APPROACH: Assessing Pain, Patient Reported Outcomes and Complementary and integrative Health (A National VA Demonstration Project)

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APPROACH: Assessing Pain, Patient Reported Outcomes and Complementary and integrative Health (A National VA Demonstration Project): Phase 2/UH3

Principal Investigators: Stephanie Taylor, PhD and Steven Zeliadt, PhD

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Abstract

Provide a summary of the study (recommended length: less than 500 words).

Background: In 2016, Congress passed the Comprehensive Addiction and Recovery Act (CARA) mandating expansion of Complementary and Integrative Health (CIH) therapies in VA. In response, 18 VA regional networks committed $5 million/year to implement CIH therapies at their sites beginning in 2018, focusing on six evidence-based therapies: acupuncture, chiropractic, therapeutic massage, Tai Chi/ Qigong, mindfulness, and yoga. The VA's Office of Patient Centered Care and Cultural Transformation (OPCC&CT) is charged with developing policy and operational guidance to promote evidence-based CIH therapies across VA. They also are charged with routinely reporting to Congress on the progress VHA is making on offering CIH therapies and, as such, is collecting quality improvement data through two large patient-reported outcome survey efforts, one focusing on evaluating the implementation of the Whole Health flagship initiative and a second survey focused on understanding patient experiences associated with receipt of CIH ("The CIH Experience Survey").

Design, site location and three study arms: This research project is one of 11 pragmatic trials funded by the NIH-DoD-VA Pain Management Collaboratory. Given it is a pragmatic trial, we are not conducting an intervention nor enrolling or surveying patients. Instead, we will primarily conduct a secondary data analysis of electronic medical record data from the Corporate Data Warehouse (CDW) combined with VA OPCC&CT's above-mentioned CIH Experience Survey of data collected from patients who have used CIH therapies and have chronic musculoskeletal pain at the 18 Whole Health Flagship sites. Based on CIH use, we will place Veterans in one of three study analytic cohorts/arms: 1) those using only practitioner-delivered therapies (acupuncture, chiropractic, therapeutic massage); 2) those using only self-care therapies (Tai Chi/Qigong, mindfulness, yoga); or 3) those using a combination of practitioner-delivered and self-care CIH therapies.

Hypothesis, sample size, data sources: The hypothesis being tested is whether adding self-care CIH therapies to practitioner-delivered CIH therapies is more effective than either strategy alone. We will use a pragmatic trial framework to assess study outcomes for Veterans in the 3 study arms. Our primary analysis is a secondary data analysis of existing data from OPCC&CT's quality improvement CIH Experience Survey on patient-reported outcomes (n ~ 18,000). The primary outcomes are pain intensity and pain interference. The secondary outcomes are symptoms of anxiety, symptoms of depression, general well-being, quality of life, and opioid use. We also are measuring Veterans' self-empowerment to take care of their health as a potential mechanism of action.

Our instrumental variable evaluation– Business practice nudges: We will prospectively collect one type of data – "nudges" (methods or business practices) that VAMCs use to promote Veterans' use of CIH therapies to Veterans. We will use this information to construct a variable which will serve as a surrogate for randomization to the three study arms. (Because we are only conducting a secondary data analysis, we cannot randomize anyone, but want to simulate that to increase our analytic abilities.) Specifically, those nudges/business practices are rapidly evolving and include things such as developing dedicated CIH facilities, educating providers about the CIH referral processes, and conducting CIH outreach activities (such as telephone calls to Veterans) to encourage CIH use. We will closely monitor these CIH nudges/business practices and utilize variation in them over time and across the study sites to serve as a surrogate for randomization.

List of Abbreviations

CDW - Corporate Data Warehouse

CIH – Complementary Integrative Health

DOD – Department of Defense

EHR - Electronic Health Records

ESP - Evidence Synthesis Program

HIPAA - Health Insurance Portability and Accountability Act

HSR&D – Health Services Research & Development

ISO – Information Security Officer

NIH – National Institute of Health

OPCC&CT - Office of Patient Centered Care and Cultural Transformation

PHI - Protected Health Information

VA - Veteran Affairs

VHA – Veterans Health Administration

VINCI - VA Informatics and Computing Infrastructure

VISN – Veterans Integrated Service Network

Contents

1.0 Study Personnel

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2.0 Introduction

Background and Research Question. Over half of Veterans report chronic musculoskeletal pain. Complementary and integrative health (CIH) therapies are important non-pharmacologic treatment options for these conditions. The evidence base for individual CIH modalities and pain management is well established. While practitioner-delivered therapies (i.e., massage, acupuncture or chiropractic) are promising, providers would like patients to be more active in their pain management by using self-care (i.e., meditation, tai chi, yoga) instead of relying solely on practitioner-delivered care. A critical question for the field is whether adding self-care CIH to practitioner-delivered CIH is a more effective approach than either strategy alone.

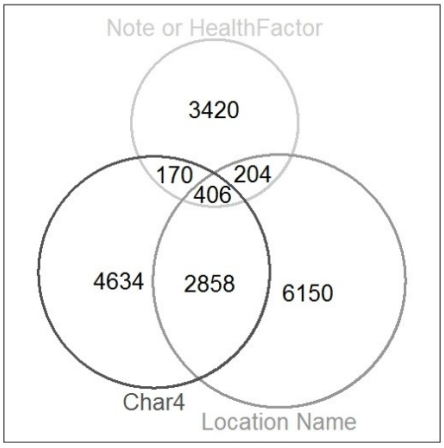
VA OPCC&CT and the CIH Experience Quality Improvement Survey. In 2016, Congress passed the Comprehensive Addiction and Recovery Act (CARA) mandating expansion of CIH therapies in VA. In response, 18 VA regional networks committed $5 million/year to implement CIH therapies at their 18 "Whole Health Flagship" sites beginning in 2018, focusing on six evidence-based therapies: acupuncture, chiropractic, therapeutic massage, Tai Chi, mindfulness, and yoga. The VA's Office of Patient Centered Care and Cultural Transformation (OPCC&CT) is charged with developing policy and operational guidance to promote evidence-based CIH therapies across VA. They also are charged with routinely reporting to Congress on the progress VHA is making on offering CIH therapies and, as such, is collecting a variety of quality improvement data. One set of data will be collected from the "CIH Experience" quality improvement effort, which will collect patient reported outcomes from Veterans at the 18 Whole Health Flagship sites who use CIH therapies.

Overall Design. We propose addressing the above critical question regarding the relative value of practitioner-delivered and self-care CIH therapies by capitalizing on the CARA expansion of CIH being provided to Veterans in 18 VA Whole Health Flagship sites. Specifically, we propose to conduct a secondary data analysis of VA OPCC&CT's CIH Experience quality improvement survey data. Their survey is collecting information on patient reported outcomes and CIH use. We will link that data to Veterans' clinical outcomes (e.g., opioid use) found in VA electronic health records. Based on what CIH therapies Veterans report using, they will be placed in one of three study arms: 1) those using only practitioner-delivered therapies (acupuncture, chiropractic, therapeutic massage); 2) those using only self-care therapies (Tai Chi, mindfulness, yoga); or 3) those using a combination.

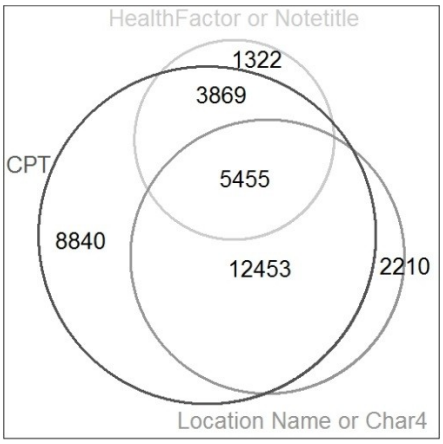
We Are Only Collecting Nudge/Business Practice Information. We will collect information from 1-2 staff at the 18 medical center study sites on nudges/business practices that they employ to encourage Veterans to use self-care CIH therapies. That information will serve as an instrumental variable (a method to reduce confounding and selection bias in our analysis). We are only conducting a secondary data analysis and although sites are not randomizing patients to types of CIH, the variation in nudges/business practices will serve as a surrogate for randomization in our analysis; See Section 5.6 for additional details.

The funding mechanism for this study is a UG3/UH3 mechanism entitled the NIH-DOD-VA Pain Management Collaboratory and all eleven funded studies are pragmatic trials focused on non-pharmacological approaches to pain. **The source of funding for this study is VA HSR&D**.

During the two-year UG3 Planning Phase (5/2018-4/2020) we : 1) reviewed administrative records from CDW to determine how much self-care and dual-care Veterans really use. 2) We also have been identifying nudges/business practices that the 18 VA medical center Flagship sites to examine variation in how sites encourage Veterans' use of CIH therapies. We also are learning that site nudges/business practices are rapidly evolving with hiring of additional CIH providers, agreements with community clinics, and active outreach by Whole Health Coaches. During this phase, we have refined methods for extracting CIH utilization based on how sites are entering information about CIH visits into the electronic health record. As described in the figure below, data coding varies across multiple methods for capturing CIH use including note titles, healthfactors, CPT codes, Char4 codes, stop codes and clinic location names. In these examples, meditation visits are captured across diverse coding practices while for chiropractic care, the use of CPT codes alone captures the majority of visits, although some also are coded with note titles, or other data entry mechanisms.



A. Sources of identifying unique meditation visits, a CIH therapy without CPT codes, in the VHA electronic health record



B. Sources of identifying unique chiropractic care visits, a CIH therapy with CPT codes, in the VHA electronic health record

In the table below, we summarize the frequency of CIH therapy use across the three study analytic arms for select clinics during FY18 in the UG3 planning phase 1, noting that dual use/combined care is under 10%.

Clinic Locations	Unique Patients	Dual Use/Combined Practitioner-Delivered and Self-Care	Practitioner-Delivered CIH Only	Self-Care CIH Only
A	652	1%	74%	25%
B	872	3%	37%	60%
C	607	8%	81%	12%
D	663	8%	68%	23%
E	1577	6%	68%	26%
F	942	11%	38%	51%
G	3227	6%	74%	20%
H	913	9%	79%	12%

Total	**9453**	**7%**	**66%**	**27%**

During the UH3 trial phase (5/2020-4/2024), we will identify eligible CIH users (n~120,000) and assign them to one of three study analytic arms based on the CIH they used. These CIH users will be linked with the nudge/business practice data at the locations where the received CIH as well as linked with available patient reported outcomes from OPCC&CT's "CIH Experience Survey" (n~18,000).

3.0 Objectives

Building on the planning efforts completed in the planning phase (UG3), the objectives of the trial phase (UH3) are:

Aim 1a: Conduct a 3-arm comparative effectiveness trial using a pragmatic encouragement design based on nudge/business practices associated with Veterans' use of CIH therapies at the 18 VA Whole Health Flagship sites to compare the effects of Veterans' use of 1) only practitioner-delivered therapies (acupuncture, chiropractic, therapeutic massage); 2) only self-care therapies (Tai Chi/Qigong, mindfulness, yoga); or 3) a dual/combination of practitioner-delivered and self-care CIH therapies.

Aim 1b: Assess the effectiveness of site nudges/business practices on encouraging dual/combination use vs practitioner-only and self-care only CIH use.

Aim 2: Identify how individual CIH therapies drive the overall treatment effects of the pragmatic trial.

These aims will be carried out by conducting a secondary data analysis by combining data from 3 sources:

1) **Medical Record Review** -Data from the CDW on Veterans' use of CIH and clinical pain management outcomes including opioid use across the 18 Flagship sites (n~120,000), linked to
2) **Secondary use of OPCC&CT CIH Experience Quality Improvement Survey Data** - Data on patient reported CIH use and outcomes found in VA OPCC&CT's CIH Experience Survey for Veterans who use CIH at the 18 Flagship sites (n~18,000), linked to
3) **Nudge/Business Practice Data Collection -** Data we collect in this study on the nudges/business practices that the 18 VA medical centers use to encourage Veterans to try self-care CIH therapies. This information is our instrumental variable (what we will use as a surrogate for randomization).

4.0 Resources and Personnel

Research personnel will follow all necessary procedures for accessing, extracting and analyzing Veteran medical record information as well as processes for accessing and analyzing non-research VA data resources.

Medical Record Review. Study aims require the review of patient data in medical records. We will utilize the CDW through VINCI. Study activities will be conducted by personnel located at the Seattle and Los Angeles HSR&D Centers. All personnel accessing CDW data will be VA employees and will follow all relevant CDW procedures.

Secondary use of OPCC&CT CIH Experience Quality Improvement Survey Data. Available data from the OPCC&CT's CIH Experience QI survey will be requested through Data Use Agreements with OPCC&CT or through a research repository that is being established to make OPCC&CT's data available to researchers.

Nudge/Business Practice Data Collection. Study personnel will collect business practices throughout the study period through qualitative interviews and tracking sheets (as noted in Appendix A). These administrative/non-human subjects data will be maintained on VA servers at VA Puget Sound behind the VA firewall and only the analysts and PIs will have access to them.

Study Staff Table

Name	Location	Project Role	PHI Access	Data Analysis
Stephanie Taylor, PhD	Los Angeles	PI and Site PI	Yes	Yes
Steven Zeliadt, PhD	Seattle	PI and Site PI	Yes	Yes
Barbara Bokhour, PhD	Bedford	Co-Investigator	No	No
Claudia Der-Martirosian	Los Angeles	Co-Investigator	No	No
Joy Toyama, DrPH	Los Angeles	Biostatistician	Yes	Yes
Danna Kasom	Los Angeles	Research Assistant	No	No
A. Rani Elwy, PhD	Boston	Co-Investigator and Site PI	No	No
Karl Lorenz, MD	Palo Alto	Co-Investigator and Site PI	No	No
Marlena Shin, JD, MPH	Boston	Co-Investigator and Site PI	No	No
Scott Coggeshall	Seattle	Biostatistician	Yes	Yes
Michael McGowen	Los Angeles	Program Assistant	No	No
Alissa Simon, MA	Los Angeles	IRB Consultant	No	No
Briana Lott	Los Angeles	Project Director	No	No
Jamie Douglas	Seattle	Data Analyst	Yes	Yes
Alexander Kloehn	Seattle	Project Coordinator	No	No
Michelle Upham	Seattle	Project Manager	No	No
Lawrence Swanson	Seattle	Database Manager	Yes	Yes
Xiaoyi Zhang	Seattle	Data Analyst	Yes	Yes
Raziel Gamboa, MA	Palo Alto	Research Assistant	No	N0
Melissa Medich	Los Angeles	Qualitative Analyst	No	No
Spencer Hilde	Seattle	Project Coordinator	Yes	No
Nathan Tomlanovich	Seattle	Data Analyst	Yes	Yes
Rian DiFranco	Seattle	Data Analyst	Yes	Yes

5.0 Study Procedures

1.1 Study Design

Assignment into each of the three analytic study arms will be based on a Veteran's CIH use at one of the 18 Whole Health Flagship locations. Each of the 18 VISNs has selected a Flagship site to serve as a model for establishing Whole Health and CIH programs of care: 1 Boston; 2 New Jersey; 4 Erie, Pa; 5 Beckley, WV; 6 Salisbury, NC; 7 Atlanta; 8 Tampa; 9 Tennessee Valley; 10 Saginaw, MI; 12 Tomah, WI; 15 St. Louis; 16 Little Rock; 17 San Antonio; 19 Salt Lake City; 20 Portland; 21 Palo Alto; 22 Tucson; 23 Omaha.

Identification of CIH Users (n~120,000). CIH users will be identified from CDW data, and eligible patients with chronic pain will be identified. Based on their CIH use over the subsequent 6 months following their initially being identified, each CIH user will be assigned to one of the three study arms. We estimate that approximately 120,000 Veterans with chronic pain will utilize CIH since the beginning of the Flagship initiative and throughout the study period (October 2017- March 2024).

Flagship Site Nudges/Business Practices. We will use virtual meetings with site leads to collect information about CIH therapies available at each of the Flagship sites, how availability of these therapies changes over the study period, and the nudges/business practices the sites are using to encourage Veterans' use of CIH, especially self-care CIH, therapies. For this, we will use a structured table (see Appendix A). For example, Grand Island, Nebraska, one CBOC within the Omaha VAMC, established a comprehensive **wellness clinic** in 2018 that encourages/nudges Veterans to try their acupuncture, chiropractic, massage, Tai Chi, yoga, or meditation programs. Among Veterans who initiate CIH therapies in that CBOC, preliminary data indicate that over 80% of these Veterans go on to use both practitioner-delivered and self-care CIH therapies. In contrast, Veterans at nearby facilities **with no wellness clinic that encourages use of these CIH therapies** are instead referred *outside* the VA to the community to receive their acupuncture because VA acupuncturists have not yet been hired. **In this case, the nudge is site's having a wellness clinic that encourages use of these therapies or not**. Preliminary data suggest few (<5%) of these Veterans who initiate acupuncture go on to participate in other self-care CIH services such as meditation, Tai Chi, and yoga. We will maintain a database based on the information we collect about business practices about of whether each Veteran who initiated CIH use is 1) exposed or 2) not exposed to a nudge/business practice that encourages them to try a combination of practitioner-delivered and self-care CIH.

Coding of business practice/nudges. After collecting business practice/nudge information from each site, we will create a complete list of nudges and assign each site a code of 1 if they have that particular nudge (in the Omaha example above, an "encouraging" wellness clinic) and a 0 if they don't. We imagine from site to site, some nudges will be similar but not be exactly the same. For example, Omaha might have an encouraging "wellness clinic", but Tucson might have a "Whole Health" clinic that is functionally similar to Omaha's clinic in that the Tucson's clinic encourages/nudges Veterans to try their acupuncture, chiropractic, massage, Tai Chi, yoga, or meditation programs. As such, both Omaha and Tucson would each be assigned a code of 1 for having an encouraging wellness clinic. If we find 7 total nudges across the 18 sites, we will create 7 instrumental variables. For each variable, we will assign a "1" to each site having that nudge, and a "0" if they do not have the nudge. There is almost no subjective aspect to nudges – either a site has a nudge or it does not.

Sites' provision of business practice/nudge information. The individuals from whom we will collect the nudges are the 18 Whole Health Flagship site leads. These are individuals at the site who oversee the various CIH therapy programs and, as such, have content expertise and can answer our questions (and whose names are available on VA OPCC&CT's website). We have an existing relationship with all. In Phase 1 of this study, VACO/OPCC&CT introduced us to them via email. We then had introductory calls to explain the study and talk about the next steps of our gathering information on their nudges. Also, as noted below, the individuals should not in any way feel coerced to provide this information. They understand it is a mutually beneficial information exchange. Additionally, we will not be recording the telephone calls we make to obtain information. The operational site leads will only see data from their site which they would see during the normal course of their work. However, as noted in the next paragraph, when a site requests us to share their best practice nudges with the other 18 Whole Health Flagship sites, we will do so. Further, they will not be making any judgements or changes in their sites, based on our study design, using the data they report during the data collection process. "

Nudge reports (Aim 1b). Given sites will be providing information on their nudges, we realized it would be helpful to them if we provided them with reports on how their nudges were doing (i.e.,how much each nudge got people to try self-care or dual care CIH therapies). As such, in our introductory calls, we offered to share two reports with them on a quarterly basis once the study began. As shown in Appendix A, those are the 1) nudge audit and feedback reports and 2) "radar" reports. The nudge reports will show the volume of CIH use associated with each nudge. The radar reports will provide CIH use volume for each of the codes the sites use to track CIH usage, so we can ensure we have the latest accurate list of codes (CIH coding can be dynamic). All were very excited about this collaborative relationship that was a two-way information exchange. They realized they could use our reports to determine which nudges could be considered "best practices" that could be shared with other sites. Whole Health Flagship sites are very collaborative, as they all struggle together to implement and sustain CIH therapies**.** As such, when a site requests us to share their best practice nudges with the other 18 Whole Health Flagship sites, we will do so. **Most important**, this activity is what we mean by Aim 1b "evaluating the nudges". We included that sub-Aim not because our study is about determining nudge effectiveness – it is not. We included the sub-Aim because we did not want to include in our analysis an instrumental variable that was associated with a nudge that wasn't effective – using such an instrumental variable would not help our analysis. As such, we need to look at the CIH use data associated with each nudge to make sure that nudge actually works and nudges people to self or dual CIH care.

Direct Comparison and Instrumental Analysis Comparison. The study will use the full sample of all CIH users (n~120,000) to first conduct a direct comparison of the three treatment arms: 1) practitioner-delivered CIH only; 2) self-care CIH only; and 3) combined use of practitioner-delivered and self-care CIH. This analysis will adjust for available patient characteristics including history of conditions associated chronic pain in the Corporate Data Warehouse and other available EHR-based clinical and demographic characteristics.

However, because of variation in CIH associated with the changing availability of CIH at each Flagship site and other underlying business practices, we will conduct a two-stage instrumental variable analysis (See Analysis 5.6). This analysis will allow us to identify the effect of participating in combined use of practitioner-delivered and self-care CIH compared to either practitioner-delivered CIH only or self-care CIH only.

Clinical Outcomes and Patient-Reported Outcome. These study analyses will be conducted on CIH users who participate in OPCC&CT's CIH Experience QI survey between 2021 and 2024 (n~18,000). The primary outcomes are pain intensity and interference. Secondary outcomes are symptoms of anxiety, symptoms of depression, general well-being, quality of life, and opioid use. We also are measuring Veterans' self-empowerment to take care of their health as a potential mechanism of action.

1.2 Recruitment Methods

No subjects will be recruited.

1.3 Informed Consent Procedures

No subjects will be recruited.

1.4 Inclusion/Exclusion Criteria

The full analytic sample will include all Veterans with chronic pain who initiate CIH therapy during the study cohort accrual period – 4/2021 to 4/2023.

CIH is defined as:

- Chiropractic care, therapeutic massage, acupuncture, yoga, Tai Chi, Qigong, or meditation coded in VA data or community care data.

Chronic pain is defined as:

- ICD10 codes for musculoskeletal pain conditions identified by NIH/VA/DOD Pain Collaboratory coded within 30 days of the CIH visit and coded on at least one additional previous encounter in

the -365 to -335 days prior to the CIH visit.

- Pain Numerical Rating Scale (NRS) Score of ≥ 4 within 30 days of the index CIH visit.

Additional inclusion criteria:

- Veteran
- VA user at one of the Flagship sites during the cohort accrual period.

Additional exclusion criteria:

- Patients with evidence in CDW of ICD10 codes for severe behavioral disorders in the year prior to index visit will be excluded. These include: Schizophrenic/delusional disorders Manic/bipolar disorder severe; Dissociative/conversion disorders; Paranoid/Unstable personality disorder; Mental retardation; Pervasive speech/language development disorders
- Patients with cognitive impairment and/or dementia
- Patients > age 90 at time of initial/index CIH visit
- Patients with spinal cord injury
- Patients with hospitalization 30 days prior to index visit

1.5 Study Evaluations

The primary sources of human subjects research data are retrospective medical records to ascertain CIH utilization and clinical pain management outcomes, and secondary use of non-research quality improvement survey data from OPCC&CT. The use of the CDW to review retrospective records about utilization of CIH as well as ascertain pain management outcomes within the 6-month period of initiating CIH will continue from the planning work during the initial UG3 phase. Request for secondary access to OPCC&CT's CIH Experience Survey (the quality improvement effort being fielded at the 18 Flagship sites) will be made through the Patient Centered Care Research Repository, following that repository's approved IRB protocol procedures.

5.5.1. Flagship Site Nudge/Business Practices (Non-human subjects data). Appendix A. As noted above, we will collect non-human subjects information about CIH nudges/business practices using both qualitative and quantitative approaches. We will collect the qualitative information from the individual CIH therapy providers and CIH Program Directors at each of the study sites to determine which CIH therapies they provide and if they use any business practices to nudge patients to theme, using the form and protocol shown in Appendix A. After we collect this, we will extract quantitative data from CDW on the number of Veterans using these CIH therapies among Veterans newly initiating CIH, and present it in a report for each specific nudge/business practice the site uses. We will produce quarterly nudge/business practice reports and will review them with site staff to identify potential changes in their CIH nudges/business practices, such as hiring of chiropractic or acupuncture staff.

1.6 Data Analysis

In general, randomization is the gold standard for yielding unbiased findings to appropriately control for selection bias, confounding and other challenges to casual inference. If potential imbalances among the cohort groups are observed it suggests that unmeasured selection to a particular treatment may be present. Using an as-treated approach adjusting for patient differences is one approach for addressing some forms of bias. Given we are only examining existing data and not randomizing subjects to an intervention, our analytic first step will be to identify potential imbalances in observable patient characteristics across the 3-arms. We will then use a direct adjustment approach for imbalanced covariates, acknowledging that alternatives such as propensity score weighting using boosted regression to account for the 3 treatment arms may also be considered if severe imbalances are observed. Our proposed direct adjustment approach will use a generalized linear mixed effect model (GLMM) to account for patients who are nested within site clusters.

The focus of this research study is to use the novel information from business practices to supplement

statistical adjustment approaches to addressing selection bias. Because randomization to specific CIH treatments is impractical at the Flagship sites as it would require withholding or restricting patients from receiving pain care options, a pragmatic approach using variation in business practices to serve as a surrogate to randomized treatment assignment is appealing. Business practices serve as nudges or encouragements to receipt of treatment, although patients may or may not fully comply with the encouragements. Pilot data from the Grand Island CBOC highlight that some locations due to hiring, space and other business practices can encourage dual care rates as high as 80%, while overall use of dual care is less than 10%. Because of the rapidly changing business practices associated with CIH in the flagship sites, variation in business practices are analogous to a natural experiment in which CIH use is constrained by factors such as availability reducing selection bias and confounding-by-indication as potential sources of bias. The assumption that there is a partial random component in variation in treatment is consistent with previous studies of encouragement designs and preference-based instruments.

The instrumental variable approach we will use is a two-stage least squares approach, which has been shown to yield consistent estimators of average causal effects over a wide range of scenarios including in the presence of weak instruments. In the first stage, we will estimate allocation to the treatment arm as a function of available patient characteristics and the presence of one of several business practice encouraging combination of practitioner-delivered and self-care CIH using a linear probability model. As noted earlier, if we find 7 total nudges across the 18 sites we will create 7 instrumental variables. For each variable, we will assign a "1" to each site having that nudge, and a "0" if they do not have the nudge. In the second stage, the estimated treatment values from the first stage, as well as available patient characteristics, are modeled to estimate the effect of treatment (e.g. patients who used combined practitioner-delivered and self-care CIH services compared to those who used practitioner-delivered CIH alone due to business practices encouraging their use). Separate models for each of the study outcomes and study cohorts will be fit including one model (n~120,000) for patterns of opioid use 6 months after initiating CIH, and a second model on self-report improvement in functional pain outcomes (n~18,000) for patients with available patient-reported outcome data.

Minimum size of smallest arm needed to detect 10% difference in patient reported outcomes among the study arms	
ICC = 0.01 (small site effect)	350
ICC = 0.03 (moderate site effect)	650
ICC = 0.06 (strong site effect)	2100

Sample Size. The most critical assumption underlying the potential power of the study is potential variation in effectiveness, which is unknown but likely to be present, and in combined use of CIH. In preliminary data for FY2018, approximately 7% of Veterans used combined CIH overall (ranging from 1-11%), although the goal across the 18 Flagship Sites is to increase this substantially in upcoming months with hiring of additional CIH providers. We have estimated the minimum sample size necessary to detect a 10% difference between study arms. This effect size was guided by OPCC&CT as the minimum effect size that would support specific policy recommendations. The null hypothesis is that the treatment effects are equivalent across study arms. Effect size changes are based on patient-reported outcome of pain interference over time among Veterans. We used a conservative power estimate (0.90) and assume a two-sided alpha of 0.017 to account for multiple testing among the three arms. The table on the right demonstrates the necessary sample size for a range of potential clustering effects by site. Note, even with a distribution of CIH utilization leading to one arm/group as small as 2100 Veterans (approximately 2% of the full sample of 120,000 CIH users, 12% of the anticipated 18,000 Veterans with available patient reported outcomes), we will have sufficient power even when there is substantial variance by site as represented by the ICC. In preliminary findings from the planning phase, the smallest group of CIH users were those who utilized combined practitioner and self-care modalities – 7% overall – which is rapidly increasing due to hiring of additional CIH providers. A manuscript describing the analytic plan and simulation studies has been requested for publication by the journal Clinical Trials.

1.7 Withdrawal of Subjects

We are not recruiting subjects.

6.0 Reporting

The primary risk of harm is inadvertent breach of confidentiality or data security protocols. These events will be reported as stipulated in VHA handbook 6500.

6.1. Data Safety Monitoring Plan. The Co-Principal Investigators (PIs) will be responsible for ensuring protection of study data and for reporting Serious Adverse Events (SAE) and Unanticipated Problems to CIRB, Information Security Officers and Privacy Officers, as required. Because the study is only evaluating retrospective care activities, there are few potential risks of harm to subjects. The main possible risk is breach of confidentiality, which will be minimized as described below in Privacy and Confidentiality.

Data Quality and Management. In accordance with planned milestones, quarterly evaluations of the progress of the study will be conducted which will review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. The PI or study analysts will review data obtained from the three data sources: 1) CDW, 2) OPCC&CT's CIH Experience Survey, and 3) Nudge/Business Practices data collection. This review will summarize total counts of patients for whom data has been extracted/received, and location of data storage behind the VA Puget Sound firewall (described below). Reports of use of PHI to link records between the data sources will be prepared, including number of records successfully linked. This effort will be used to continually examine data management procedures for potential risks of inadvertent breach of confidentiality. Annual reports of records accessed and changes in study staff accessing records will be reported to local R&D and CIRB as part of routine reporting requirements.

Upon discovering an Unanticipated Problem or unexpected and related SAE at any time during the study, study staff will contact appropriate regulatory officials within 48 and provide the CIRB with a report describing the duration (start and stop dates and times), severity, outcome, potential reason for the problem or SAE and relation to study activity, and remedies for avoiding further SAE or problems. Additional regulatory personnel including Privacy Officer and Information Security Officer will also be notified simultaneously with CIRB.

7.0 Privacy and Confidentiality

1.8 3 Data Sources

- **CDW data on Veterans' use of CIH and opioids at the 18 sites (n~120,000**): This data will be maintained on the VA Puget Sound secure server behind the VA's firewall. Only authorized APPROACH Study data analysis project team members in good standing will have access to the PHI data. Data will not be shared with anyone outside the research team. PHI data including visit dates and medical record numbers will be used to identify subjects in the CDW and link the data sources. Once the data have been extracted, identifiers will be removed from analytic dataset and replaced with a coded identifier. A separate crosswalk allowing the coded identifier to be re-linked to the CDW data will be maintained in a location separate from the analytic file within the study's secured data location behind the VA firewall.
- **Secondary use of OPCC&CT CIH Experience Quality Improvement Survey Data** at the 18 sites (n~18,000): This patient reported outcome data and identifiers will be obtained directly from VA OPCC&CT through a research repository that is being established to make OPCC&CT's data available to researchers.
- **Nudge/Business Practice Data at the 18 sites:** Non-human subjects data on the business practices sites used to encourage patients to try CIH therapies will be collected via phone or VA-approved video conference platforms. Study teams will take notes, which will be uploaded to an excel file stored on the restricted-access study folder on the GLA secure research server behind the VA firewall. Notes will be shared via email and/or verbally with corresponding site leads for verification purposes.

1.9 Data Destruction

Identifiers will be stored on VINCI and research servers at VA Puget Sound until the close of the study, approximately 6 years after the data has been collected and analyzed. At that time a de-identified dataset will be created. All data, along with the identifiers, will be transferred to the Seattle and GLA research data archives for the 6 year retention period, as required by VA policies, and removed from the VINICI workspace. After the retention period has been reached, the data will be destroyed in accordance with ORD Records Control Schedule (RCS).

1.10 Data Security

All gold-standard data security protocols will be in place:

- A VA data custodian will ensure that access to data is aligned with data security protocols for this project.
- No project data will be printed, faxed or shipped, nor will it be stored on desktop computer hard drives (other than initial recording download), laptops, or thumb drives.
- Access to the data files will be limited to the minimum number of individuals necessary to achieve the approved purpose and to those individuals on a need-to-know basis only.

Data will be coded, with identifiers removed from the analytic datasets. Exceptions are utilization dates in the CDW data.

8.0 Communication Plan

Central IRB submissions will include all applicable forms for local site approval. The project coordinator will work with the IRB consultant to ensure that IRB deadlines are met, that submissions are complete and that IRB approved protocols are followed. We will also take appropriate action if an engaged site is no longer needed as part of the study's research activities. All project personnel will be trained on relevant data security procedures. Regular project meetings will communicate the need for protocol changes and compliance updates. A shared folder on the research server at the Greater Los Angeles VA, behind the VA firewall, will be used by all study sites to manage CIRB protocols. All study staff at all study sites will be provided access to this server.a