Official Title:	EHR Embedded Comparative Effectiveness Studies--CPS (EHR-CPS)
NCT number:	NCT04520009
Document Type:	Study Protocol; Statistical Analysis Plan
Date of the Document:	08.05.21

PROTOCOL TITLE: EHR Embedded Comparative Effectiveness Studies

D-HH IRB OVERSIGHT:

One of the following must be true in order to submit to the D-HH IRB. Please check all that apply:

☐ The Principal Investigator is employed by D-H
☐ The study will utilize any D-H data or specimens
☒ The study will enroll D-H patients or recruit from D-H sites
☒ The study will utilize any D-H resources, e.g. study procedures will occur at D-H locations and/or use of D-H equipment or shared resources

PROTOCOL TITLE:

EHR Embedded Comparative Effectiveness Studies

PRINCIPAL INVESTIGATOR:

Tor D. Tosteson, ScD
Professor of Biomedical Data Science
Director, Division of Biostatistics
603 653-3677
Tor.tosteson@dartmouth.edu

Clinical Co-Investigators:

John A. Batsis, MD, FACP, AGSF, FGSA, FTOS
Associate Professor of Medicine and The Dartmouth
Institute for Health Policy & Clinical Practice
Section of General Internal Medicine
John.A.Batsis@hitchcock.org

Auden C. McClure, MD, MPH
Assistant Professor of Pediatrics & Medicine
Auden.C.McClure@hitchcock.org

Adam M. Pearson, MD, MS
Assistant Professor of Orthopaedics
Adam.M.Pearson@hitchcock.org>

Dawne M. Mortenson, RN
Center for Pain and Spine
Dawne.M.Mortenson@hitchcock.org

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
4	092320	Change language for WWC clinic changes due to COVID and process modification; change from single-site to multi-site trial; change to tear-off sheet to gather patient contact information for CPS (done via Redcap in WWC)	Yes

Table of Contents

Study Summary

Study Title	EHR Embedded Comparative Effectiveness Study
Study Design	Survey and interview assessment of parallel group randomization embedded into clinical processes and EHR Systems
Primary Objective	Evaluation of the feasibility, quality, and acceptability of informatics systems and consent procedures for EHR embedded comparative effectiveness research.
Secondary Objective(s)	
Research Intervention(s)/ Investigational Agent(s)	The demonstration interventions are: Initial visit with Dietitian (RD) then Health Coach (HC) or initial visit with Health Coach (HC) then Dietitian (RD) in Weight & Wellness Center (WWC); and activity restriction versus activity as tolerated post discectomy (see below for full descriptions)
IND/IDE #	N/A
Study Population	1) Patients and providers in the D-H Weight & Wellness Center (WWC) of the Department of Medicine enrolling in obesity management programs; 2) patients undergoing spine surgery for disc herniation in the DH Center for Pain and Spine (CPS).
Sample Size	For the WWC: 30 for RD then HC initial visit, 30 for HC then RD initial visit; For the CPS: 30 for activity restriction/30 for activity as tolerated.
Study Duration for individual participants	6 months of follow-up for CPS patients; follow-up for WWC patients is dependent on when the intervention was completed which could range from 1-6 months.
Study Specific Abbreviations/ Definitions	Health Coach (HC); Registered Dietitian (RD) Weight and Wellness Clinic (WWC); Dartmouth Hitchcock Medical Center (DHMC); Center for Pain and Spine (CPS)

Objectives*

- Evaluation of the feasibility, ease of use, quality, and acceptability of informatics systems and consent procedures for EHR embedded comparative effectiveness research.

- Estimate survey-based patient-participation, approval of EHR processes, and assigned treatment completion rates for embedded randomization procedures in the Weight and Wellness Clinic comparing visit order for initial Health Coach (HC) and Registered Dietitian (RD) visits (part of initial WWC multidisciplinary evaluation at approximately 2 weeks).
  Hypothesis: Patients participation and approval rates of the process will be greater than 80%.

- Estimate survey-based patient-participation, approval of EHR processes, and assigned treatment completion rates for embedded randomization procedures in the Center for Pain and Spine comparing activity restriction versus activity as tolerated following discectomy in the Center for Pain and Spine (CPS).
  Hypothesis: Patients participation and approval rates of the process will be greater than 80%.
  Following study completion, verify treatment status and determine EHR outcomes through chart review and records from the D-H data warehouse.

Background*

It is commonly acknowledged that patient-clinician decision making is inadequately supported by evidence on the comparative effectiveness of alternative therapies. In response to this need, efforts to reform health care delivery—such as the Affordable Care Act—have included large investments in improving electronic health record systems (EHR) as a potential source of evidence development. The expectation is that the large quantity of organized and accessible health care records will ultimately provide a resource for conducting comparative effectiveness research on an ongoing basis to guide "learning health care systems." [IOM (Institute of Medicine). Digital Data Improvement Priorities for Continuous Learning in Health and Health Care: Workshop summary. Washington, D.C.: The National Academies Press; 2013.]

This protocol will evaluate the feasibility, quality, and acceptability of informatics systems and consent procedures for EHR embedded comparative effectiveness research based in eDH, our Dartmouth-Hitchcock EHR.

Two initial demonstrations evaluating the new systems will be conducted targeting obesity interventions in the D-H Weight & Wellness Center (WWC): initial visits with

Dietitian (RD) then Health Coach (HC) or initial visits with Health Coach (HC) then Dietitian (RD); and in the CPS: activity restriction versus activity as tolerated following discectomy.

In the WWC, the demonstration will focus on patients who are returning for their RD and HC visit. These visits are scheduled after the initial provider visit. These visits are a part of normal clinical care and are scheduled interchangeably as part of the initial WWC multidisciplinary evaluation.

In spine surgery, patients undergoing lumbar discectomy commonly have post-operative restrictions related to bending, twisting, and lifting, as well as return to work. However, it is also common to have these activities allowed as tolerated [Carragee EJ, Helms E, O'Sullivan GS. Spine;1996;21(16):1893-1897], and both approaches are used in the DHMC Center for Pain and Spine.

Study Endpoints*

WWC: System recorded activity and patient surveys/interviews for the quality, and acceptability of informatics systems and consent procedures.

CPS: System recorded activity and patient surveys/interviews for the quality, and acceptability of informatics systems and consent procedures. Treatment status and patient reported outcomes as available retrospectively in the EHR.

Study Intervention/Investigational Agent

In the WWC obesity and related complications are managed by a WWC provider and obesity specific medications are prescribed as needed. Team care is provided by dietitians and health coaches. Progress is monitored at provider visits every 1-3 months with an aim to provide skills and support for sustained lifestyle change with a goal of 5-10% weight loss. Due to the COVID19 pandemic visits are now offered as a hybrid of in-person and telehealth visits.

In the WWC, the demonstration will focus on patients eligible and willing to be randomized for the order of their initial RD and HC visits. Both visits are offered as part of routine clinical care following the first provider visit and are consistent with current best practice medical guidelines for obesity.

WWC Arm A: Scheduling the initial RD visit first and then the HC visit as part of standard care.

WWC Arm B: Scheduling the initial HC visit first and then RD visit as part of standard care.

CPS Arm A: Standard post-operative activity instructions (i.e., no bending, twisting, or lifting more than 10 lbs for 4 weeks, no return to work until cleared to do so).

CPS Arm B: Instructions advising activity as tolerated and return to work based on patient discretion

Procedures Involved*

The software will identify patients for consent and randomized treatment assignments in obesity treatment and spine surgery. Eligible patients will be identified and approached during patient visits to consent for participation.

Initial pilot testing will take place at each demonstration center. Clinicians and support staff will be trained in using the EPIC based systems and clinical workflows. This feedback will be used to make final revisions to the systems and procedures for the demonstrations as necessary.

All potentially eligible patients in demonstration protocols will be initially identified through EPIC system alerts. Alerts will be triggered by surgeon orders for discectomy in the CPS and by entering into the pathway order screen in the WWC.

If the clinicians confirm that eligibility criteria are met, the patients will be asked if they would consider participation in a research project. If the patient is in person and agrees, the demonstration protocol will be explained and information sheet will be handed out. If the patient is not in person the information sheet will be mailed or emailed out to the participant via RedCap link. They will be asked to consent to be assigned randomly to one of the comparative effectiveness interventions and to participate in the follow-up survey and potentially a follow up semi-structured interview (see below). This follow up survey may be done in person via paper survey, sent via RedCap link, or participants can answer the survey questions verbally over the phone and a research assistant will enter responses directly into RedCap.

The software will return a computer-generated treatment assignment, with random block sizes chosen to balance the number in each comparison group. A code will be stored in the patient record to indicate the assigned treatment. The provider will be notified of the assigned treatment and place the proper orders in EPIC. In the WWC, this will be done using the pre-defined pathway order screen in EPIC.

We will use a brief post-visit survey (<5 min) with all patients who are approached about participating in the two studies. The survey will focus on the consent process, reasons for deciding to consent or to not consent, and a few demographics (e.g., gender, age, race, education level). The survey will be anonymous and will be given to the patient at the end of their visit or after their consent phone call. This brief post-visit survey may be done in person via paper survey, sent via RedCap link, paper survey via mail, or participants can answer the survey questions verbally over the phone and a research assistant will enter responses directly into RedCap. Invitations to participate in the survey will be sent up to four times by mail or email,

For patients in the CPS who have decided to enroll we will use the sheets to also gather their contact information for possible interviewing. To allow us to get feedback from unenrolled patients, the information sheet will have a tear off section with blanks for the patient's contact information. That sheet will be torn off before being given to an unenrolled patient who will remain anonymous.

All the demonstration interventions are considered standard of care at DHMC. Risks will be monitored according to clinical standards as currently employed in the participating clinics.

A follow-up survey will be sent after 1 to 6 months to ask whether they received the assigned treatment, their perceptions of the study processes, and some basic demographic information. The survey and semi-structured interviews will be conducted by the Center for Program Design and Evaluation at Dartmouth (CPDE) and overseen by Dr. Schifferdecker, study Co-I. Identifying information (e.g., name, email, address, phone number) will only be used to contact the participant and send them a survey or administer it by phone, and to assess their interest in being interviewed. Invitations to participate in the survey will be sent up to four times by mail or email, and paper surveys will be mailed as a last resort to non-respondents with a paid return envelope.

Participants who agree to be contacted for the semi-structured interview will be asked their preference for setting up an interview (e.g., by email or phone). CPDE staff will use the participant's preference to contact them to set up an interview time. All interviews will be conducted by phone, audio-recorded, and transcribed for analysis.

Following study completion treatment status and patient reported outcomes determined through retrospective chart review based on EHR data.

Data and Specimen Banking*

Study data are derived from responses to the surveys. Patient level data files will be maintained until a final report is released. Full name, email and phone number will be entered into RedCap database and will only be stored with the study team.

Sharing of Results with Subjects*

Summary results from the demonstrations will be available as a published final report from the funding agency (PCORI), and in scientific publications. Information on the location and timing of summary results will be communicated to participating patients during the consent process.

Study Timelines*

The anticipated start date for enrollment into the study is September 1, 2020. Approximately three months is expected for enrollment. Patients will be contacted 1-6 months following enrollment for follow-up surveys. The estimated date for completion of the last enrollment is December 1, 2020, with the last follow-up survey completed by March 1, 2021. The primary data analyses will be executed on a blinded basis as survey data are accrued, and summarized by the end of March.

Inclusion and Exclusion Criteria*

CPS
Inclusion Criteria: Adults (>18) able to consent, with sufficient fluency in English; indications for discectomy; able to restrict activities or to resume activities as tolerated.
Exclusion Criteria: Pregnant women; Prisoners; Children (<18).

WWC
Inclusion Criteria: Adults (>18) able to consent, with sufficient fluency in English; initial RD and HC visits are part of routine care as recommended by the provider; willing to be randomized.
Exclusion Criteria: Pregnant women; Prisoners; Children (<18).

Vulnerable Populations*
N/A

Local Number of Subjects
WWC: 60 patients total, 30 in each treatment arm.
CPS: 60 patients total, 30 in each treatment arm.

Recruitment Methods
Patients will be identified during clinic visits using pre-defined events recorded in the EHR. For WWC, the identifying event will be entering into the program order entry program during the second clinic visit for patients enrolling in obesity pathways. For the CPS, the identifying event will be the surgeon ordering discectomy. Following confirmation of eligibility criteria, recruitment and consent process will be initiated.

Risk descriptions will be provided for both the standard of care options in the WWC and CPS according to established clinical practice.

Withdrawal of Subjects*
It is unlikely that patients will be withdrawn unless the study terminates prematurely. In this case, participating patients and providers will be notified. Partial withdrawal from procedures will not affect the continued data collection, unless the patient also withdraws permission to use their data. No plans are in place to collect survival data.

Risks to Subjects*

No clinical risks beyond those of standard of care treatment are anticipated. Patients will be informed of these risks according to currently used procedures in the clinics and during the consent process. Patients will be contacted for follow-up questionnaires, and risks/protections regarding privacy will be discussed in the consent process.

Potential Benefits to Subjects*

There are no direct benefits.

Data Management and Confidentiality*

Data collected through the surveys and interviews will be subject to strict confidentiality safeguards. The brief post-visit survey and follow up survey may be conducted using DH RedCap account, which is a standard and secure online survey platform. Interview audio recordings will be transcribed and analyzed; the audio will be destroyed at the completion of the full study (around March 2021). In addition, the following procedures will be used to minimize risk: 1) unique identifiers will be assigned to each participant, and any potential identifiers (e.g., name) in surveys or transcripts will be removed prior to entering data into software for analysis; and 2) only the members of the study team will have access to a list linking unique IDs to participants; this list will be stored on a password protected computer. Information will be kept on password-protected secure computers and electronic files.

Access to retrospective EHR data is requested following study completion for all study participants to examine clinical and outcomes for assessing the quality and feasibility of the EHR process. The following data elements are requested:

For WWC:

- Age
- Sex
- Race
- Ethnicity
- Date of enrollment/treatment group assignment
- Date of initial Health Coach and Dietitian visits
- Patient Weight and Height at initial and subsequent visits
- Patient Reported Outcomes: PROMIS quality-of-life measure functional status questionnaire, and self-efficacy

For CPS:

- Age
- Sex
- Race

- Ethnicity
- Date of enrollment/treatment group assignment
- Date of surgery
- Patient discharge instructions for chart review by resident to verify activity restrictions
- Patient Reported Outcomes: PROMIS quality-of-life measure functional status questionnaire.
- Oswestry Disability Index

The following table gives estimates of the accuracy of the estimates for the primary outcomes with the planned demonstration sample sizes, with a range of participation and adherence rates.

Parameters for Sample Size	90% CI half-width for participation and adherance rates in each arm
N	30
Rate: 80%	13%
Rate: 70%	15%
Rate: 60%	16%

Provisions to Monitor the Data to Ensure the Safety of Subjects*

The interventions are all standard of care and considered to be minimal risk. Safety concerns will be addressed as part of routine clinical practice.

Provisions to Protect the Privacy Interests of Subjects

For the surveys and interviews, de-identified data are only linked through separate logs that are stored on password protected computers.

Compensation for Research-Related Injury

The WWC and CPS assigned treatments are considered standard of care and minimal risk. There will be no compensation to participants for study-related injuries beyond those offered in routine clinical practice.

Economic Burden to Subjects

No costs outside of usual care are anticipated. Those patients being asked to participate in interviews at either the beginning or end of the study will be given/sent $30 VISA gift cards, and those patients responding to surveys at the end of the study will be sent $20 VISA gift cards.

Consent Process

The consent process may take place in person at the WWC, or over the phone, or via videoconference. The participant will be asked to provide their preferred email during this conversation or address if they do not have email or internet Both phone and videoconference process will be standardized and involve using the script provided for the WWC for the initial RD and HC visit order. The information sheet will be emailed to the participant via a RedCap link or mailed if unable to be emailed.

In CPS for the post-discectomy Activity Restriction/Activity as Tolerated, following the SOP: Informed Consent Process for Research (HRP-090).

Process to Document Consent in Writing

Given the minimal risk, a waiver of documentation of written consent is requested for this protocol. Note that all data are collected via anonymous survey, and no HIPPA data are collected.

Note that both WWC and the CPS have reviewed and approved this protocol. Consent scripts are attached as well as a detailed information sheet for each comparison, covering all required consent elements.
A waiver of HIPPA authorization is requested for the retrospective use of EHR data and chart reviews for patients who are no longer participating in the study. The data are requested to assess the feasibility of our embedded systems and processes, and, as in other retrospective EHR chart reviews, it is not practicable to obtain consent. The privacy risks are mitigated by the use of deidentified analytic data sets, which are securely stored. The files linking the study IDs to patient records will be destroyed at the conclusion of the study. PHI will not be reused or disclosed following the conclusion of the study.

Setting

The study will be conducted in the Department of Medicine D-H Weight & Wellness Center Clinic and in the Department of Orthopedic Surgery Center for Pain and Spine. All interventions are standard of care and will be performed at these sites. The DH Research Ethics Committee serves as an advisory board and includes community representation.

Resources Available

There are approximately 150 patients per year/75 per 6 months who undergo lumbar discectomy at DHMC, of whom we plan to enter 30 to each of the two arms for activity restriction following discectomy.

Current WWC volume is estimated at approximately 600 patients per year (300 during the randomization period of 6 months, with capacity for up to 30. We plan to enroll 30 in the RD then HC initial visit, 30 for HC then RD initial visit;

The participating clinic investigators are all part of the research team and have been meeting multiple times per month since the beginning of the study to plan the procedures and informatics. The first two weeks of the accrual period will be used to conduct the testing and provide final guidance for the clinical staff.

The facilities used for conducting the research include the clinic sites, the Department of Biomedical Data Science, Divisions of Biostatistics and Biomedical Data Sciences, The Dartmouth Institute, and the D-H Analytics Institute. The project supports approximately 40% FTE for the Investigators and Co-Investigators and 120% FTE for staff in supporting roles as research assistants and programmers. Informed consent will be performed by clinic investigators and clinic assistants, most of whom are regular participants in team meetings. Scripts and training will be reviewed prior to initiation of the demonstration projects.

Multi-Site Research*

One of our Co-Investigators, Dr. John Batsis, has moved to the University of North Carolina (UNC). To maintain his involvement in this and other of his studies at Geisel and at Dartmouth-Hitchcock, we have changed the designation of this trial to a multi-site trial, including UNC. The appropriate materials for this change were uploaded in MOD00011236.