></p>
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## 2 INTRODUCTION: BACKGROUND INFORMATION & SCIENTIFIC RATIONALE

### 2.1 Background Information

#### **A brief description of the health problem that the study will address**

Pain commonly occurs after common dental procedures, though there is a lack of knowledge about patient's post-procedure pain experiences and how best to alleviate pain. Because of the expectation that pain will occur after dental procedures, dentists often provide strategies to manage acute pain. However, guidelines for acute pain management are based upon the 3<sup>rd</sup> molar extraction model and pain intensity for 24-48 hours post-surgery. There is limited data about pain following other common dental procedures, as well as the full pain experience beyond the short-term period. Consequences of unmanaged, worse than expected pain may include physical, psychological, and emotional restrictions in sleeping and eating, as well as sleep disturbances. Mismanaged and misunderstood pain is described as one of the factors contributing to the opioid crisis, which has been associated with lost school days, reduced efficiency and productivity at work, lost wages and employment, increased health care expenditures due to disability compensation, and injudicious use of healthcare resources. Prospectively capturing post-procedural orofacial pain is the first step to understand the pain experience associated with dental procedures and may offer insights towards improving pain management. Patient self-report is a critical component of comprehensive pain assessment, given the subjective and multi-dimensional nature of pain. Patient-reported outcomes (PROs) allow clinicians to directly assess a patient's symptoms, symptom burden, functional status, health behaviors, health-related quality of life, and care experiences, and offer opportunities to deliver value-based care. Furthermore, emerging health information technologies (HIT), such as mobile health applications and secure messaging, which effectively collect PRO data to inform clinical care and promote patient engagement in medicine, remain largely unexplored in dentistry.

## **Discussion of important research relevant to the study that provides background and scientific justification for the study**

(1) Patient Reported Outcome measures (PROs) provide an essential perspective on the quality of health care provided to patients. The primary reasons for seeking care among dental patients include addressing a disturbing symptom, restoring function and/or promoting wellbeing. Therefore, a patient's assessment of his/her health status following dental treatment is an important indicator of quality. By promptly collecting patient health assessments, we will offer practitioners an opportunity to assess the effectiveness of their treatment modalities in order to improve their patients' experiences and health outcomes.

(2) Growing evidence suggest that mobile phones are an effective platform for assessing patients' symptoms, symptom burden, health status, health behaviors and health-related quality of life. A recent study by Stein et al explored the feasibility of using smartphone applications to triage dental emergencies. Another study from the UK revealed that mobile applications motivated dental patients to maintain better oral hygiene. Research on the use of various forms of health information technology (HIT) is promising. For example, mPOWER enables patients to provide feedback on the condition of their surgical incision site following discharge from the hospital, while other mobile apps that collect PRO data enable patients to monitor their chronic health conditions, such as diabetes. Additionally, participants in a chemotherapy treatment group using a web based PRO questionnaire platform to report on their symptoms had fewer hospitalizations and emergency room visits and overall higher survival rates. This study will demonstrate the extent to which PROs provide actionable data. It may also serve as a model for implementing new HIT by taking workflows into account and following a user-centered design approach.

(3) Equally critical is the practitioner experience described by Bodenheimer et al as the quadruple aim. By relying on a user-centered design process and performing workflow analyses, we will identify operational barriers to implementing FollowApp.Care at the Network participating dental offices. We will also evaluate practitioner acceptance and its impact on the clinical workload and satisfaction with treatment.

### **2.2 Rationale**

- Prospectively capturing post-procedural pain in a systematic manner is the first step to understanding the full pain experience and improving pain management. Patient self-report is a critical part of comprehensive pain assessment, given the subjective and multi-dimensional nature of pain. By promptly collecting patient health assessments, we will also offer practitioners an opportunity to assess the effectiveness of their treatment modalities in order to understand their patients' experiences and health outcomes. Robust and comprehensive PRO data collection will occur through 21 days after the patient's procedure for a variety of dental surgical procedures, to understand the acute pain experience and extent to which lingering pain may occur.
- In this study dental practitioners will be able to respond in real time to PROs for post-operative pain management. Existing means to address unexpected post-operative discomfort following a dental procedure include either prescribing in advance pain medication that

might not be needed or having the patient call/visit the dental office before the regular scheduled follow-up time period.

- Growing evidence suggests that mobile phones are an effective platform for assessing patients' symptoms and symptom burden. Mobile apps can be effective in collecting and utilizing PROs to tailor care, however, are rarely used in dentistry to collect PROs. This study will use a validated mHealth platform to communicate PROs between practitioner and patient.

### **A brief description of the study's overall goal**

Our proposed study seeks to address the gap in knowledge by implementing an existing mHealth system technology (FollowApp.Care) for research purposes into the real-world dental office setting in the National Dental Practice-Based Research Network (Network). Through this platform, we will actively track pain and other complications following dental procedures. We expect to promptly and precisely identify specific pain experiences associated with surgical dental procedures. We will also collect information about pain management strategies and medications recommended by the practitioner and utilized by the patient. The results of this study will provide insight on pain and other postoperative complications experienced by patients through approximately 3 weeks following common dental procedures. We will also be able to gauge to what extent practitioners are interested in adopting mHealth technology and we will learn how patients like to be engaged with text messaging to report post-operative pain and complications.

## **2.3 Potential Risks and Benefits**

### **2.3.1 Potential Risks**

Potential risks to patients due to research participation are minimal. There will be no physical risk or discomfort for subjects who participate in the research. There is a potential for psychological harm (e.g., embarrassment) if the data were to be acquired by someone outside the study team. For both practitioner and patient participants, there is the potential risk for breach of confidentiality. To mitigate this risk, practitioner and patient data entered into the National Coordinating Center's (NCC; Kaiser Permanente Center for Health Research; Portland, OR) web-based electronic data capture system (EDC) will be stored on encrypted servers maintained by the NCC. All practitioners and network staff accessing the EDC will be authenticated by NCC systems prior to gaining access to the data collection systems. All study analysis data sets will be limited datasets. NCC and FollowApp will use the same codes to identify participants to assist with record linking when the NCC receives data from FollowApp.

University of Texas Houston (UTH) will store qualitative data temporarily on computers, that similarly will require valid UTH login credentials for authentication and access; all data will be

encrypted. All laptops and computers will be encrypted and will be kept in a locked office. Practitioners will use their own computers/devices to access the web-based system in order to enter data on the eCRF form or to access the FollowApp.Care platform. Their computers/devices require authentication to access.

Practitioner and patient data entered into the FollowApp.Care platform will be encrypted at rest. No unencrypted data will be stored to disk. All FollowApp.Care staff accessing the data will be authenticated by the FollowApp.Care platform prior to gaining access to the data. All study analysis data sets will be limited datasets. NCC and FollowApp will use the same codes to identify participants to assist with record linking when the NCC receives data from FollowApp.

There are two potential consequences of text messaging: accidents and thumb and joint pain. Texting while driving or walking could increase the risk of accidents. Frequent texting may increase the risk of thumb and joint pain. The number of texts involved in this study is not likely to result in thumb and joint pain.

### **2.3.2 Potential Benefits**

Participation by patients in this research may help to improve how pain-related information is provided to their dental practitioners. Patients in general may benefit from the findings of this study, if the results of this study provide insight on how mHealth can help facilitate the capturing of patient reported outcomes (PROs) in ambulatory settings.

## **3 OBJECTIVES**

### **3.1 Study Objectives**

The study objectives of the full-scale study are as follows:

#### **Primary objective**

**Objective 1: Assess post-operative pain experiences by dental procedure type through 21 days post-procedure as reported by patients following dental procedures; and assess patients' satisfaction with pain management following dental surgical procedures.**

#### **Secondary objectives**

**Objective 2: Assess post-operative pain management strategies at one week following dental surgical procedures, as recommended by practitioners and reported by patients.**

**Objective 3: Evaluate practitioner and patient acceptance of FollowApp.Care.** We will evaluate FollowApp.Care usage, perceived usefulness, ease of use, and impact on clinical workload.

The results of this study will provide insight on how mHealth technology can help facilitate the capturing of pain and other post-operative complications after dental procedures. Study findings

will also help gauge the extent to which practitioners are interested in adopting mHealth technology and patients are engaged with text messaging to report post-operative pain and complications related to dental care.

### **3.2 Study Outcome Measures**

We have selected two primary outcomes for this study which reflect 1) pain experience and 2) patient pain management satisfaction.

#### Primary Outcomes:

*Pain experience* refers to both Pain Intensity and Pain Interference:

Pain Intensity will be collected during days 1, 3, 5, 7, 14 and 21 using the mHealth questionnaire with questions based on the PROMIS Item Bank v.1.0 – Pain Intensity Scale. The response categories range from “No pain” to “Worst imaginable Pain” on a 10-point Likert scale. Pain intensity is a relatively homogeneous dimension and most measures of pain intensity tend to be interchangeable. It was selected because of its relevance to dental patients and practitioners, applicability to all conditions, including acute postoperative dental pain for the assessment of symptoms, ease of administration, and the relative accuracy with which most adult patients gauge pain.

On days 1, 3, 5, 7, 14 and 21 patients are asked: “What is your level of pain right now?”

On day 7 patients are also asked: “How intense was your pain at its worse since the procedure?”

Pain interference refers to the extent to which patients have experienced interferences that have prevented them from activities of daily living (ADL), falling asleep, and staying asleep. This measure will be captured on Day 7 using the mHealth questionnaire with questions based on the APS-POQ-R and OHIP 14 instruments. If on days 14 and 21 patients answer the pain intensity question (“What is your level of pain right now?”) as positive (>0), they will also be asked the pain interference questions.

*Patient pain management satisfaction* refers to the level with which patients are satisfied with the overall pain management following their procedure and shared pain management strategies. This measure will be captured on Day 7 using the mHealth questionnaire with questions based on the APS-POQ-R instrument.

#### Secondary Outcomes:

*Analgesic medications used by patients.* We will collect analgesic medications taken from patient reported data through FollowApp.Care; frequency and dose prescribed captured through the eCRF completed by the practitioners; adherence to pain medications prescribed collected from patient reported data through FollowApp.Care.

*Concordance with pain management strategy* as recommended by the practitioner (reported on the eCRF) and reported by the patient will be measured. The pain management strategy of each practitioner will be captured on the eCRF, and the mHealth questionnaire will capture the corresponding patient adherence. Concordance will be measured using several diagnostic measures: the Cohen's Kappa coefficient, or the correlation coefficient.

*Other pain management strategies* used by patients, assesses post-op pain management strategies including usage of other pain management strategies, such as non-medicine methods for pain relief.

*Practitioner acceptance* with the platform will be measured by the UTAUT questionnaire to evaluate FollowApp.Care usage, perceived usefulness, ease of use and impact on clinical workload.

*Patient and Practitioner perceived usability* with the platform will be measured by the System Usability Scale (SUS) questionnaire to measure usefulness and ease of use of the FollowApp.Care platform

*Other complications* related to immediate postoperative complications - bleeding and increased swelling.

Other covariates being collected:

*Baseline pain intensity* will be collected through the welcome message

*Patient demographic* variables will be collected through the welcome message

*Type of procedure* (CDT) will be collected through the eCRF.

*Practitioner demographic* variables will be collected through the practitioner's enrollment questionnaire (EQ)

This information is already available in the practitioner database and enrolled practitioners will be asked to update their EQ before the study.

*Practitioner specialty* will be collected through the practitioner's enrollment questionnaire (EQ)

This information is already available in the practitioner database and enrolled practitioners will be asked to update their EQ before the study.

*Practitioner years in practice* will be collected through the practitioner's enrollment questionnaire (EQ)

This information is available in the practitioner database as the year of graduation from dental school.

Practitioner assessment of *expected pain intensity* will be collected through the eCRF

#### 4 STUDY DESIGN

This is a prospective, longitudinal cohort study that will be conducted in the National Dental PBRN, which is a network of participating dental practitioners who conduct practice-based oral health research. This study will utilize the resources of the ARC and NCC. The node coordinators will utilize ARC’s established communication methods to inform prospective dental practitioners about the study opportunity. Enrolled practitioners will recruit and enroll patients prior to undergoing specific dental surgical procedures. Participating patients will utilize the FollowApp.Care platform to comprehensively record their pain experience over a three-week post-operative period.

Means of Data Collection: A mobile health (mHealth) platform (FollowApp.Care®) will be utilized to collect PRO data (pain experiences) from patients after dental procedures.

Collection Time frame: For patients, the expected collection time frame is approximately 4 weeks: 3 weeks (Days: 1, 3, 5, 7, 14, and 21) completing mHealth surveys (based on the PROMIS, APS-POQ-R and OHIP-14 questionnaires) regarding their pain experiences (pain intensity and pain interference) following their procedure; at the end of the 1<sup>st</sup> week (day 7) we will also assess the patients’ satisfaction with their post-operative pain management using an additional mHealth survey (based on the APS-POQ-R questionnaire); and at the 4<sup>th</sup> week following their procedure patients will be asked to complete the last mHealth survey regarding the usability of the platform (day 23). For those patients who participate in the ramp-up study which will include a debriefing/interview session, the total study time will increase to approximately 8 weeks. Practitioners, who will recruit and enroll their patients in the study, will participate for the entire study period, including the patient recruitment and data collection phase, completion of a practitioner satisfaction survey, and some will participate in a debriefing/interview session (approximately 26 months); for those who also participate in the ramp-up study, the total study time will increase to approximately 32 months.

Study Population: The practitioner study population will include those who perform endodontic, periodontal, oral surgery, and/or implant dental surgical procedures. Starting with approximately 170 practitioners, and up to 215 will participate in the full-scale observational study and will recruit and enroll up to a target of 3147 adult patients undergoing specific dental surgical procedures. National Dental PBRN practitioners from all 6 geographic regions will be recruited for study participation.

Using the sequence listed below, we will execute the study protocol:

<u>Task</u>	<u>Description of implementation/operationalization</u>
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<p>1. Network Site Selection</p>	<p>We anticipate that all Network practices stratified by state, urban/rural and practice size, will be eligible to participate. We will work with the Network coordinators to assure all sites are informed of the study protocol and opportunity to participate.</p>
<p>2. Practitioner Recruitment and training</p>	<p>The Network site coordinators will use established protocols to recruit practitioners. The study team will work with the coordinators and the Network Communications Director to assure dissemination of the study opportunity. The study team will provide the coordinators with all on-line training materials. Coordinators may decide to add an in-person training component. Study personnel will be available remotely via video conference/phone calls to support all training efforts.</p>
<p>3. Patient screening and enrollment</p>	<p>Each participating office will decide if practitioners or office staff will screen/enroll patients into the study. Office staff who enroll patients will need to have successfully completed appropriate training. Each participating office will maintain a log of screened and enrolled subjects. On a weekly basis, office staff will record their summary screening/enrollment information in the EDC.</p> <p>Practitioners will enroll patients via a consecutive process that best suits their practice situation, i.e., they will approach any patient who may meet the inclusion criteria during the days and/or times when the office is participating in research activities.</p>
<p>4. FollowApp.Care platform activation</p>	<p>Enrolled practitioners will individually be able to set their FollowApp.Care notification preferences, for example, they can choose to receive notifications by email or text. Notifications will be sent to practitioners based on predefined thresholds as defined in the MOP.</p>
<p>5. Patient evaluation (Usability questionnaire)</p>	<p>Patients will complete a Usability survey (SUS) on day 23 using the FollowApp.Care platform.</p>
<p>6. Practitioner evaluation (debriefing/interview session and UTAUT questionnaire)</p>	<p>Once the patient component of the study has been concluded, we will administer the UTAUT Questionnaire to all participating practitioners, to assess their perceived usefulness and perceived ease of use of FollowApp.Care as predictors of their usage behavior. Thereafter, we will conduct</p>



	telephone debriefing/interviews with up to 45 purposefully selected practitioners to qualitatively evaluate their experiences with using FollowApp.Care for managing their patients' post-op pain including, its impact on their clinic workload, workflow patterns, and satisfaction with the effectiveness of pain management. These debriefing/interview discussions will be audiotaped and transcribed for analysis.
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**Ramp-up study:** Prior to implementing the full-scale observational study, a small ramp-up study will be conducted with up to 15 Network practitioners in all six geographic regions combined and their eligible patients (2-5 patients per practitioner; up to 30-75 total). During the ramp-up study, all study procedures will be performed to directly observe the use of FollowApp.Care in the provision of clinical care. The ramp-up study, including the use of FollowApp.Care will occur in Network practices and will ensure functionality of the platform, allow for streamlined data collection and will assess usability and workflow within dental offices. Usability testing, fidelity monitoring and workflow analyses will be conducted.

## 5 STUDY ENROLLMENT AND DISCONTINUATION

- For the full-scale study, up to 215 practitioners in all six geographic regions will be enrolled for an expected/active participation of up to 150 practitioners. Practitioners will enroll up to a target of 3147 patients.
  - As a first step, approximately 170 practitioners will be made study ready
  - We expect a 10% dropout rate among practitioners
    - If the dropout rate among practitioners is higher than 10%, we will recruit additional practitioners (up to 215) and/or request that the remaining practitioners increase individual recruitment.
  - We expect a 40% missing data rate among patients.
    - If the dropout rate among patients is higher than 40%, all practitioners will be expected to increase recruitment accordingly.
- The expected breakdown is as follows:
  - Inclusion Across the Lifespan
    - Patient study participation will be limited to adult patient-subjects 18 years or over.
  - Inclusion of Women and Minorities
    - Women: approximately 51% of enrolled population

- Minorities: approximately 23% of enrolled population
- We do not exclude pregnant women.

We will include women and minorities in this study. For the proposed study, there are no exclusions based on gender, race or ethnicity. Pregnant women may be enrolled in the study. The study does not pose any additional risk to this population.

- Subject Inclusion Criteria

In order to be eligible to participate in this study, a practitioner must meet all of the following criteria:

- Be a National Dental PBRN practitioner deemed as study ready.
- Be a dentist who performs at least one of the identified CDT procedures per week:
  - Endo CDT codes D3000-D3999, excluding D3110, D3355, D3356, D3357, D3911, D3921
  - Perio CDT codes D4200-D4299, excluding: D4265, D4274
  - Oral Surgery CDT codes D7000-D7999, excluding D7287, D7288, D7880, D7881, D7899, D7921
  - 12 CDT codes from Implant Services D6010, D6011, D6012, D6013, D6040, D6050, D6100, D6101, D6102, D6103, D6104, D6081
- Have access and willingness to use the platform through an internet browser using a smartphone, tablet, computer or laptop, that is provided by the practice for patient care purposes.

In order to be eligible to participate in this study, a patient must meet all of the following criteria:

- Willing and able to comply with all study procedures
- **Age  $\geq$  18 years, except in Nebraska where the age of majority is  $\geq$  19 years**
- Planning to undergo one or more of the following surgical procedures:
  - Endo CDT codes D3000-D3999, excluding D3110, D3355, D3356, D3357, D3911, D3921
  - Perio CDT codes D4200-D4299, excluding: D4265, D4274
  - Oral Surgery CDT codes D7000-D7999, excluding D7287, D7288, D7880, D7881, D7899, D7921
  - 12 CDT codes from Implant Services D6010, D6011, D6012, D6013, D6040, D6050, D6100, D6101, D6102, D6103, D6104, D6081
- Has access to and willingness to use their smartphone for study purposes.

- Has not already participated in the study previously.

## 5.1 Strategies for Recruitment and Retention

### 5.1.1 Practitioner and Patient Recruitment

All Network dentists will be approached for interest in study participation and queried about meeting inclusion criteria. Active Network practitioners who are “research ready” will have been oriented to the Network and will have completed any institutionally required human subjects research protection training. In general, it has been the policy of the Network that Node Coordinators from each region will be responsible for recruitment of practitioners. The National Coordinating Center (NCC) will maintain the practitioner database to facilitate recruitment and track Network practitioner training.

Practitioners who are “study ready” and their office staff will undergo study-specific training in-person or virtually, provided by the Node Coordinators. All training materials will be available in electronic formats, and practitioner/office staff training will be recorded and tracked by the NCC prior to participating and enrolling patients in the study.

Office staff may provide an information sheet and instruct the patient to discuss the study with the practitioner. All adult patients presenting at participating Network practices may be considered for eligibility after screening by the practitioners and/or trained office staff. The practitioner or other appropriately trained staff members will ask the patient if he or she wants to enroll in the study, provide the patient with an information sheet if the patient does not already have one and will obtain the verbal authorization to put their information on the HUB and into FollowApp.Care. Some regions may also obtain HIPAA consent per region requirements. Neither the office staff nor the appropriately trained individual will obtain specific study-related consent from the patient. The patient will provide consent by clicking on the link when receiving the welcome message. Office staff can enter PHI into the HUB and screening logs. Each office should have the latitude to designate tasks to office personnel in a manner that will work best within the normal operations of the practice. Further, each practice will develop a method for screening patients and will maintain a screening log.

*UH3 Phase Ramp Up Study:* The Ramp up study will involve up to 15 practitioners across all 6 geographic regions combined if possible, and each of whom will enroll approximately 2-5 patients, up to 30-75 patients total. The study will occur in a ramp-up manner, beginning in one or two regions and then expand across the entire Network. We anticipate that practitioner participants will be recruited by Network Node Coordinators. Participants will be remunerated for each of the separate tasks that are part of the workflow testing.

Practitioners and Patients who participate in the Ramp up study will be asked to engage one time in a debriefing/interview session with the study team by phone or in person, and at the end of that session will be asked to complete a SUS.

*Full Study:* Practitioners who participated in the UH3 phase Ramp up study are allowed to participate in the full study if they so desire. Each participating practitioner will be asked to recruit a target of approximately 3 consenting patients per month although recruitment targets will be further refined once the number of enrolled practitioners is clear. Practitioners may enroll patients at a rate and consecutive process (i.e., one day per week, one week per month, etc.) that best suits their practice situation. Node Coordinators and study staff will have access to the online study portal, where they will be able to monitor patient enrollment for practitioner study participants.

Some practitioners who participate in the full study will be asked to engage one time in a debriefing/interview session with the study team by phone or in person. All practitioners will be asked to complete the UTAUT. All patients will complete the SUS at the end of their participation in the study (day 23).

### **5.1.2 Practitioner and Patient Retention**

Retention will be facilitated through practitioner and patient remuneration for each of the separate study procedures. *Patients* will be eligible for remuneration once they complete the mHealth questionnaire on day 23 by clicking on a link immediately at the end of the closing screen. The total remuneration amount will be dependent on the number of mHealth questionnaires completed. *Practitioners* will be eligible for remuneration at the end of the ramp-up phase, and at the end of the observational study phase, after completing the UTAUT questionnaire. Those who participate in the debriefing/interview session will receive additional remuneration. Practitioner remuneration will be proportional to the effort provided.

### **5.2 Subject Discontinuation**

Practitioners may withdraw voluntarily from the study or the study team may terminate a practitioner's participation at any time.

Patients may discontinue voluntarily from the study or the practitioner may terminate a patient's participation at any time. Patients who discontinue from the study for any reason will have the date and reason for discontinuation recorded (if known), but no additional study data will be collected. Patients who discontinue from the study may continue to receive normal clinical care as patients of the participating dentists.

### **5.2.1 Reasons for Discontinuation**

Participants are free to discontinue from participation in the study at any time upon request.

An investigator may discontinue a participant from the study if/when:

- Any medical condition, event or situation occurs such that continued participation in the study would not be in the best interest of the subject.
- The subject meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
- A patient's cross-covering practitioner is not a Network practitioner participating in the study (and the patient's practitioner is on leave any time during the 21-day study period after the procedure).

### **5.2.2 Handling of Subject Discontinuation**

Once participants have discontinued from the study, they will not be contacted. Discontinued individuals will not be replaced as the power calculation has accounted for them. If the discontinuation rate is high, the study team PIs will discuss with the Network and NIDCR how to proceed.

## **5.3 Premature Termination or Suspension of Study**

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party. If the study is prematurely terminated or suspended, the principal investigator will promptly inform the IRB and will provide the reason(s) for suspension or termination.

Circumstances that may warrant termination include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects.
- Insufficient adherence to protocol requirements.
- Data that are not sufficiently complete and/or evaluable.
- Determination of futility.

## **6 STUDY SCHEDULE**

The [Schedule of Events](#) has been provided in the Protocol Summary section at the beginning of this document. A detailed timeline is also available in the [MOP](#).

## 6.1 Screening & Registration

For patients: Practitioners, their delegates and/or other appropriately trained office staff members will screen and invite patients to participate in the study at the time of appointment and register their information in the HUB.

Practitioners/office staff will record results of the screening activities for tracking purposes on the screening/enrollment logs as detailed in sections 6.1.2 and 6.1.3 of the MOP. All office staff can enter PHI into the HUB and activities logs.

On a weekly basis, clinic staff will record the summary screening information in the EDC (HUB).

## 6.2 Enrollment/Baseline

For those patients who agree to study participation and meet inclusion criteria, verbal authorization will be obtained as described below in order to put the patient's information on the HUB and into FollowApp.Care.

Before or during the dental surgical procedure, patients will be registered by the office staff on FollowApp.Care (a mobile phone text messaging system) with their mobile phone number. After registration, patients will receive the first text message (welcome message), which will contain a link to the patient information sheet. Clicking the link to advance the survey (and as such indicating they received the welcome message) will serve as tacit consent to study participation. If the patient does not receive the link, staff will verify the mobile number and try to re-register the patient. Once the patient clicks successfully on the welcome message the patient is considered enrolled. This will also send an alert to the practitioner that the patient is now enrolled and that the eCRF needs to be completed.

### Enrollment/Baseline Visit (Visit 1, Day 0)

- Verify inclusion/exclusion criteria. Inclusion/Exclusion criteria will be available on paper or in [electronic format](#).
- Explain the study to the patient, provide the patient with an information sheet if the patient does not already have one and
- Obtain HIPAA authorization if required by state law
- Once verbal agreement is obtained, the practitioner/appropriate office staff register the patient in the EDC (HUB) with their name, phone number and address.
- As part of the registration process staff will attest in the EDC that the patient provided authorization to provide information (name, phone number, address) and they are eligible to participate.
- Once information is entered in the EDC, a tracking ID is assigned to the patient and that tracking ID number is recorded on the screening & enrollment log.
- Practitioner/Office staff will register patient on FollowApp.Care platform

- Practitioner/Office staff will ensure patient has received a ‘welcome’ text. Patients will have access to the study information sheet via a link in the welcome text.
- Practitioner will provide usual care as per the nature of the visit
- Practitioners will complete the day 0 eCRF after the appointment, attesting on the eCRF that they received a notification from FollowApp that the patient is enrolled, and the patient was given a study information sheet, able to ask questions, and then provided informed consent.

### **6.3 Early Intermediate Data Collection Timepoints (electronic data collection independent of in-office visits)**

#### **Day 1, 3, and 5**

- At 9:00 am on Days 1, 3, and 5 following their procedure, patient participants will receive a text notification prompting them to respond to a series of questions about their pain experiences, for which they will have 48 hours to respond. 9 AM is a set time point due to platform restrictions.

### **6.4 Late Intermediate Data Collection Timepoints (electronic data collection independent of in-office visits)**

#### **Day 7, 14, 21 and 23**

- At 9:00 am on Day 7 following their procedure, patient participants will receive a text notification prompting them to respond to a series of questions about their pain experience and pain management strategies.
- At 9:00 am on Days 14 and 21 following the procedure, patient participants will receive a text notification, for which they will have 48 hours to respond, prompting them to respond to a series of questions pertaining to potential lingering pain. 9 AM is a set time point due to platform restrictions.
- Practitioners will complete the day 21 eCRF on day 21. The data capture system will have a mechanism for alerting practitioners when an eCRF is due to be completed, and the NCC will provide an online mechanism for completing the eCRF.
- At 9:00 am on Day 23 following the procedure, patient participants will receive a text notification prompting them to complete the System Usability Scale (SUS) questionnaire to measure usefulness and ease of use of the FollowApp.Care platform, for which they will have 48 hours to respond. 9 AM is a set time point due to platform restrictions.

## **6.5 Withdrawal Visit**

Not applicable, subjects who withdraw from study participation will not undergo a withdrawal visit.

## **7 STUDY PROCEDURES/EVALUATIONS**

### **7.1 Study Procedures/Evaluations**

#### **7.1.1 Ramp Up Study**

A limited usability/workflow feasibility test of FollowApp.Care will be conducted across the six geographic regions of the Network. During the ramp up, all study procedures will be performed to directly observe the use of FollowApp.Care in the provision of clinical care. Interactions in the FollowApp.Care system between patients and practitioners will be analyzed, patient survey completion times will be tracked, and practitioner response times will be tracked from the time when practitioners are prompted for survey completion by the FollowApp.Care system.

At the end of the ramp up period, practitioners and patients will be invited to participate in separate debriefing sessions (in-person or virtual), where the study team will inquire about user experiences, potential barriers to a seamless office workflow integration, and suggestions for enhancements (e.g., pain threshold). Final recommendations for customizations will be compiled and transmitted to the FollowApp.Care developers.

Participating practitioners and patients will also be asked to evaluate the usability of the FollowApp.Care system by completing the SUS.

Finalization of the FollowApp.Care configuration: Using the recommendations from the ramp up phase with input from the study team, the FollowApp.Care developers will finalize any needed changes or configurations, including dashboard appearance, text message notification modalities/specifications, routing protocols, and case handling/escalation processes.

#### **7.1.2 Longitudinal Prospective Cohort Study**

Patients will be enrolled in the study prior to having a dental surgical procedure by a participating Network practitioner. At baseline, on Day 0 patients will receive a welcome message, and data about baseline pain intensity and patient demographics will be collected. On Days 1, 3, 5, 7, 14 and 21 following the dental surgical procedure, data about pain intensity, and pain interference will be collected in FollowApp.Care after being prompted for data collection via text messages. Practitioners will be able to see and resolve patient generated alerts using their smartphone or laptop/computer. On Day 7 after the procedure, patients will be requested to complete an additional questionnaire regarding patient satisfaction with pain management and shared pain management decision making. On Day 23 after the procedure, patients will be



requested to complete the System Usability Scale (SUS) questionnaire to measure usefulness and ease of use of the FollowApp.Care platform.

After completion of the patient component of the study, all participating practitioners will be invited to complete the UTAUT questionnaire, assessing perceived usefulness and perceived ease of use of the platform. Up to 45 practitioners will also be invited to participate in debriefing/interview to qualitatively evaluate their experiences with using FollowApp.Care for managing their patients' post-op pain, including its impact on their clinic workload, workflow patterns, and satisfaction with the effectiveness of pain management. The invitation to participate in these debriefing/interviews will be sent by the Node Coordinators and once the maximum number of participants has been reached, enrollment will be closed. Dr. Walji and a study team Research Assistant (RA) will facilitate the debriefing/interview sessions. These debriefing/interview discussions will be audiotaped and transcribed for analysis using a computer-assisted qualitative data analysis package, which allows for the efficient coding, retrieval, and searching of text.

## 7.2 Questionnaire Administration

### 7.2.1 mHealth Questionnaires

The mHealth Questionnaire #1 includes questions about Pain Intensity and Pain Interference. *Pain Intensity* is an assessment of how much a patient hurt and will be collected during days 1, 3, 5, 7, 14 and 21 using our mHealth questionnaire #1. The validated PROMIS Item Bank v.1.0 – Pain Intensity Scale response categories range from “No pain” to “Very severe” on a 10-point Likert scale. On days 1, 3, 5, 7, 14 and 21 patients are asked: “What is your level of pain right now?” On day 7 patients are also asked: “How intense was your pain at its worst since the procedure?” Pain intensity is a relatively homogeneous dimension and most measures of pain intensity tend to be interchangeable.

*Pain Interference* refers to the level with which patients have experienced interferences that prevented them from activities of daily living (ADL) (e.g., falling asleep and staying asleep). The response categories range from “Does not interfere” to “Completely Interferes” on a 10-point Likert scale. This mHealth item is designed to evaluate how pain interferes with functioning and well-being in the dental, clinical outpatient setting. It was taken from the validated OHOP-14 and APS-POQ-R questionnaires to focus attention on the small subset of activities (e.g., sleep) common to post-operative dental patients. This measure will be captured on Day 7 using our mHealth questionnaire #2 with three questions based on the APS-POQ-R instrument and two questions based on the OHIP-14 instrument. If on days 14 and 21 patients answer the pain intensity question (“What is your level of pain right now?”) as positive (>0), they will also be asked the six pain interference questions.

The mHealth Questionnaire #2 includes questions from the 1<sup>st</sup> mHealth questionnaire and also questions about patient pain management satisfaction. *Patient pain management satisfaction* refers to the level with which patients are satisfied with the overall pain management following

their procedure. The response categories range from “Extremely dissatisfied” to “Extremely Satisfied” on a 10-point Likert scale. Additionally, it encompasses whether the patient participated in the decision making regarding their treatment. The response categories range from “Not at All” to “Very Much So” on a 10-point Likert scale. This measure will be captured on Day 7 using the mHealth (2) Survey with questions based on the APS-POQ-R instrument.

Each item in the mHealth Questionnaires was selected because of its relevance to dental patients and practitioners, applicability to all conditions, including acute postoperative dental pain for the assessment of symptoms, ease of administration, and the relative accuracy with which most adult patients gauge pain.

### **7.2.2 System Usability Scale (SUS)**

*FollowApp.Care* usability as perceived by patients and practitioners will be measured by the system usability scale (SUS) questionnaire to measure usefulness and ease of use of the *FollowApp.Care* platform. The validated SUS is a simple questionnaire that uses a ten-item attitude Likert scale giving a global view of subjective assessments of usability.

### **7.2.3 Unified Theory of Acceptance and Use of Technology (UTAUT)**

*Practitioner acceptance* with the *FollowApp.Care* platform will be measured by the Unified Theory of Acceptance and Use of Technology (UTAUT) questionnaire to evaluate *FollowApp.Care* usage, perceived usefulness, ease of use and impact on clinical workload. The UTAUT model measures the relationships between use intention and two independent constructs – performance expectancy and effort expectancy. The UTAUT model integrates eight major theories and has been tested and validated using large real-world data sets.

### **7.3.4 Overview of the Instruments**

The following table provides an overview of the instruments used in the POPS study

<b>Instrument</b>	<b>Completion Time</b>	<b>Content</b>	<b>Completed by</b>
Debriefing and Interview Session results	Once (Ramp-up study); end of year 1	Feedback on use of <i>FollowApp.Care</i> platform	Practitioner Patient
System Usability Scale (SUS)	Ramp-up study: end of year 1 Full study: Day 28 Year 2 to 3)	Practitioners and patients' perceptions of usability of the <i>FollowApp.Care</i> user interface	Ramp-up study: Practitioners and Patients

			Full study: Patients
mHealth Questionnaire #1	Days 1, 3, 5 and 14 and 21 (Full study): Year 2 to 3	-Pain intensity levels, types of medications used, and bleeding and swelling -Pain interference	Patients
mHealth Questionnaire #2	Days 7 (Full study): Years 2 to 3	-Pain intensity levels, types of medications used, swelling -Pain interference -Satisfaction with pain management treatment	Patients
UTAUT Questionnaire	Year 5 (Full Study): Years 3 to 4	Explores four core constructs: performance expectancy, effort expectancy, social influence and facilitating conditions as direct determinants of behavioral intention and behavior	Practitioners
electronic Case Report Form (eCRF)	Days 0 and 21 (Full study): Years 2 to 3	Two eCRFs: 1. Practitioner info - Practitioner characteristics 2. Patient info - Patient demographics - Diagnoses and procedures - Pain levels - Pain management plan - Complications	Practitioners  Practitioners

## 8 ASSESSMENT OF SAFETY

### 8.1 Specification of Safety Parameters

Safety monitoring for this study will focus on Unanticipated Problems (UPs) involving risks to participants, including unanticipated problems that meet the definition of a serious adverse event.

Safety events will be recorded and reported into the National Dental PBRN safety event reporting system maintained by the NCC. Study Multiple PIs, Drs. White and Walji, will be informed via the safety event system when events are reported.

## **8.2 Definitions of Safety Parameters**

### **8.2.1 Adverse Events**

An adverse event (AE) is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

#### **8.2.1.1 *Serious Adverse Event***

A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect
- Based upon appropriate medical judgment, the event may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

#### **8.2.1.2 *Unanticipated Problems***

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to subjects or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 8.3 Reporting Procedures

Incidents or events that meet the OHRP criteria for unanticipated problems require the creation and completion of an [unanticipated problem report form](#). OHRP recommends that investigators include the following information when reporting an adverse event, or any other incident, experience, or outcome as an unanticipated problem to the IRB:

- appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- a detailed description of the adverse event, incident, experience, or outcome;
- an explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

To satisfy the requirement for prompt reporting, unanticipated problems will be reported using the following timeline, understanding that the Network is developing new guidelines and any changes will be reflected once the guidelines are finalized:

- Unanticipated problems that are serious adverse events will be reported to the single IRB (sIRB) within 1 week of the investigator becoming aware of the event.
- Any other unanticipated problem will be reported to the sIRB within 2 weeks of the investigator becoming aware of the problem.
- All unanticipated problems should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within one month of the sIRB's receipt of the report of the problem from the investigator.

All unanticipated problems will be recorded in the National Dental PBRN safety event system and will be reported concurrently with reporting to the IRB. These reports will be submitted to NIDCR's centralized reporting system via Rho Product Safety:

- Product Safety Fax Line (US): 1-888-746-3293
- Product Safety Fax Line (International): 919-287-3998
- Product Safety Email: [rho\\_productsafety@rhoworld.com](mailto:rho_productsafety@rhoworld.com)

General questions about SAE reporting can be directed to the Rho Product Safety Help Line (available 8:00AM – 5:00PM Eastern Time):

- US: 1-888-746-7231
- International: 919-595-6486

## 9 STUDY OVERSIGHT

The investigators will be responsible for study oversight, including monitoring safety, ensuring that the study is conducted according to the protocol and ensuring data integrity. Study progress and safety will be reviewed monthly by the PIs, when data will be reviewed for safety concerns and data trends. Reportable events that arise during the conduct of the study will be promptly submitted to the IRB.

If necessary, additional steps may be taken to ensure data integrity and protocol compliance.

## 10 CLINICAL SITE MONITORING

Clinical site monitoring is not required for this study. The NIDCR maintains the right to conduct ad hoc monitoring visits if necessary.

Node Coordinators will provide study training to practitioner sites. Remote monitoring activities will be conducted at the NCC and ARC Nodes to evaluate study processes and documentation based on NIDCR standards and principles of good clinical practice.

Remote monitoring activities will primarily involve quality management (QM) procedures to ensure completeness and accuracy of data collection. These QM procedures are detailed in the protocol, Section 13, as well as the study-specific Manual of Procedures ([MOP](#)), and Data and Quality Management Plan ([DQMP](#)). This study will follow the general guidelines for conducting monitoring for the Network's observational clinical studies documented in Chapter 6 of the National Dental PBRN Network Operating Procedures. The NOP and all study-specific documentation will be stored on the Hub website and accessible to all study team members.

The NIDCR reserves the right to conduct independent audits as necessary.

## 11 STATISTICAL CONSIDERATIONS

### 11.1 Study Hypotheses

Ramp Up study

Not applicable since the ramp-up study will assess study feasibility and flow processes.

Full Study

Hypothesis 1

There is a significant difference in pain intensity measured over time and the dental procedure groupings, after adjusting for pain management strategies and other complications. More

specifically, are there significant variations in pain intensity due to different treatments after adjusting for:

- a. pain management strategy (e.g., pain medications used, adherence to pain management strategy, the usage of non-medicine methods for pain)
- b. other complications

#### Hypothesis 2

There is a significant difference in pain interference measured over time and the dental procedure groupings, after adjusting for pain management strategies and other complications. More specifically, are there significant variations in pain interference due to different treatments after adjusting for:

- a. pain management strategy (e.g., pain medications used, adherence to pain management strategy, the usage of non-medicine methods for pain)
- b. other complications

#### Hypothesis 3

There is a significant difference in patient satisfaction measured at the end of the 7-day period and dental procedure groupings, after adjusting for pain management strategies and other complications. More specifically, are there significant variations in patient satisfaction due to different treatments after adjusting for:

- a. pain management strategy (e.g. pain medications used, adherence to pain management strategy, the usage of non-medicine methods for pain)
- b. other complications.

#### Hypothesis 4

Reported technology acceptance metrics (performance expectancy (PE), Effort expectancy (EE), and the Social Influence (SI), behavioral intention (BI) will be consistent with high acceptance of the FollowApp.Care platform.

Key associating factors:

1. CDT treatment codes and their corresponding groupings will be provided in both the eCRF (CDT codes) and FollowApp.Care (groupings). Procedure groupings will be defined by the ADA CDT codes categorized by types of service. As part of the study inclusion criteria, the types of services included derive from 4 groups: Endodontics, Periodontics, Implant Services and Oral Surgery.
2. Pain management metrics measured by the eCRF and the FollowApp.Care mHealth questionnaire (i.e., Medication use)
3. Other complications, measured by the eCRF and FollowApp.Care mHealth questionnaire (i.e., swelling, bleeding).

## 11.2 Sample Size Considerations

Sample Size Estimation for Aims 1 and 2 in UH3: A minimum of 150 and up to 215 dental providers will be recruited. During the course of the 9-month provider participation period (within an 18-month total recruitment period), each provider will be expected to enroll an average of 21 patients (3 per month), for a total of 3,147 patients. Assuming a 40% missing data rate among enrolled patients throughout the duration of the study, there will be 1,888 patients remaining. This includes patient non-response rate as well as item non-response rates for the outcome of interest during the study period. Given a sample of 1,888, the GLMM model for repeated measures will be able to detect a 20% reduction in pain intensity between procedure groups over time with 80.0% power. The minimum sample size was derived by the “longpower” sample package in the R statistical computing environment. All statistical analyses will be performed at the standard significance level ( $\alpha=0.05$ ) using R and Stata Statistical Software release 15 for StataCorp LP.

- *Outcome measure used for calculations (almost always the primary variable)*

There are two primary PROs for this study - Pain Experience and Patient Satisfaction. *Pain experience* refers to both Pain Intensity and Pain Interference.

- *Test statistic*

The pain intensity data have a repeated measure structure whereby patient data will be collected over 6 timepoints. In order to test whether the null hypothesis of “no association” between pain intensity, pain interference, or patient satisfaction and the treatment categories (Endo, Perio, OS, and Oral Implant), a GLMM will be performed for count data. There will be a total of three models representing each outcome. The pain intensity, patient satisfaction, and pain interference models will report the relative risk measure of association.

We will use a standard Type I error rate of 0.05 and Type 2 error rate of 0.20.

- *Method for adjusting calculations for planned interim analyses, if any*

1. Insufficient procedure variation among our collected procedures (divided in “procedure groups”): If there is low variability within groups, we will consider two adjustment methods: 1) combining data from similar treatment groups and 2) dropping specific groups with low cell counts.

2. The patient response rate is insufficient (patients complete only some of the mHealth questionnaires but not for all days): To address this missing data type, we may employ multiple imputation methods. Pain intensity has an average score of 5 and SD of 1.

- *Assumed dropout rates*
  - We expect a 40% dropout rate among patients.
  - We expect a 10% dropout rate among practitioners



- *Approach to handling discontinuation and protocol violations, i.e., to what extent data from discontinued subjects will be evaluable, whether discontinued subjects will be replaced.*
  - Opened but unanswered mHealth questionnaires will be discarded
  - Answering only 1 day out of the six questionnaires will not be discarded
  - Answering one day with one question will not be discarded unless the only question answered is the first question.
  - We will not replace the *discontinued* subjects unless recruitment is not reaching minimum recruitment goals.

<b>Patient Sample Size by Participating Practitioners</b>	<b>Expected number of Participating Practitioners</b>
	$n_3 = 150- 215$
<i>Expected number of patients enrolled over the 18-month period (enrolling an average of 3 patient per month per practitioner over 36 weeks)</i>	3147
<i>Expected 40% dropout rate among patients (what we expect to be left with)</i>	1888
<i>Estimated power for detecting 20% effect difference between treatment groups</i>	80%

- The standard level of power to detect differences is 80% which provides sufficient power for addressing our secondary objectives.
  - 1) type and frequency of pain relief medications taken;
  - 2) post-operative complications (bleeding and visible swelling)

### 11.3 Final Analysis Plan

Quantitative Analysis Plan: In addition to the analyses described for the pain evaluation, descriptive statistics will be used during the course of the project as part of the data management procedures for monitoring data quality.

Standard descriptive statistics will be used to describe both patient and practitioners' characteristics using 5 data capture methods: 1) the SUS questionnaire, 2) the mHealth Questionnaire distributed on pre-specified days post procedure, 3) the UTAUT questionnaire, 4) the debriefing/interviews, 5) and the practitioner eCRF. Summary statistics such as means, medians, and ranges will be produced for all measured continuous variables. Frequencies and percent contributions will be computed for all categorical and ordinal variables. Graphical methods like X-charts will be used to examine distributions over time and identify potential influential time points. The balance of baseline characteristics and measures between groups will be compared using appropriate tests, including chi-squared tests, student t tests and Wilcoxon rank-sum tests.

To assess the dental pain experience (intensity, interference) and patient satisfaction, we will analyze the distribution of reported pain following painful procedures in all Network regions. This will allow us to assess clinical factors such as treatment type-category, medications used, and potential complications as a result of treatment. As an initial study, the analysis plan should help to demonstrate the program replicability and sustainability in other clinics/offices and study environments.

This observational study offers insight into the distribution of patient reported outcomes, while also capturing information on strategies used by practitioners for pain management. However, a challenge for this non-randomized study is confounders – pre-existing variables that affect the outcomes and differ between the treatment groups. In order to reduce bias, potential confounders variables will be adjusted for in regression models for the analysis. We will create a missing category for all missing data and assess the need of any imputation methods.

With the eligible Network patient cohort, we will estimate the difference in intensity, pain interference, and patient satisfaction dependent on the treatment type. The relative risk (RR) will be the measure of association reported along with 95% confidence intervals. Pain, interference, and satisfaction at the end of the study will be compared among the treatment categories.

To model the differential treatment (CDT Grouping) effect on patients' pain intensity, interference and satisfaction, we will use GLMMs using a Poisson link. Models will include time, treatment type, age, gender, race/ethnicity, medications and no medication methods as fixed effects. Dentist and Network region will be included as random effects in the models to account for correlations within clusters.

A secondary analysis will be considered for additional evaluation of the FollowApp.Care platform by the practitioners including:

1. *Assessment of the usability.* It is essential to ensure that practitioners are not unduly burdened by the technology and that it fits seamlessly into their workflow. The factors that affect the individual's intention to adopt a new technology are its perceived usefulness and perceived ease of use. We will administer the UTAUT Questionnaire to all participating practitioners, post-implementation, to evaluate FollowApp.Care usage,

perceived usefulness, ease of use and impact on clinical workload as predictors of their usage behavior.

2. *Data analysis:* At the practitioner level, to ensure that our Health IT intervention is implemented as intended, we will comprehensively evaluate **fidelity**. Means and corresponding estimates of precision (e.g., standard deviations and 95% confidence intervals) and frequency distributions with percentage contributions will be used to report the distribution of each metric. We will conduct a confirmatory factor analysis (CFA) for multilevel data to test the reliability and construct validity.

<b>PATIENTS</b>
1. FollowApp.Care Profile created
2. Received FollowApp.Care information sheet
3. Received email notification on specified days
4. Completed mHealth pain intensity survey (using FollowApp.Care)
5. Completed mHealth satisfaction survey (using FollowApp.Care)
6. Completed SUS usability survey
<b>PRACTITIONERS</b>
1. Completed training
2. Verified FollowApp.Care practitioner profile
3. Received FollowApp.Care dashboard notifications
4. Dashboard response time
5. Completed SUS usability survey (Ramp Up)
6. Completed UTAUT usability survey (Full Study)

The UTAUT questionnaire will be used to describe the 4 latent constructs: performance expectancy, effort expectancy, social influence and behavioral intention. The relationships between the constructs will be given by the estimated factor loadings. There are several goodness of fit indices that will be used to determine how well the CFA model performs; the Chi-squared test, the root mean square error of approximation, Akaike information criterion, and the Bayesian information criterion.

## 12 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Study staff will maintain appropriate dental and research records for this study, in compliance with ICH E6, Section 4.9 and regulatory and institutional requirements for the protection of confidentiality of subjects. Study staff will permit authorized representatives of NIDCR and regulatory agencies to examine (and when required by applicable law, to copy) research records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress and data validity.

Summary of Source Data/Documents:

- Usability testing, debriefing/interview sessions – Audio recordings of qualitative data recorded electronically (ramp up study)
- Patient mHealth data – collected electronically through FollowApp.Care (provided to study team as limited dataset)
- Practitioner Questionnaire data, UTAUT – collected via eCRFs completed by practitioners, entered into NCC-managed data management system

## 13 QUALITY CONTROL AND QUALITY ASSURANCE

Quality Management (QM) is the overall process of establishing and ensuring the quality of processes, data, and documentation associated with clinical research activities. It encompasses both quality control (QC), and quality assurance (QA) activities. Quality management processes are detailed in the study-specific Quality Management Plan ([DQMP](#)) and involve review of consent procedures and electronic case report forms (CRFs) for completeness, timeliness and accuracy; if irregular trends or other ongoing issues are identified, virtual or in-person monitoring visits may be conducted. The NCC, with input from the study team and ARC, will develop a study-specific Quality Management Plan (DQMP) that sets up a continuous quality control process with the goal of reducing the turnaround time between error detection and correction.

Data and safety monitoring will be the joint responsibility of the study team, ARC and the NCC. The NCC will develop a data management system for study data collection and safety event reporting. Study progress and safety will be reviewed monthly by the PIs utilizing reports provided by the NCC. The PIs will maintain primary responsibility for reporting of safety events to ensure participant safety and reviewing protocol deviations and considering study modifications if needed to ensure data integrity.

Practitioner Surveys/Questionnaire data will be obtained electronically through the NCC-managed study-specific electronic data system. The EDC provides: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation; 3) access to study datasets that can be imported into common statistical packages; and 4) procedures for importing data from external sources.

Patient Surveys/Questionnaire data will be obtained electronically via the FollowApp.Care system. FollowApp.Care has standard operating procedures within its data analytics and software

development groups for quality control of data, assuring accuracy and standardization. FollowApp.Care software engineers who develop the scripts for data extraction verify the quality of their scripts through an internal code review and a thorough testing process prior to implementation. Once data extraction methods are in place, FollowApp.Care monitors the success and accuracy of the extractions through comparison with known data points. Extraction from FollowApp.Care's databases occurs through sFTP (Secure File Transfer Protocol) and https (Hypertext Transfer Protocol Secure), ensuring secure transfer methods of the data. Data for this study will flow from FollowApp.Care to the research team, and each entity will follow its own processes and procedures for quality control.

### Subject Accrual and Compliance

#### a. Measurement and reporting of subject accrual, adherence to inclusion/exclusion criteria –

Review of the rate of patient subject accrual and adherence to inclusion/exclusion criteria will be provided by the NCC as part of the study monitoring reports. The reports will be made available on a set schedule, as detailed in the Data Quality Management Plan, throughout the 18-month recruitment period for the study. The study team will review monthly to ensure that participants meet eligibility criteria and diversity goals outlined in the grant proposal. If the enrollment sample shows an imbalance with respect to clinical procedures, or patient characteristics/ demographics, the research team might request modifications to recruitment strategies, such as increasing recruitment at certain offices to offset the imbalance.

b. Measurement and reporting of participant compliance to treatment protocol – Study progress and safety will be reviewed quarterly (and more frequently if needed). Data on adherence to the protocol will be collected monthly by research staff and reviewed quarterly by the PIs with the research team and the study statistician. The study team will review reports as part of their monthly agenda. Compliance will be reviewed with the NIDCR, ARC and NCC at the quarterly meeting and if the study team has concerns about whether compliance has reached a level that might inhibit the ability of the study to test its primary hypotheses, a correction plan will be developed with NCC/ARC/NIDCR and study team input. There is no available data on expected compliance to the proposed FollowApp.Care protocol that can be used to determine a 'trigger point' for this action.

### **13.1 Data quality management**

The NCC will provide the study team with QC reports that include information on data completeness and accuracy as well as protocol compliance. The QC reports will be updated on a set schedule and accessible through the HUB website. A statement reflecting the results of the review will be sent to the NIDCR in the annual report. Data quality will be assessed using measures such as time from study visit to data entry, time to resolution of data queries, number of missing forms, and proportion of all study variables queried. Guidelines for concern regarding these measures are included in the Data and Quality Management Plan.

The NCC will make all reports available on the HUB for review, as needed. The schedule of report posting will be detailed and maintained in the Data and Quality Management Plan

### **13.2 Plans for data quality assessment**

Data quality will be formally assessed on an annual basis for each data source (e.g., FollowApp.Care data, eCRF data). A data quality report will be generated annually that summarizes findings, provides recommendations based on best practices, and suggests follow-up actions.

## **14 ETHICS/PROTECTION OF HUMAN SUBJECTS**

### **14.1 Ethical Standard**

The investigators will ensure that this study is conducted in full conformity with the principles set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, as drafted by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (April 18, 1979) and codified in 45 CFR Part 46 and/or the ICH E6.

### **14.2 Institutional Review Board**

The protocol, informed consent form(s), recruitment materials and all participant materials will be submitted to the sIRB for review and approval. Approval of both the protocol and the consent form will be obtained before any participant is enrolled. Any amendment to the protocol will be reviewed and approved by the sIRB before the changes are implemented in the study.

### **14.3 Informed Consent Process**

All consent forms and related documents will be sIRB- approved. For participating patients: An information sheet describing the study procedures and risks will be available to the participating patient by clicking on a link in the welcome message and will be provided when the study is explained to the patient. HIPAA information as required by state law will be shared with the patient. The practitioner or appropriate trained office staff will explain the research study to the patient and answer any questions that may arise. The rights and welfare of the patients will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study. By clicking on the link in the FollowApp.Care welcome text, the participating patient will provide tacit consent to participate in the study.

All study participants may withdraw consent at any time throughout the course of the study.

### **14.4 Exclusion of Women, Minorities, and Children (Special Populations)**

For the study, there are no exclusions based on gender, race or ethnicity. Study participation will be limited to adults aged 18 and over.

### **14.5 Participant Confidentiality**

1. Protection of Subjects - all study data will be kept in strict confidence. No information will be given to anyone without permission from the subject. This statement guarantees confidentiality. Confidentiality is assured by use of identification codes linked to the subject. Health Information Portability and Accountability Act (HIPAA) guidelines of all Network clinical sites will be followed.
2. Confidentiality during safety event reporting – Safety event reports and annual summaries will not include subject identifiable material. Each will include the identification code only.

Participant confidentiality is strictly held in trust by the investigators, study staff, and the sponsor(s) and their agents.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

Authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the investigator, including but not limited to dental records for the study participants. The clinical study site will permit access to such records.

#### Certificate of Confidentiality

To further protect the privacy of study participants, a Certificate of Confidentiality will be obtained from the NIH. This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.

#### **14.6 Future Use of Stored Specimens and Other Identifiable Data**

No identifiable data will be stored or used in the future. Three years after the final federal financial report (FFR) has been accepted by NIH, all data will be deleted from the FollowApp.Care platform.

### **15 DATA HANDLING AND RECORD KEEPING**

The investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible

manner to ensure accurate interpretation of data. The investigators will maintain adequate case histories of study participants, including accurate CRFs, and source documentation.

### **15.1 Data Management Responsibilities**

The PIs in collaboration with the NCC will review reports of data completeness and accuracy as well as protocol compliance on an ongoing basis throughout the study. A statement reflecting the results of the review will be sent to the NCC/NIDCR in the annual report. Data quality will be assessed using measures such as time from study visit to data entry, time to resolution of data queries, number of missing forms, and proportion of all study variables queried. The process and timeline for review will be detailed in the study-specific Data Quality Management Plan.

### **15.2 Data Capture Methods**

Practitioner Case Report Forms will be captured through the NCC's electronic data capture system, as described in the study-specific data management plan developed and maintained by the NCC.

Patient surveys/questionnaires will be captured through the FollowApp.Care system. The FollowApp.Care databases are accessible only to FollowApp.Care engineering and data analytics teams. Data that is accessible by FollowApp.Care account holders (i.e., office practitioners and admin, members of the research team) is password protected, and all passwords are filtered from FollowApp.Care logs and are one-way encrypted in the database using PBKDF2 with HMAC-SHA1, 128-bit salt, 256-bit subkey, 1000 iterations. FollowApp.Care has implemented strong encryption via TLS throughout our application. By using encryption, FollowApp.Care minimizes the chances of someone possibly intercepting username-password combinations and/or other sensitive data. FollowApp.Care also maintains a robust application audit log to include security events such as user log in and data changes. FollowApp.Care ensures that the software and its dependencies are up to date eliminating any potential security vulnerabilities and employs a wide range of monitoring solutions for preventing and eliminating attacks.

The data will also be securely transferred to the NCC utilizing Kaiser Permanente Center for Health Research's secure data transfer site. This is a secure file transfer (SFT) system that features FIPS 140-2-compliant encryption for files at rest and two-factor authentication via a one-time password token for maximum security.

The research team will only have access to a limited dataset from the FollowApp.Care system throughout the study period. The NCC will make a limited dataset available to the study team for the purposes of analysis. The NCC will also provide summary reports to the study team to allow for the review and monitoring of study progress.

The NCC needs to be able to link the FollowApp.Care data with the eCRF patient data. This will be done in the following manner to ensure consistency: (1) the patient will be registered in the NCC system "National Dental PBRN Hub" main central website by the practitioner with the patient's name and address (to facilitate patient remuneration and study data linkage); (2) this



will create a date of visit; and (3) the patient is assigned a tracking ID; (4) the patient’s information is entered into FollowApp.Care; (5) once the patient clicks on the welcome message the patient is considered enrolled and FollowApp.Care will create a Subject ID; (6) FollowApp.Care will send the practitioner a message that the patient is enrolled; (7) the practitioner completes the Day 0 eCRF and attest on the eCRF that the patient is enrolled.

Debriefing/interview sessions will be conducted in person or virtual. The debriefing/interview sessions will be recorded and later transcribed for analysis. The recordings will then be destroyed and there will be no link to any individual identifiers. De-identified transcripts will also be stored in the NCC data management system.

### 15.3 Schedule and Content of Reports

#### 15.3.1 Schedule

<b>Ongoing Data Review Meetings</b>	<b>Schedule</b>	<b>Content</b>
Study team meetings	Weekly	Ongoing data review
Study Team PI with NIDCR PO Calls	Monthly	Ongoing data review
Study team Biostatistician meeting with NCC	Monthly	Ongoing data review
Study Team PI and Executive Team	Quarterly	Study update
<b>Interim Report</b>	<b>Schedule</b>	<b>Content</b>
Enrollment Report	Monthly	Weekly data from FollowApp.Care
Interim Data Analysis Report	Quarterly	eCRF, activities logs, Source Documents
Quality Management Summary Report	Annually	Results of QM activities
Annual investigator meetings (RPPR)	Annual	Study progress, interim data analyses, next year’s goals, publications
Study Monitoring Reports (developed and provided by NCC)	Monthly	

#### 15.3.2 *Plans for interim data analysis and interim and final study reports*

Interim and final study reports covering preliminary and final findings will be developed by the study team for review by the NCC and ARC. At the annual project meetings interim study reports will be discussed, eliciting the full investigator team's feedback.

The study team's biostatistician and FollowApp.Care staff will develop the analysis and reports for data from the FollowApp.Care platform.

The NCC will develop the reports from the source documents that are located in the NCC database.

The study team's biostatistician will merge the data from the NCC and FollowApp.Care for certain reports.

### **15.3.3      *Steps for locking the database prior to analysis***

The NCC is responsible for locking the database. After a proper quality check and assurance, the final data validation is run. If there are no discrepancies, the datasets are finalized in consultation with the study team biostatistician. A pre-lock checklist is used to confirm completion of all data management activities prior to database lock. Once the approval for locking is obtained from all stakeholders, the database is locked, and clean data is extracted for statistical analysis. In case of a critical issue and after NCC approval, privileged users can modify the data even after the database is locked. Proper documentation and an audit trail will be maintained with sufficient justification for updating the locked database. Data extraction is done from the final database after locking. This is followed by its archival along with posting of a deidentified dataset(s) to the National Dental PBRN public website.

## **15.4      Study Records Retention**

Study records will be maintained for at least three years from the date that the grant federal financial report (FFR) is submitted to the NIH. Records that were housed by the NCC will be maintained with the NCC; records that were housed by the study team will be maintained by the study team.

## **15.5      Protocol Deviations**

A protocol deviation is any change, divergence, or departure from the study procedures described in the IRB-approved clinical study protocol. The deviation may be on the part of the participant, the investigator, or study staff.

Consistent with the investigator obligations in the ICH E6 Guideline for Good Clinical Practice, the Principal Investigator will document in study source documents and explain any deviation from the IRB-approved protocol. The Study Team PI will report to the IRB any deviations or changes made to eliminate immediate hazards to participants and any changes that increase risk to participants and/or significantly affect the conduct of the study.

Protocol deviations will be assessed for their impact on safety, study operations, and data integrity. Appropriate corrective and preventive actions will be implemented if warranted.

## 16 PUBLICATION/DATA SHARING POLICY

**Scientific Publication** - Publication policy /authorship will be based on the relative scientific contributions of the MPIs and key personnel. One of the MPIs will likely be senior author of manuscripts related to this project.

Roles and responsibilities of authors and contributors are based on the “Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals” as published by the International Committee of Medical Journal Editors (ICMJE – [www.icmje.org](http://www.icmje.org)). As outlined by the ICMJE “authorship confers credit and has important academic, social, and financial implications”, and “implies responsibility and accountability for published work.” Additionally, authors should be able to identify which co-authors are responsible for what other parts of the manuscript and have confidence in the integrity of all work produced. Designated authors need to be able to meet the following four criteria; contributors who do not meet all four criteria should be acknowledged.

This project will follow the ICMJE recommendations that authorship be based on the following 4 criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

These criteria are intended to assign authorship to those responsible for the development of the content of the manuscript. The criteria are not meant to disqualify eligible colleagues from authorship. Hence, all individuals who have met the first criterion will be offered the opportunity to participate in the review, drafting, and final approval of the manuscript.

If the author group is large, all members of the group need to meet all four criteria to be named as authors and individually complete disclosure forms as required by the journal the manuscript will be submitted to.

**Data Sharing** - The MPIs will share their respective research results with other Co-investigators, key personnel, and consultants.

This study will comply with the [NIH Public Access Policy](#), which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive [PubMed Central](#)

upon acceptance for publication. As needed we will also refer to the Network's publication policy which is publicly available at <https://www.nationaldentalpbrn.org/publications/>.

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## SUPPLEMENTAL MATERIALS

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

- [\*Essential Document Binder\*](#)
- *Manual of Procedures*
- Data [\*Quality Management Plan\*](#)
- *Statistical Analysis Plan*
- *Time Line*
- Study Questionnaires
  - [\*System Usability Scale and feedback questions \(SUS\)\*](#)
  - [\*Practitioner acceptance questionnaire \(UTAUT\)\*](#)
- Data Collection Forms
  - [\*Electronic case report form \(eCRF\)\*](#)
  - [\*Patient mHealth questionnaires using FollowApp.Care\*](#)
- Debriefing/Interview
  - [\*Semi-structured\*](#) interview questions

## **APPENDICES**

The following list of documents are officially affiliated with the protocol and will be submitted to the IRB as a part of the protocol. As such, changes to these items will require a protocol amendment.

- Appendix A: Schedule of Events (table and diagram)

### APPENDIX A: Schedule of Events

#### Patient Study Group

Procedures	Screening (Day -7 to -1)	Study Visit 1 (Day 0)	Study Visit 2 (Day 1)	Study Visit 3 (Day 3)	Study Visit 4 (Day 5)	Study Visit 5 (Day 7)	Study Visit 6 (Day 14)	Study Compl etion (Day 21)	Prematur e Discontin uation
Provide Information Sheet		X							
Assessment of Eligibility Criteria	X	X							
Enroll in FollowApp.Care		X							
Send Welcome message		X							X
Send mHealth Survey			X	X	X	X	X	X	X
Obtain implied consent by clicking on link			X	X	X	X	X	X	

#### Practitioner Study Group

Procedures	Screening (Day -28 to -1)	Study Visit 1 (Day 0)	Stud y Visit 2 (Day 1)	Stud y Visit 3 (Day 3)	Stud y Visit 4 (Day 5)	Stud y Visit 5 (Day 7)	Stud y Visit 6 (Day 14)	Study Compl etion (Day 21)	Post Stud y	Premat ure Discon tinuatio n
Assessment of Eligibility Criteria	X									
Complete training	X									

Enroll in FollowApp.Care	X									X
Receive daily chats and reports			X	X	X	X	X	X		X
Participate in debriefing/interview									X	
Complete UTAUT Questionnaire									X	