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Embedded emergency department physical therapy versus usual care for acute low back pain: a protocol for the NEED-PT randomised trial

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ABSTRACT

Introduction Low back pain is a common problem and a substantial source of morbidity and disability worldwide. Patients frequently visit the emergency department (ED) for low back pain, but many experience persistent symptoms at 3 months despite frequent receipt of opioids. Although physical therapy interventions have been demonstrated to improve patient functioning in the outpatient setting, no randomised trial has yet to evaluate physical therapy in the ED setting.

Methods and analysis This is a single-centre cluster-randomised trial of an embedded ED physical therapy intervention for acute low back pain. We used a covariate-constrained approach to randomise individual physicians (clusters) at an urban academic ED in Chicago, Illinois, USA, to receive, or not receive, an embedded physical therapist on their primary treatment team to evaluate all patients with low back pain. We will then enrol individual ED patients with acute low back pain and allocate them to the embedded physical therapy or usual care study arms, depending on the randomisation assignment of their treating physician. We will follow patients to a primary endpoint of 3 months and compare a primary outcome of change in PROMIS-Pain Interference score and secondary outcomes of change in modified Oswestry Disability Index score and patient-reported opioid use. Our primary approach will be a modified intention-to-treat analysis, whereby all participants who complete at least one follow-up data time point will be included in analyses, regardless of their or their physicians' adherence to their assigned study arm.

Ethics and dissemination This trial is funded by the US Agency for Healthcare Research and Quality (R01HS027426) and was approved by the Northwestern University Institutional Review Board. All physician and patient participants will give written informed consent to study participation. Trial results will be submitted for presentation at scientific meetings and for publication in peer-reviewed journals.

Trial registration number ClinicalTrials.gov (NCT04921449)

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This single centre trial randomised emergency physicians to receive or not receive an embedded physical therapist on their primary treatment team to evaluate patients with acute low back pain using a strict intervention protocol.
⇒ Physicians were randomised using a covariate constrained method, which controlled imbalance in physician characteristics relevant to the primary and secondary outcomes of interest.
⇒ Individual patients with acute low back pain are enrolled and followed to the primary endpoint of 3 months, using a primary outcome of change in PROMIS Pain Interference and secondary outcomes of change in Oswestry Disability Index and patient-reported opioid use.
⇒ Outcomes are assessed using multiple methods, including direct patient report, the electronic health record and prescription filling data, with assessors blinded to group allocation.
⇒ This trial is limited by its single centre design and inability to blind patients and physicians to group allocation.

INTRODUCTION

Low back pain is a common problem affecting an estimated 7% of the world's population at any given time.[1] It is the leading cause of disability worldwide.[2] In the USA, low back pain accounts for nearly 4 million annual emergency department (ED) visits[3] and more healthcare spending than any other health condition.[4] Because the vast majority of low back pain is non-specific, emergency care for low back pain tends to focus on relieving patient suffering.[5 6] Back pain is the most common reason opioids are prescribed from US EDs,[7] with nearly half of all ED back pain visits receiving an opioid prescription in.[8] Despite this focus on symptom relief, 48% of patients report persistent functional impairment 3 months after an ED visit for low back pain and 19% report continued opioid use.[9]

Several randomised controlled trials have demonstrated that physical therapy interventions for low back pain are efficacious in the outpatient setting,[10 11] where patients are referred to physical therapy after an initial clinical evaluation by a primary care physician. In the USA, physical therapy interventions are increasingly being offered directly in the emergency care setting (ie, ED physical therapy, ED PT), whereby patients with low back pain are evaluated by both an emergency physician and physical therapist during the same encounter. Although direct integration of physical therapists into accident and emergency rooms is common in the UK and Australia, it is uncommon in the USA with only a small number of US hospitals recently adopting this care model and continuing to rely on a consultative model of care.[12]

In a prior observational study we demonstrated that ED PT for low back pain is associated with greater improvements in pain-related functioning and lower utilisation of analgesic medications compared with usual care.[13] However, because ED physical therapists evaluate patients only when consulted by the treating ED physician, observational studies are confounded by physician discretion in which patients receive ED PT versus usual care. Thus, we sought to more rigorously evaluate the effect of ED PT versus usual care on pain-related functioning in a cluster-randomised clinical trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) protocol for acute low back pain.

METHODS AND ANALYSIS

Study setting and overview

NEED-PT is a cluster-randomised trial conducted at an urban academic hospital ED in Chicago, Illinois with >91 000 annual visits. This trial was registered on ClinicalTrials.gov on 10 June 2021, and the trial launched on 12 July 2021. The estimated primary completion date is 30 September 2023 (ie, collection of final data for the primary outcome measure at the primary endpoint), and the estimated study completion date is 30 June 2024 (ie, collection of final data for the outcome measures at the exploratory endpoints). This report adheres to the Standard Protocol Items: Recommendations for Interventional Trials guidelines for clinical trial protocols.[14 15]

We consented, enrolled and randomised (1:1) attending emergency physicians to receive or not receive an 'embedded' physical therapist (NEED-PT) on their primary treatment team to routinely evaluate patients with eligible reports. Individual patients meeting study eligibility criteria are then enrolled and allocated to either the NEED-PT or usual care study arm, depending on the randomisation assignment of their treating physician. We will follow participants for 3 months after their initial ED visit and compare pain-related functioning across study arms.

Eligibility and recruitment

Physician participants

All attending emergency physicians in active clinical practice were eligible to participate. Physicians received an email describing the study and containing a link for electronic informed consent using Research Electronic Data Capture (REDCap) eConsent (Vanderbilt University, Nashville, Tennessee, USA). Physicians were not offered any financial incentive for study participation. A total of 44 of 46 eligible physicians were consented and enrolled prior to the start of patient enrolment. If new physicians are hired during the conduct of the trial, we will conduct additional waves of physician enrolment and randomisation as needed to accommodate new staff.

Patient participants

Research assistants will monitor the electronic trackboard for ED patients with a chief report relating to low back pain and subsequently screen patients for study eligibility. Inclusion criteria are age ≥18 years, evaluated by a participating study physician during normal business hours (Monday to Friday, 08:00 to 16:00), anatomic low back (defined using the consensus international definition of pain located between the 12th rib and buttocks),[16] symptom duration ≤30 days and ability to complete follow-up data collection in English. We will exclude patients with chronic low back pain (defined using the US National Institute of Health Task Force on Research Standards for Chronic Low Back Pain),[17] any prior lumbar spine surgery, inability to ambulate at baseline, or any of the following as determined by the treating physician: obvious non-musculoskeletal aetiology for low back pain (eg, shingles, kidney stone), other concomitant injuries or pain (eg, closed head injury and low back pain), red-flag symptoms indicating life-threatening pathology (bladder/bowel incontinence, saddle anaesthesia, debilitating motor weakness), or likely to be admitted to the hospital. We will also exclude patients unable to consent, under police custody, or known to be pregnant. Patients will be recruited during their ED visit and will give informed consent to study participation, which involves providing follow-up information over seven defined time points over the next year. Patient participants will be offered up to US$70 in total for study participation, or US$10 gift card for each data collection time point.

Randomisation

We selected a physician-randomised approach based on patient stakeholder feedback from our preliminary work. Additionally, randomisation at the physician level allowed for evaluation of the effect on the intervention on exploratory outcomes relating to ED visit characteristics, such as diagnostic imaging utilisation and length of stay.

Due to the inherent risk of cluster-level covariate imbalance between study arms in cluster-randomised trials, we selected a covariate-constrained randomisation technique to control for possible imbalance in key physician characteristics such as likelihood of working night versus

day shift, likelihood of working a particular zone (eg, fast-track vs high acuity zone), opioid prescribing rate and physician characteristics (self-reported gender, race/ethnicity and years of experience). Covariate-constrained randomisation methods tend to ensure the most efficient control over covariate imbalance between study arms at randomisation.[18]

With 44 total physicians enrolled, there were over 2.1 trillion ways (44 choose 22) in which we could achieve equal allocation of physicians across study arms. The constrained randomisation technique involved simulating a large number (10 000) of possible random allocations of physicians across the two arms, evaluating imbalance on key covariates for each simulation, constraining the randomisation space to a subset (in this case 374 possible scenarios or 3.74%) that do not surpass a pre-specified threshold of allowable imbalance for each of the aforementioned covariates, and randomly selecting an allocation scheme from this smaller subset. Thus, the process preserves the 'randomness' element in the allocation process and statistical analyses may be model-based or randomisation-based.[19 20] Because we use physician-level covariates in the constrained randomisation procedure (eg, propensity to work a certain 'zone' of the ED), and zone is a surrogate measure of patient-level characteristics that might affect the primary outcome (eg, overall health status), this will translate to control over imbalance at the participant level.

Interventions

NEED-PT

Physicians randomised to NEED-PT will have a physical therapist embedded on their primary ED treatment team, traditionally defined as the emergency physician, nurse and technician. The physical therapist will be seated with the ED treatment team and will routinely evaluate patients with a chief report relating to low back pain. This departs from the standard model of consultative care in which physical therapists are rarely involved in ED patient care and only on a discretionary basis, and often late in the overall ED treatment course. The emergency physician will also perform an independent evaluation of the patient in accordance with their usual and customary practice.

The clinical components of the ED PT evaluation are administered according to a standardised clinical care algorithm. This algorithm was developed based on existing evidence-based practices and customised to the emergency care environment using the input and feedback of an External Advisory Board. We then pilot tested the embedded care model and the clinical care algorithm prior to the trial start in two non-participating physicians. The evidence base, development and pilot testing of the clinical care algorithm will be described in detail in a separate publication, but in brief: the ED physical therapist matches the patient's history and examination findings to an appropriate treatment classification consisting of directional preference exercises, manual traction, stabilisation exercises or non-thrust manipulation and mobilisation. Patients are also provided with education, prognostic guidance and reassurance, and referred to an outpatient physical therapist for follow-up as needed. The multiple algorithm branch points and respectively matched interventions reflect the vast clinical heterogeneity of low back pain diagnoses and the biological and psychosocial aspects of pain.

Usual care

Physicians randomised to usual care will not receive an embedded physical therapist and will continue to conduct clinical care as per their usual and customary practice. This may include diagnostic imaging, patient education and reassurance and administration and/or prescribing of analgesic medications.

Blinding and masking

Given the nature of the intervention, treatment assignment will be unblinded to both the patient and the treating physician during the index ED visit. However, study investigators will be blinded to participant treatment assignment, as will research assistants performing follow-up data collection. All participant data will be maintained in a unified REDCap database lacking an identifier for study arm.

Randomisation adherence

Adherence to randomisation assignment will be assessed by determining actual receipt of ED PT during the index ED visit, defined as the presence of an ED PT consult order or ED PT note. We will report the proportion of NEED-PT and usual care participants who receive a PT evaluation during the index ED visit; interarm contamination will be defined as an NEED-PT participant not receiving a PT evaluation or a usual care participant receiving a PT evaluation. We will also report the applicable treatment classification determined by the clinical care algorithm among all participants receiving a PT evaluation, regardless of randomisation assignment.

Main outcomes and measures

While randomisation occurs at the physician level, key primary and secondary analyses will occur at the participant level. All outcome measures will be collected by secured REDCap survey link at defined time points: the index ED visit, and 1 week, 1 month, 2 months and 3 months after the index ED visit. The primary endpoint will be at 3 months; additional exploratory time points will include 6 months and 1 year. REDCap survey links will be provided by text message through a secure, HIPAA-compliant research platform (Mosio)[21] or by email, depending on the patient's preference.

The primary outcome is the change in pain-related functioning at 3 months, as measured by PROMIS Pain Interference (PI) score. PROMIS-PI measures the self-reported consequences of pain on relevant aspects of a person's life, including social, cognitive, emotional, physical and recreational activities. Scores are standardised to

the US population, with a score of 50 representing the population mean and 10 points representing 1 SD.[22] We will use the PROMIS-PI computer adaptive testing (CAT) instrument in order to minimise respondent burden; the minimum clinically important difference of the PROMIS-PI CAT for low back pain is 3.5 points.[23 24]

The secondary outcomes are change in modified Oswestry Disability Index (ODI) score and change in patient-reported opioid use at 3 months. ODI is a legacy measure of low back pain-related disability and will facilitate comparison to extant literature. We will use the modified ODI, which contains 10 questions relating to low pain intensity and inter-reference with personal care, lifting, walking, sitting, standing, sleeping, social life, travel ability and employment,[25] with scores ranging from 0 (no disability) to 100 (maximum disability) and an estimated minimum clinically important difference of six points for acute low back pain.[26]

Patient-reported opioid use will be collected via a medication use survey instrument from our previous work.[27] In brief, this instrument lists common analgesic medications by brand and generic name and asks participants to indicate any medications taken within the last 24 hours. The 24-hour timeframe was selected to maximise accuracy in patient recall. A 'yes' response to any medication triggers an additional query asking the participant to specify the medication dose (eg, oxycodone 5 mg) and quantity (eg, four pills). Opioid use will be reported as a binary outcome and as a continuous outcome using the total opioid dose in morphine milligram equivalents.[28 29]

We will also evaluate an exploratory outcome of patient-reported prescription analgesic use via the same survey instrument, which includes opioids, benzodiazepines, skeletal muscle relaxants and gabapentinoids. Additional exploratory outcomes will include prescription analgesic filling in the Illinois prescription monitoring programme, Numeric Pain Rating Scale (NPRS), Global Rating of Change Scale (GROC), 4-item Pain Catastrophising Scale (PCS-4), 4-item Pain Self-Efficacy Questionnaire (PSEQ-4), advanced healthcare resource utilisation and ED diagnostic imaging utilisation. NPRS ranges from 0 to 10, with 0 being 'no pain at all' and 10 representing the 'worst pain imaginable;' participants will rate their average level of back pain over the last 24 hours.[30 31] GROC is a single-item survey widely used by clinicians and researchers to evaluate the overall effectiveness of therapy in low back pain.[11 32] PCS measures the degree to which an individual catastrophises in response to pain[33]; higher scores are associated with progression from acute to chronic pain.[34–36] PSEQ measures the belief that one can perform tasks or activities despite pain.[37] We will use the 4-item versions of PCS and PSEQ to minimises respondent burden.[38 39]

Advanced healthcare resource utilisation includes additional healthcare visits attended (eg, primary care doctor, orthopedist, chiropractor, physical therapist), diagnostic imaging obtained (eg, MRI), and any surgical procedures or interventions received relating to low back pain. ED diagnostic imaging utilisation, and other ED visit care variables, will be extracted from the electronic medical record using structured query language. Finally, in those patients receiving ED PT, we will query participants on the number of times they performed the recommended home exercises in the last week.

Covariates of interest will include sex, age, STarT Back Score, race/ethnicity, education level, marital and employment status, baseline activity level, household income, nature of injury, duration of low back pain episode, primary diagnosis and medications prescribed and administered during the initial ED visit. The STarT Back Score is a 9-item screening tool that categorises patients as low, medium or high risk of a poor outcome.[40]

Safety outcomes will be captured by patient report at each follow-up survey time point and will include serious adverse events (SAEs) and sinister diagnosis triggers. SAEs will include any event that is life threatening or results in death, hospitalisation, persistent disability, congenital anomaly or birth defect, or an important medical event requiring intervention to prevent one of the above. All SAEs will undergo a determination of relatedness to the study intervention on a scale of unrelated, unlikely, possible, probably and definite. At the end of study participation, we will also query the electronic medical record for potential adverse events (eg, hospitalisation) that were not captured by patient report. Sinister diagnosis triggers include patient-reported symptoms that may indicate a serious underlying aetiology of low back pain requiring urgent medical evaluation: bladder or bowel incontinence, saddle anaesthesia, debilitating motor weakness and unintentional weight loss of greater than 10%. Although these symptoms are expected to be related to the clinical condition of interest rather than intervention itself, we may become aware of these serious symptoms during our collection of follow-up outcomes. Any research team member becoming aware of a sinister diagnosis trigger will immediately alert the study principal investigator, who will then contact the participant for additional details and arrange for an immediate medical evaluation if clinically appropriate.

Power and sample size

We used 'The Shiny CRT Calculator' to explore varying assumptions on cluster size (ie, average number of participants per physician), number of clusters (or physicians) and intracluster correlation (ICC). Under the parallel-arm, 'cohort' design, with baseline measurement of the primary outcome, the calculator also allows for an assumption on correlation between baseline and follow-up. The table in the Statistical Analysis Plan (SAP, online supplemental appendix file 1) illustrates power to detect at least a 3.5 mean difference across study arms if we assume just two time points (baseline and 3 months, which we deem conservative as we will have up to seven time points of observation, including baseline) per participant with a correlation of approximately 0.50. We conservatively estimate that we will need to enrol up to 360 total participants to account for worst-case (20%)

scenario dropout for both physicians and participants. Thus, after accounting for physician and participant dropout, a final sample size of 16 physicians per arm and 7 participants per physician (n=224 total or 112 per arm) achieves 84% power to detect a mean between-arm difference of 3.5 PROMIS-PI points assuming SD of 10 points, ICC coefficient of 0.10, and a two-sided 5% level of significance.

In our pilot work, we found a small ICC (0.01–0.04),[13] indicating minimal within-physician effects that were not significant; however, we use a more conservative estimate of the ICC at 0.10 in the event that greater than anticipated within-physician effects are encountered. In the event that ICC is lower than expected or dropout rate is lower than 20%, we anticipate often over 90% power to detect a meaningful difference across arms. Since our target final analytic sample size is 224 total participants, if we can reach our target with fewer participants enrolled than 360, we will consider stopping enrolment under the guidance of the Data Safety and Monitoring Board (DSMB). We will plan to monitor dropout rates, ICC, SD, and within-participant correlation throughout the course of the trial and will formally present these data to the DSMB at regular intervals.

Analytical data set

Primary and secondary outcomes will be evaluated across arms under a modified intention-to-treat principle, whereby all participants will be included in analyses, regardless of their or their physicians' adherence to their assigned study arm, and only participants contributing at least one follow-up data point will be included (ie, we will exclude patients who provide no follow-up data). We plan to conduct a number of sensitivity analyses, including but not limited to excluding patient participants: (1) who are ultimately admitted to the hospital at the index ED visit, (2) with an alternative diagnosis after enrolment that would have deemed them otherwise ineligible (eg, discovery of kidney stones after enrolment and (3) who cross over to the study arm to which their physicians was not assigned (ie, per-protocol analysis). If this occurs frequently, we may explore instrumental variables or propensity score methods as sensitivity analyses.

Power and sample size considerations allow for some dropout at the physician and patient participant level (20%); however, in the event of large amounts of missing within-participant data (ie, more than 10% of follow-up time points), multiple imputation analyses will be explored. We will examine rates of missing data for all variables and determine whether the rates vary by participant characteristics. These summarisations will inform potential biases resulting from missing data. Mixed effects models planned for longitudinal analysis are generally robust for unbalanced data across study time points. Additional sensitivity analyses may be explored to evaluate overall trial robustness.

Data analysis plan

We will use descriptive statistics to summarise baseline patient and physician-level variables both overall and by arm. Analyses will involve normal theory methods in general, and in cases of violations of assumptions, we will consider transformation, non-parametric, and/or exact methods as appropriate. Analyses will assume a two-sided 5% significance level. We do not plan to control for multiple hypothesis tests. All primary efficacy analyses are pre-specified in the accompanying SAP; any deviations from planned analyses or post hoc analyses will be labelled as such.

In analyses for each outcome, we plan to control for the respective outcome value at baseline (ie, in an analysis of covariance approach). Analyses for the primary outcome (Y) will involve a linear mixed model (LMM) with repeated measures with fixed effects for: study arm, baseline outcome score (Y0), time point, time point-by-arm interaction and known influential predictor effects (age, sex, Keele STarT score). Inference will focus on treatment impacts for the outcome at 3 months. We will include a random physician effect to account for both within and between physician variability and also to allow for ICC estimation. The repeated measures on the same participant over time will also introduce a correlation structure across time points, providing the justification for modelling the correlation structure at the participant level over time. We will use an unstructured correlation matrix to account for the repeated measures within a participant as this has the least assumptions. If the model does not converge or parameters cannot be estimated under this unstructured covariance pattern, we will explore simpler covariance patterns using residual estimated maximum likelihood comparisons. Including repeated measures per participant will allow us to make most use of all participant data after baseline. We will use assume an unstructured covariance across time.

To evaluate efficacy, the Wald model type III test for fixed arm effect will be evaluated assuming a two-sided 5% type I error rate. The primary contrast of interest involves the comparison of the model-estimated mean outcome score at 3 months across study arms. This modelling strategy is robust to unbalanced (ie, incomplete) data across study time points. We will also provide results for unadjusted analyses (ie, without accounting for the pre-specified covariates). Analyses of additional outcomes will follow the same general analytic strategy: LMM with fixed arm, baseline outcome value, influential baseline covariate effects and a random physician effect and covariance patterns to account for repeated measures within participants.

Analyses for outcomes that are either binary or count will follow the same general approach as above; however, they will involve generalised linear mixed effects models with the appropriate distributional (eg, binomial or Poisson) and link (eg, logit or log) assumptions. Modelling the covariance structure for these outcomes may result in unstable model estimates. If this occurs, we

anticipate removing the random physician effect and including a random participant effect instead to account for correlation. We will also conduct pre-specified moderator and mediator analyses, which are detailed in the SAP as exploratory analyses.

Patient and public involvement

Patients and the public were not formally involved in the trial design or dissemination plan. However, in an ancillary study to our pilot work, we conducted focus group discussions and gauged patient receptiveness towards a hypothetical patient-randomised clinical trial of ED PT for low back pain. The resulting thematic analysis informed our selection of a cluster-randomised trial design and affirmed our choice of pain-related functioning as a patient-centred primary outcome.

Trial oversight

We have assembled an External Advisory Board (EAB) and a DSMB to inform the design of this trial and provide regular recommendations and trial oversight. The EAB is composed of five clinician–researchers in emergency medicine and PT and functions to provide advice and feedback regarding encountered trial obstacles and potential responses. The DSMB is composed of five members with expertise in clinical trial conduct and biostatistics; the DSMB receives a formal report of trial progress, including SAEs and potential relatedness and provides formal recommendations to continue, modify or discontinue the study at twice-yearly meetings. The DSMB Charter is attached as online supplemental appendix file 2.

ETHICS AND DISSEMINATION

The trial is funded by the US Department of Health and Human Services, Agency for Healthcare Research and Quality (R01HS027426) and was approved by the Northwestern University Institutional Review Board (STU00213134). Physician and patient participants will give formal written consent to study participation (online supplemental appendix file 3). In addition to this trial protocol, we plan to publish the clinical treatment algorithm used in the NEED-PT trial arm to facilitate intervention replication. The main results pertaining to the outcomes and analyses described in this protocol will be published in a timely manner following trial completion. We also anticipate publishing additional reports relevant to this trial, including but not limited to a larger analysis of ED visit characteristics among physician participants randomised to NEED-PT versus usual care. Study data will be made available on formal request to the principal investigator and completion of a data use agreement.

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Version 1.0

STATISTICAL ANALYSIS PLAN (SAP)

A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

October 8, 2021

Version 1.0

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Version 1.0

STATISTICAL ANALYSIS PLAN (SAP)

A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

Principal Investigator: Howard S. Kim, MD MS
Statistical Team: Jody D. Ciolino, PhD; Jacob M. Schauer, PhD

1. INTRODUCTION

This document outlines the proposed analyses for the NEED-PT study. Briefly, NEED-PT is a physician-randomized (i.e., physicians serve as clustering or randomization units) trial evaluating efficacy of an embedded emergency department (ED) physical therapist in comparison to usual care. Individual ED patients will be consented and enrolled during their index ED visit and will follow the randomization assignment of their treating physicians. The primary outcome data will be analyzed at three months after the index ED visit, with additional data collection up to 12 months for evaluation of longer-term effects and exploratory endpoints.

Study Aims
The overarching study aims are as follows. **This SAP will focus on the details for Aim 2 analyses, which will guide the reporting of the primary study findings**. We reserve details of analyses surrounding additional aims for separate document(s):

Aim 1: Develop and field-test the Northwestern "Embedded" ED Physical Therapy (NEED-PT) intervention protocol for the routine co-evaluation of all ED patients with acute low back pain.
We will co-locate the ED physical therapist with the ED physician as part of the primary treatment team in order to remove biases in treatment selection and allow for earlier integration of ED-PT into patient care. A formalized protocol will enhance intervention fidelity in Aim 2 and facilitate dissemination of our care model.

Aim 2: Conduct a single-center, physician-randomized trial (n=40) comparing NEED-PT to usual care among ED patients (n=360) with acute low back pain to evaluate a primary outcome of pain-related functioning at three months and a secondary outcome of opioid use at three months.
H1: Patients receiving NEED-PT will report greater improvement in pain-related functioning compared to patients receiving usual care, as measured by average PROMIS Pain-Interference score
H2: Patients receiving NEED-PT will use fewer daily opioids on average.

Aim 3: Compare rates of diagnostic imaging utilization for ED visits with low back pain among ED physicians randomized to NEED-PT versus usual care.
H1: ED physicians randomized to NEED-PT will have a lower rate of diagnostic imaging utilization for low back pain compared to ED physicians randomized to usual care.

For patients enrolled in the study, study time points include baseline assessment (completed at the index ED visit), Week 1, Month 1, Month 2, Month 3 (primary endpoint), Month 6, and Month 12.

2. STUDY OUTCOMES

Primary Outcome
The primary efficacy outcome is **PROMIS-Pain Interference Score (PROMIS-PI)** three months after the index ED visit. PROMIS-PI measures the self-reported consequences of pain on relevant aspects of a person's life, including social, cognitive, emotional, physical, and recreational activities. We will use the computer-adaptive format to minimize respondent burden. Scores are standardized to the general U.S. population, with a score of 50 representing the population mean and a standard deviation of 10 points. The time frame of interest for the PROMIS-PI is "in the past 7 days," meaning that participants provide responses based on their symptoms over the last week. The minimum clinically important difference for low back pain is in the range of 3.5-5.5 points. We will treat this variable as continuous in analyses.

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Secondary Outcomes

Secondary efficacy outcomes include:

1) **Oswestry Disability Index (ODI)** at three months. *ODI* is a disease-specific instrument that contains 10 questions relating to low back pain intensity, personal care, lifting, walking, sitting, standing, sleeping, social life, traveling, and employment/homemaking. The ODI score ranges from zero (no disability) to 100 (maximum disability), with an estimated minimum clinically important difference of six points for acute low back pain. The time frame of interest for the ODI is "today," meaning that participants provide responses based on their current symptoms on the day of survey response. The modified ODI replaces an item from the original ODI pertaining to sex life with a new item pertaining to employment/homemaking. We expect this outcome to be largely correlated with PROMIS-Pain Interference. We will treat this variable as continuous in analyses.
2) **Patient-Reported Opioid Use** at three months. This will be collected using a customized instrument assessing whether participants have taken any opioid medication in the last 24 hours. The 24-hour timeframe was selected to maximize accuracy in patient recall and has been used previously. In brief, opioid medications are listed by brand and generic names; a "yes" response to any medication triggers an additional query asking the participant to specify the medication dose (e.g., oxycodone 10mg) and quantity (e.g., four pills), allowing for standardization by morphine milligram equivalents (MME). We anticipate treating this variable as either count or a binary (any dose vs. none), or continuous (MME) for analyses.

Exploratory Outcomes

We expect the following outcomes to be related to the primary and the major secondary outcomes of interest. We deem the more exploratory in nature, and they thus carry less weight in analyses and overall inferences regarding efficacy of intervention.

1) **Opioid Prescription Filling** will be queried in the state prescription monitoring database. We anticipate treating this variable as count, binary, or continuous (MME).
2) **Patient-Reported Prescription Analgesic Use** in the last 24 hours will be collected using the same customized instrument described above for opioid use. Prescription analgesics include: opioids, benzodiazepines, skeletal muscle relaxants, and gabapentinoids. We anticipate treating this variable as either count or binary.
3) **Prescription Analgesic Filling** will be queried in the state prescription monitoring database. Prescription analgesics include: opioids, benzodiazepines, skeletal muscle relaxants, and gabapentinoids. We anticipate treating this variable as either count or binary.
4) **Numeric Pain Rating Scale (NPRS)** measures pain intensity from 0 to 10 and is easily understood by laypersons, clinicians, and researchers. We will assess a single item relating to average pain intensity over the last 24 hours. We plan to treat this as a continuous outcome, but we anticipate requiring transformation or nonparametric analyses, as this variable will likely be skewed and exhibit flooring / ceiling effects.
5) **Global Rating of Change (GROC)** is a single-item survey widely used by clinicians and researchers to quantify functional disability in low back pain and evaluate the overall effectiveness of therapy. This item ranges from zero (a very great deal worse) to 14 (a very great deal better). We plan to initially treat this measure as continuous, but we anticipate exploring this outcome as a count variable, requiring transformation, or using nonparametric analyses.
6) **Pain Catastrophizing Scale (PCS-4)**. The original PCS is a 13-item survey measuring the degree to which an individual catastrophizes in response to pain. PCS scores correlate closely with pain intensity and disability over time; higher PCS scores are associated with progression from acute to chronic pain. We will utilize the brief 4-item PCS measure containing original items 3, 6, 8, and 11 to reduce respondent burden. We will treat this variable as continuous in analyses.
7) **Pain Self-Efficacy Questionnaire (PSEQ-4).** The original PSEQ is a 10-item survey measuring the confidence with which individuals can do things despite pain. We will utilize the brief 4-item PSEQ measure containing original items 4, 6, 8, and 9 to reduce respondent burden. We will treat this variable as continuous in analyses.
8) **Advanced Healthcare Resource Utilization.** We will assess the proportion of participants who utilized advanced healthcare resources for low back pain after their index ED visit, defined as advanced imaging (e.g., magnetic resonance imaging) or procedures/surgery (e.g., epidural steroid injection, lumbar discectomy).

9) **ED Diagnostic Imaging Utilization.** We will assess the proportion of ED visits in which diagnostic imaging of the lower back was performed, including plain radiography, computed tomography, and magnetic resonance imaging.
10) **Additional outcomes (not discussed in detail in this SAP) that are a part of the third study aim include:** ED length of stay, ED disposition (admit, observation, discharge), total costs/charges.

3. DEMOGRAPHICS AND BASELINE ASSESSMENTS

The following are specific demographic / baseline assessments of interest for analyses. **Primary analyses will adjust for these covariates as we anticipate they will influence outcome**. We plan to report both model-adjusted and simple unadjusted intervention effect estimates:

1) Sex
2) Age
3) Keele STarT Back Screening Tool: a nine-item survey which assesses risk for progression to chronic base pain

Additional demographics and clinical characteristics we plan to collect and summarize (i.e., we **do not plan to include as covariates in analyses**) include:

1) Race / ethnicity
2) Education level
3) Marital status
4) Employment status
5) Activity level at work for those that are working at baseline
6) Income level
7) Physical activity level according to self-report
8) Nature of injury
9) Length of pain at baseline
10) Primary diagnosis
11) Medications administered / prescribed during initial ED visit

Note that some additional exploratory analyses may examine these additional variables as covariates and/or effect modifiers as well. We will label any exploratory analyses involving additional potential covariates as post hoc in any dissemination materials.

4. DATA STORAGE

Data will be collected and managed using Research Electronic Data Capture (REDCap) housed at Northwestern University's Clinical and Translational Sciences Institute (CTSA), NUCATS (1, 2) . REDCap is a secure, web-based application designed for research studies that provides an intuitive interface for validated data entry, audit trails for tracking data manipulation and export procedures, and automated export procedures for seamless data downloads to common statistical packages, and procedures for importing data from external sources. Individualized REDCap survey links will be sent to participants using Mosio, a secure text messaging research platform that is 21 CFR Part 11 compliant and integrates with REDCap.

5. RANDOMIZATION METHODS

We plan for equal allocation (1:1) of physicians across study arms; thus, there will be inevitable imbalance in patient numbers across study arms. Physicians will be randomized to either the intervention (NEED-PT) or "control" (usual care). Physicians randomized to the NEED-PT intervention will have a physical therapist assigned to their treatment team who will automatically evaluate all patients with low back pain. Physicians randomized to "usual care" will not have a physical therapist assigned to their treatment team, and their patients with low back pain will not be automatically evaluated by the physical therapist. Due to the inherent risk of cluster-level (i.e., physician-level) covariate imbalance between study arms in cluster-randomized trials, we will employ covariate-constrained randomization techniques to control for possible imbalance in key physician-level characteristics. Covariate-constrained randomization methods tend to ensure the most efficient

control over covariate imbalance between study arms at randomization (3, 4). With 40 total physicians, there are over 137 billion ways (40 choose 20) in which we can achieve equal allocation of physicians across study arms. The constrained randomization procedure will involve:

1) Enumerating a 10 thousand possible allocation schemes at the 1:1 physician allocation ratio.
2) Calculating imbalance in the following baseline physician-level variables across study arms for each of the schemes simulated in step 1:
    a. Physician gender
    b. Physician years' experience (since first year of residency)
    c. Physician race
    d. Physician opioid prescription rate
    e. Number of "fast track" zone shifts for a physician per month, on average – fast track shifts are those with the highest likelihood of receiving low-back pain patients
        i. This variable is highly correlated with the number of day shifts a physician tends to have per month
        ii. It is also correlated with the mean number of patients the physician sees per hour
        iii. While we will control imbalance in the randomization algorithm for this "fast track" zone variable, we anticipate reporting summary statistics on day shifts and patients per hour
3) Constraining the randomization space to a subset of allocation schemes that do not surpass some threshold of "allowable" imbalance for each of the variables (a-e in step 2) above. The thresholds will be guided by the following restrictions; however, the distribution of these physician-level variables may require modification(s) to these thresholds. Any updates will be documented in a later version of this SAP:
    a. Physician gender counts may not differ by more than two for any one category across study arms.
    b. Mean number of years' experience may not differ more than one year.
    c. Physician race will likely require dichotomization into White vs. Minority for randomization. We will not allow physician racial category counts to differ by more than two for any one category across arms.
    d. Mean physician opioid prescription rate may not differ by more than 0.5 standard deviation units across study arms.
    e. Mean number of orange or red zone shifts may not differ by more than 0.25 across study arms.
4) Of the possible allocation schemes meeting the criteria outlined in Step 3, randomly select one for implementation in the study.

6. STATISTICAL METHODS

We plan to use descriptive statistics to summarize baseline patient and physician-level variables both overall and by arm. We will use mean±standard deviation (or median and interquartile range [IQR] as appropriate) for continuous variables and frequency / percentage for categorical variables. Specifically, we will summarize age, sex, Keele STarT score, baseline patient-reported outcome scores (PROMIS-PI and ODI), analgesic medication prescription at ED discharge, and the variables listed above. Analyses will involve normal theory methods in general, and in cases of violations of assumptions, we will consider transformation and / or nonparametric / exact methods as appropriate.

Analyses will assume a two-sided 5% significance level. All primary efficacy and safety analyses will be pre-specified as outlined in this SAP, and deviations from planned analyses or post hoc analyses will be labeled as such in any reports or dissemination materials. We do not plan to control for multiple hypothesis tests.

In analyses for each outcome, we plan to control for the respective outcome value at baseline (i.e., in an analysis of covariance [ANCOVA] approach). Analyses for the primary outcome (Y) will involve a linear mixed model (LMM) with repeated measures with fixed effects for: study arm, baseline outcome score (Y0), timepoint, timepoint-by-arm interaction, and known influential predictor effects (age, sex, Keele STarT score). Inference will focus on treatment impacts for the outcome at three months. We will include a random physician effect to account for both within and between physician variability and also to allow for estimation of the intra-cluster correlation coefficient (ICC). The repeated measures on the same participant over time will also introduce a correlation structure across time points, providing the justification for modeling the correlation structure at the

participant level over time. We will use an unstructured correlation matrix to account for the repeated measures within a participant as this has the least assumptions. If the model does not converge or parameters cannot be estimated under this unstructured covariance pattern, we will explore simpler covariance patterns using residual estimated maximum likelihood (REML) comparisons. Including repeated measures per participant will allow us to make most use of all participant data after baseline. We will use assume an unstructured covariance across time.

To evaluate efficacy, the Wald model type III test for fixed arm effect will be evaluated assuming a two-sided 5% type I error rate. The primary contrast of interest to address the primary research aims involves the comparison of the model-estimated mean outcome score at three months (T4) across study arms. This modeling strategy is robust to unbalanced (i.e., incomplete) data across study time points. We will also provide results for unadjusted analyses (i.e., without accounting for the pre-specified covariates). Analyses of additional outcomes will follow the same general analytic strategy: LMM with fixed arm, baseline outcome value, influential baseline covariate effects, and a random physician effect and covariance patterns to account for repeated measures within participants. We chose to incorporate baseline outcome as a covariate in the model, rather than as a time point, based on clinical reasoning. As these baseline values (e.g., PROMIS-PI score at the index ED visit) are assessed pre-intervention and primary analyses aim to assess outcome(s) as follow-up accounting for pre-intervention state. Incorporating this baseline value in the analytic model as a fixed effect will increase precision and reduce bias on the intervention effect estimate for primary outcome at the time point of interest as the baseline value will likely be highly correlated with outcome at follow-up (previous data: $p<0.001$ for both PROMIS and ODI).

Residual diagnostics will assess model fit and assumptions, and in the case of violation, we will explore transformations / nonparametric methods as indicated above. In the event of poor model fit, we may explore different distributional assumptions as appropriate (e.g., Poisson for count or rate data) with the corresponding canonical link (e.g., log) function. As above, we will assess model fit via residual diagnostics and may consider transforming or nonparametric methods as needed.

Analyses for outcomes that are either binary or count will follow the same general approach as above; however, they will involve generalized linear mixed effects (GLMMs) models with the appropriate distributional (e.g., binomial or Poisson) and link (e.g., logit or log) assumptions. Modeling the covariance structure for these outcomes may result in unstable model estimates. If this occurs, we anticipate removing the random physician effect and including a random participant effect instead to account for correlation.

<u>Exploratory Analyses</u>

In addition to repeating the above analyses with exploratory outcomes, we will conduct exploratory analyses to study effects among subgroups of patients (moderator analyses) and examine the potential impact of PT use among patients in the control arm.

Planned moderator analyses will include the following moderators:

1. Opioid naivete as measured by whether patients report taking opioids within the last 24 hours at their index ED visit or have a history of opioid prescription filling in the Illinois prescription monitoring program within the last 3 months.
2. Initial symptom burden measured as “moderate/severe” if their baseline measures of PROMIS pain scores are ≥60 or their STarT score registers as “high risk,” defined as a subscore ≥4 (questions 5-9).
3. Age ≥ 65 years old
4. Primary treatment classification, as per the clinical care protocol (directional preference, traction, stabilization, manipulation, nociplastic presentation)

Analyses will focus on PROMIS-PI scores measured three months after patients’ index visits, as well as ODI scores and opioid use (proportion using an opioid within the last 24 hours) at the same time point. Analyses will involve generalized linear models with appropriate link functions (identity for PROMIS-PI and logit for opioid use) that include fixed effects for baseline measures of the outcome of interest, treatment assignment, a moderator variable, and a treatment-moderator interaction. As above, PROMIS-PI will be modeled with standard normality assumptions, which will be evaluated via residual diagnostics and appropriate transformations will be used as necessary. Separate models will be fit for each outcome and moderator. Tests for the treatment-moderator interaction will be two-sided with a 5% type I error rate, and we will report point

estimates and 95% confidence intervals. For the logistic regression involving opioid use, we will use Wald confidence intervals and Wald tests. We will not make multiple comparison adjustments.

Mediation analyses will focus on PCS and PSEQ as possible mediators. Our hypotheses are that embedding a PT in the ED can impact patients downstream pain catastrophizing and self-efficacy which will in turn lead to lower reported pain and less frequent opioid use. Our key dependent variables will be PROMIS-PI and opioid use at three months after the index visit. PCS and PSEQ measured at one month will be the mediators of interest. We will use a nonparametric approach to analyses, running separate models for each outcome and mediator (5). In addition, we will examine the possible correlation between mechanisms by using a joint nonparametric estimation framework (6).

In addition, we will conduct a complier analysis. Based on pilot data, we expect some patients in the control arm will receive a discretionary PT consultation as part of usual care. These consultations will be operationally different from those in the treatment group, as the PT will not be embedded with the care teams in the control arm. Conversely, it is possible some treatment arm patients may not receive an embedded PT consult, though we expect this will be rarer. Since we hypothesize that PT consultation will play a large role in this intervention's effectiveness, we propose to examine the impact of these differential PT consultations (discretionary, embedded) in two ways. First, we will re-create the proposed confirmatory analyses excluding control patients receiving a PT consultation and intervention arm patients who do not. Second, we will use a generalized mediation analysis that includes all patients that treats receipt of a PT consult as a mediator to estimate the direct and indirect effects of treatment assignment and PT consultation. This mediation analysis will focus on PROMIS-PI at three months post-index visit as the outcome of interest, and use a generalized nonparametric estimation approach (5).

7. ANALYTIC DATASET

Primary and secondary outcomes will be evaluated across arms under a modified intention-to-treat (mITT) principle, (1) whereby all participants will be included in analyses, regardless of their or their physicians' adherence to their assigned study arm, and (2) only participants contributing at least one follow-up data point will be included. That is, we will exclude patients who are lost to follow-up before Week 1. Sensitivity analyses will be detailed after data collection; however, we plan to conduct sensitivity analyses that would involve:

1) Excluding patients who are ultimately admitted to the hospital after their ED visit.
2) Excluding patients with an alternative diagnosis after enrollment that would have deemed them otherwise ineligible (e.g., discovery of kidney stones or shingles after enrollment).
3) Excluding patients who cross over to the study arm to which they were not assigned (i.e., per-protocol analysis). If this occurs frequently, we may explore instrumental variables or propensity score methods as sensitivity analyses.

Power and sample size considerations allowed for some missing data (20%); however, in the event of large amounts of missing data (i.e., more than 10%), multiple imputation analyses will be explored. We will examine rates of missing data for all variables and determine whether the rates vary by participant characteristics, etc. These summarizations will inform potential biases resulting from missing data. Mixed effects models planned for longitudinal analysis are generally robust for unbalanced data across study time points. Additional sensitivity analyses may be explored to evaluate overall trial robustness. These analyses will again serve as sensitivity analyses to the primary analyses, and the details of these analyses will be documented at the time of analyses (if needed).

8. POWER AND SAMPLE SIZE CONSIDERATIONS

Power calculations focus on the primary endpoint of PROMIS-PI at three months, and we desire adequate (at least 80%) power to detect the minimum clinically important PROMIS-PI score difference of 3.5-5.5 points as previous literature suggests (7). If we assume a standard deviation of 10 points, which is the defined standard deviation of PROMIS-PI, this corresponds to a desired minimal detectable effect size of d=0.35 standard deviation unit difference across arms. Power considerations also account for a 20% drop-out rate for physician clusters (e.g., physician leaves the practice or refuses participation after randomization) and a 20% lost to follow-up rate among recruited participants. We used "The Shiny CRT Calculator" to explore varying assumptions on cluster size (i.e., average number of participants per physician), number of clusters/physicians, and ICC. Under the parallel-arm, "cohort" design, with baseline measurement of primary outcome (PROMIS),

the calculator also allows for an assumption on correlation between baseline and follow-up. The table below illustrates power to detect at least a 3.5 mean difference across study arms if we assume just two time points (baseline and three months, which we deem conservative as we will have up to seven time points of observation, including baseline) per participant with a correlation between the two of approximately 0.50. We conservatively estimate that we will need to enroll up to 360 total participants to account for worst-case (20%) scenario dropout for both physicians and participants. **Thus, after accounting for physician and participant dropout, a final sample size of 16 physicians per arm and 7 participants per physician (n=224 total or 112 per arm) achieves 84% power** to detect a mean between-arm difference of 3.5 PROMIS-PI points assuming standard deviation of 10 points, ICC of 0.10, and a two-sided 5% level of significance. In our pilot work, we found a small ICC (0.01-0.04), indicating minimal within-physician effects that were not significant; however, we utilize a more conservative estimate of the ICC at 0.10 in the event that greater than anticipated within-physician effects are encountered. In the event that ICC is lower than expected or dropout rate is lower than 20%, we anticipate often over 90% to detect a meaningful difference across arms. Similar effect size in secondary outcomes (e.g., 0.35 standard deviation units difference in ODI across arms) are also detectable with at least 80% power under similar assumptions. Additionally, we plan to conduct secondary longitudinal analyses involving multiple time points per participant (i.e., more data observations) using likelihood-based methods that are robust to missing data. Therefore, we anticipate adequate power to evaluate differences across arms in outcome trajectories. **Since our target final analytic sample size is 224 total participants, if we can reach our target with fewer participants enrolled than 360, we will consider stopping enrollment.** We will plan to monitor dropout rates, ICC, standard deviation, and within-participant correlation throughout the course of the trial, and we will seek advice from the External Advisory Board and DSMB as we make any interim decisions on stopping enrollment prior to the planned 360 participants.

ICC	Physicians (Total)	Physician % Dropout	Average N participants per Physician	Participant % Dropout	Power: Mean 3.5-point Difference
0.01	40	0	9	0	97%
	40	0	8	5 to 10	95%
	40	0	7	15 to 20	92%
	38	5	9	0	96%
	38	5	8	5 to 10	94%
	38	5	7	15 to 20	90%
	36	10	9	0	95%
	36	10	8	5 to 10	92%
	36	10	7	15 to 20	89%
	34	15	9	0	94%
	34	15	8	5 to 10	91%
	34	15	7	15 to 20	87%
	32	20	9	0	92%
	32	20	8	5 to 10	89%
	32	20	7	15 to 20	85%
0.05	40	0	9	0	96%
	40	0	8	5 to 10	94%
	40	0	7	15 to 20	91%
	38	5	9	0	95%
	38	5	8	5 to 10	93%
	38	5	7	15 to 20	90%
	36	10	9	0	94%
	36	10	8	5 to 10	91%
	36	10	7	15 to 20	88%
	34	15	9	0	93%
	34	15	8	5 to 10	90%

	34	15	7	15 to 20	86%
	32	20	9	0	91%
	32	20	8	5 to 10	88%
	32	20	7	15 to 20	84%
0.10	40	0	9	0	96%
	40	0	8	5 to 10	94%
	40	0	7	15 to 20	91%
	38	5	9	0	95%
	38	5	8	5 to 10	93%
	38	5	7	15 to 20	90%
	36	10	9	0	94%
	36	10	8	5 to 10	92%
	36	10	7	15 to 20	88%
	34	15	9	0	93%
	34	15	8	5 to 10	90%
	34	15	7	15 to 20	86%
	32	20	9	0	91%
	32	20	8	5 to 10	88%
	32	20	7	15 to 20	84%

We will not need to adjust sample size calculations for the covariate-constrained randomization approach, as this merely controls imbalances across arms on physician-level (i.e. cluster) covariates, such as physician productivity (e.g., patients seen per hour) while preserving the 1:1 study arm allocation ratio. Therefore, controlling imbalance on these physician-level covariates is intended to translate to both equal allocation of physician participant numbers and comparable participant-level covariate distributions across arms. As mentioned above, we anticipate that this increased control over imbalance coupled with the analytic strategies will increased precision and reduce bias in estimating intervention effects. Since the amount of increased precision is unknown, we deem the sample size and power calculations conservative.

9. TECHNICAL DETAILS

The SAP is subject to version control, and we anticipate modifications to analytic plans be documented herein. As in any study, the analytic plan may change due to assumption violations, logistical issues, unexpected empirical distributions of study outcomes, or a combination thereof. In these cases, the SAP will be updated accordingly. All analyses will be performed via SAS version 9.4 or higher (The SAS Institute; Cary, NC) or R version 4.0.4 or higher (The R Foundation for Statistical Computing platform). Table and figure formatting and style may be dictated by mode of dissemination or specific target journal(s) for results dissemination.

10. TIMELINE FOR ANALYSES

The analysis plan does not include any formal interim statistical analyses involving hypothesis testing or any pre-specified stopping criteria for efficacy or futility on primary or secondary outcomes. Interim reports to the study team, external advisory board, or Data and Safety Monitoring Board (DSMB) will consist of process measures such as protocol adherence, missing values, missing forms, etc. We also plan to use simple descriptive statistics on primary and safety outcomes of interest in aggregate (not stratified by arm). Regular bi-weekly meetings with the study team will utilize central statistical monitoring techniques as a method of quality control and quality assurance for trial data on an ongoing basis. We foresee the DSMB requiring specific data listings or summarizations, but these will be specified at the time of the relevant DSMB meeting(s); at this time, however, we do not plan for formal statistical analyses involving hypothesis testing for DSMB interim review.

To preserve the integrity of the study, no formal statistical analyses will occur until the REDCap database has been locked and all known queries/discrepancies resolved; the date of database lock will be documented.

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DSMB Charter

A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

April 27, 2021

Version 1.0

IRB Number: STU00213134

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DATA AND SAFETY MONITORING BOARD (DSMB) CHARTER

A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

Principal Investigator: **Howard S. Kim, MD MS**
Biostatistician Co-Investigators: **Jody D. Ciolino, PhD; Jacob M. Schauer, PhD**
Clinician Co-Investigator: **Danielle M. McCarthy, MD MS**

I. INTRODUCTION

The purpose of this charter is to define the responsibilities of the DSMB and provide written guidance and documentation of the DSMB procedures. In essence, it serves as a plan of operations for the DSMB. The DSMB may refer to the International Conference on Harmonization (ICH) E6 and E9 documents in addition to the FDA Guidance on the Establishment and Operation of Clinical Trial Data Monitoring Committees for reference.

NEED-PT is a single center physician-randomized trial of an embedded emergency department (ED) physical therapy intervention for patients with acute low back pain. Individual physicians will be consented to undergo randomization to either the NEED-PT intervention (i.e., an embedded physical therapist on their primary treatment team) or usual care; patients will be individually consented and enrolled and allocated to the study group of their treating physician. The primary outcome is pain-related functioning as measured by PROMIS-Pain Interference scores over three months of follow-up; the main secondary outcome is patient-reported opioid use.

The trial is sponsored by the Agency for Healthcare Research and Quality (AHRQ) through grant award #R01HS027426; Principal Investigator: Howard S. Kim, MD MS. The investigator team and coordinating activities for the trial are located at the Northwestern University Data Analysis & Coordinating Center (NUDACC) in the Feinberg School of Medicine.

The Data and Safety Monitoring Board (DSMB) provides independent safety review and trial guidance during the course of the ongoing trial. This document outlines the formal operating procedures for the NEED-PT DSMB.

The DSMB will review safety data and primary outcome data summarizations both overall and by study arm at a minimum of every six months during the conduct of the trial. The DSMB will collectively determine whether the overall safety and feasibility of the trial remain acceptable given the information provided in the interim reports, during formal DSMB meetings, and in any communication regarding the trial in between meetings.

Specifically, the DSMB will review summary reports of all serious adverse events (SAEs), and they may review individual cases in detail if deemed appropriate or necessary to address potential safety concern(s). The investigators, sponsor representative(s), or combination may also request additional *ad hoc* DSMB review should a concern arise. The DSMB may recommend a new course of action for one or both study arms or may suggest other appropriate courses of action to address general study safety issues which may arise. If warranted, the DSMB may recommend at any time that the entire protocol be suspended temporarily or terminated permanently. These recommendations will be directed to the principal investigator (Dr. Howard Kim), who has the responsibility to accept, reject, or modify DSMB recommendations. Dr. Kim will ensure AHRQ and Northwestern University's

Institutional Review Board (IRB) receive the written DSMB recommendations and any written decisions to accept / reject / modify them.

II. ORGANIZATION OF THE DSMB

Composition of the DSMB

The DSMB membership includes **five voting members**:

1. Chair: Dr. Timothy Platts-Mills, MD, MSc
2. Dr. Rogelio Coronado, PT, MPT, PhD
3. Dr. Janel Fedler, PhD
4. Dr. Dave Lu, MD, MSCI, MBE
5. Dr. Diana Wilkie, PhD, RN

There will also be a designated DSMB Secretary to take minutes during portions of the meeting in which the study team investigators are not present (i.e., closed session); during all other portions of the meeting the study team will have a research coordinator available to take minutes.

Board members may not participate in the NEED-PT study as co-investigators, study physician participants, or study patient participants.

Conflicts of Interest

DSMB members must be free of any financial, intellectual, or other conflicts of interest. The Department of Health and Human Services Guidance on Financial Conflicts of Interest may be referenced for further information (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/financial-conflict-of-interest/index.html). Prior to initiation of DSMB service, all members will affirm they either do not have or will declare any relevant conflicts of interest. At the start of each DSMB meeting, all members will disclose any updates or changes to conflicts of interest. If a change in conflict of interest arises at any point during a member's service on the NEED-PT DSMB, then the member should notify the principal investigator, who may consider finding a replacement for that member. Updates to the charter and membership will be made as needed.

III. RESPONSIBILITIES AND FUNCTIONS OF THE DSMB

This DSMB will be coordinated by the NEED-PT study team. Each DSMB member will receive a $250 (US) honorarium for participation after each scheduled meeting. Meetings will last on average approximately two hours, and members will receive relevant materials approximately one week in advance of each meeting.

A. Initially, the DSMB is responsible for:
   1. Finalizing and signing this DSMB Charter with approval of the NEED-PT study team.
   2. Reviewing the NEED-PT study protocol, providing comment as appropriate, and approving the protocol prior to initiating enrollment.
   3. Defining, with input from the NEED-PT study team, safety and related parameters to be monitored, frequency of committee monitoring reviews and interim safety analyses, methods for review, statistical methodologies, quorum of Committee members, and establishing criteria for making recommendations to the NEED-PT study team.
   4. Documenting and approving the procedures defined above.

B. The DSMB will review study data and study safety events every six months. The designated DSMB secretary will take minutes during the closed sessions and report them to Drs. Kim and

Ciolino, who will disseminate meeting minutes and recommendations to AHRQ, IRB, and the NEED-PT study team as appropriate.

C. The DSMB will recommend one of the following actions to the investigators, in writing, following each interim data review:
   1. Continue the study according to the protocol and any related amendments.
   2. Modify the study protocol. Modifications may include, but are not limited to: changes in inclusion/exclusion criteria, frequency of visits or safety monitoring, alterations in study procedures, changes in duration of observation or follow-up.
   3. Suspend enrollment or discontinue the study.

D. After each meeting, the DSMB will issue their recommendations and minutes via a letter signed by the DSMB Chair within seven business days of receipt of the draft minutes from the NEED-PT study team. These recommendations will also be included in the final open minutes and distributed by email to the DSMB members and the NEED-PT study team.

E. In between scheduled DSMB meetings, if an SAE that meets relevant criteria (unexpected, SAEs that are determined to be possibly, likely, or definitely related to the study intervention) occurs (see DSMP), then the DSMB members will receive a narrative and relevant information surrounding that event (email is an acceptable mode of communication for these instances). The investigators will request the DSMB members review these SAEs and determine whether they merit a formal meeting, and the DSMB members may make any recommendations as in Part C above. A quorum vote via email may suffice as documentation for recommendations following these events unless the DSMB Chair or the investigators call(s) for a formal meeting.

IV. RESPONSIBILITIES AND FUNCTIONS OF THE NEED-PT STUDY TEAM

The statistical team, including Drs. Jody Ciolino and Jacob Schauer, in collaboration with the DSMB secretary, is responsible for the coordination of the DSMB activities and materials including the following items. While this is not a blinded study, every effort will be made to conceal allocations on data collection tools and outcome assessments, and data in general will not be summarized by study arm. Thus, we will ensure 'blinding' to the extent possible, especially for Dr. Kim and the co-investigators. With this in mind, the statistical team will be unblinded, and thus serve as the reporting statistician(s) to the DSMB. Drs. Ciolino and Schauer will oversee the preparation of the data to be reviewed by the DSMB and the following:

A. Recommendation of DSMB members and providing the initial DSMB Charter Draft to the members for their review.

B. Management of transfer of clinical safety data and relevant study data to the DSMB for review. Drs. Ciolino and Schauer (NUDACC-affiliated statisticians) will coordinate and oversee preparation of the interim reports containing summaries of the safety and outcome data pertinent to DSMB review as outlined in the Data and Safety Monitoring Plan (DSMP). Approximately one week prior to each DSMB meeting, the DSMB will receive two reports:
   1. An **open report** that will NOT contain any unblinded information or summarizations.
   2. A **closed report** that will contain interim summarizations grouped by 'masked' study arm (e.g., 'Arm A' and 'Arm B', while not disclosing in writing what 'A' and 'B' signify). A NUDACC representative will verbally disclose the meaning of these codes during the DSMB meeting closed session upon request from the DSMB.

   Each report will be password protected, and the DSMB members will be asked to destroy / delete each report within seven business days after each meeting. NUDACC will maintain all

interim reports in a secured location with restricted access to study team members only (and unblinded team members only for closed reports) on Northwestern University's protected servers.

C. *Ad hoc* data summaries may be prepared upon written request by the DSMB to address a specific safety concern (email is an acceptable method of communication). Ad hoc reports will be prepared by the NEED-PT study team. Drs. Ciolino and Schauer will oversee preparation of any unblinded ad hoc reports.

D. We do not anticipate that there will be serious adverse effects resulting from this non-invasive physical activity and behavioral intervention for low back pain. However, given the natural history of non-specific low back pain we expect to discover a baseline level of serious adverse events in both study arms (e.g., hospitalization, surgery) during the one-year of follow-up. We will plan to summarize and report adverse events and serious adverse events at each regularly scheduled DSMB meeting.

E. Serious Adverse Events determined to be possibly, likely, or definitely related to the study intervention will be reported to the DSMB within seven days of the NEED-PT study team becoming aware of these SAEs. Dr. Kim and Dr. Ciolino will oversee preparation of these interim SAE narratives and any additional data shared with the DSMB (e.g., laboratory data or clinical history as appropriate). Refer to Section III.E above and Section II of the DSMP for additional details.

F. Maintaining DSMB Charter, meeting minutes, and recommendation documentation in secure locations on Northwestern University's servers.

G. Maintaining the DSMB files and archives of electronic data sets and programs used to generate each summary report.

H. Making resources available in a timely fashion to the DSMB as required to carry out its designated functions including:
   1. Study documents (e.g., protocols, manuals of procedures, consent, protocol amendments).
   2. Study data.
   3. SAE reports.
   4. Additional medical records and supporting documentation as requested to address specific safety concerns.
   5. Other data/information as requested in writing by the DSMB.

CONDUCT OF DSMB MEETINGS

Scheduled Meetings

An initial meeting of the DSMB will be held before any participant enrollment in the study occurs in order for the members to finalize the DSMB charter, establish a meeting schedule, review the study protocol, and study/participant termination guidelines.

The DSMB will meet twice per year (every six months) once study enrollment begins. DSMB meetings will be conducted via teleconference. The actual frequency of convened DSMB meetings and conference calls may vary depending on participant recruitment, safety concerns, DSMB member schedules, and potentially other factors. Ad hoc meetings may occur if the study team, IRB, sponsor, or any other party related to the NEED-PT study conduct and safety deems it appropriate.

Voting
DSMB members vote on all recommendations to be submitted to the PI. To vote, a DSMB member must be present in person or over telephone/video conferencing at convened scheduled meetings. In rare circumstances, if a DSMB member cannot attend a meeting, then he/she may provide his/her vote after reviewing the DSMB interim report(s) and the draft meeting minutes following the meeting. In these instances, the meeting minutes and recommendations will be finalized after the absent member has provided his/her responses. The absent member must provide his/her absent vote and the meeting minutes must be finalized by the DSMB within seven business days of receipt of the draft minutes from the NEED-PT study team. All members present must reach a consensus at any meeting in order to pass a proposal, motion, or recommendation to the PI.

Quorum
A minimum of three DSMB members, including the DSMB chair, constitutes a quorum for the purposes of voting on recommendations to the NEED-PT Study Team.

Procedures for Communicating DSMB Recommendations to the NEED-PT Investigators
The DSMB chair will send voted and passed DSMB recommendations to the PIs in writing within seven working days of the meeting at which the recommendation was formulated and passed. The PI will have the responsibility to communicate final recommendations to the NEED-PT Study Team, IRB, and AHRQ, if required.

Minutes
Meeting minutes will be kept for each meeting of the DSMB, by a member of the NEED-PT study team for the open session and by the designated DSMB secretary for the closed session. The PI and DSMB chair will keep these meeting minutes on file for the duration of the study. If necessary, two separate versions of the minutes will be generated: 1) Open Minutes will be completely blinded to study arms; 2) Closed Minutes may contain partially unblinded information, and will be distributed to DSMB members and the unblinded statisticians (NUDACC).

Meeting Format
With the exception of the initial meeting to review the Charter and study documents, meetings will follow the same general format:

1. **Open session**: During the initial open portion of a meeting, the investigators and DSMB members will first affirm they do not have any conflicts of interest and disclose any relevant updates to their conflicts of interest. Then, the investigators will briefly review the study data and progress as outlined in the open DSMB report, and the investigators will be available for questions from DSMB members.
2. **Closed session**: During the closed session of the meeting, the DSMB members and unblinded statisticians will be present. The unblinded statisticians will review unblinded data by study arm and respond to any questions from the DSMB members regarding blinded data.
3. **Executive session**: If desired, then the DSMB members may then request the statisticians leave the meeting as they discuss any concerns, vote, and finalize recommendations. The DSMB members will keep minutes as necessary during these sessions since there will not be a study team member present.
4. **Debrief session**: If desired, then the DSMB chair may then ask a NEED-PT study team representative(s) to return to the meeting for a final, open portion in which the DSMB chair will summarize the recommendations they plan to submit to the PI.

Kim HS, *et al. BMJ Open* 2022; 12:e061283. doi: 10.1136/bmjopen-2022-061283

The secretary and unblinded statisticians (in the event of closed meeting minutes that contain unblinded information) will finalize the meeting minutes and send to the DSMB members within seven business days of the meeting. The DSMB members will have seven business days to review and provide comment on these minutes once they receive the initial draft. If, at the end of these seven days, the committee members have not provided comment, then the minutes will be considered final.

REPORTS

DSMB reports containing enrollment data, patient safety data, primary outcome data, and adverse event summaries will be reviewed at the DSMB meetings. As mentioned previously, two versions of the DSMB report will be generated:

1. An **open report** that will NOT contain any unblinded information or summarizations.
2. A **closed report** that will contain interim summarizations grouped by 'masked' study arm (e.g., 'Arm A' and 'Arm B', while not disclosing in writing what 'A' and 'B' signify). Dr. Ciolino will verbally disclose the meaning of these codes during the DSMB meeting closed session upon request from the DSMB.

Contents of these reports will be guided by the Data and Safety Monitoring Plan (DSMP) with input from the DSMB members, and they may evolve as the study progresses and DSMB member needs change.

NEED-PT Study Team Response to DSMB Findings and Recommendations

Dr. Kim will review and respond to the DSMB recommendations. If the DSMB recommends continuation of the study without modification, then no formal response will be required. However, if the recommendations request action, such as modification of the protocol or study termination, then the DSMB will request that the PI provide a formal written response indicating whether the recommendations will be followed, and the plan for carrying out the recommendations or addressing the issues over a specific timeframe.

Confidentiality

All committee members will treat DSMB reports, meeting discussions, and minutes as confidential. DSMB members' signature on this charter will serve as this confidentiality agreement. Master copies of the DSMB reports and recommendations will be kept in limited access folders on Northwestern University's secure servers. Hard copies may be stored in locked file cabinets at Northwestern; however, DSMB members must shred / destroy / delete any DSMB meeting materials within seven business days. The members may retain minutes and recommendations for their records; however, the DSMB chair may be the only DSMB member to retain closed minutes in a secure location.

AMENDMENTS TO THE DSMB CHARTER

This DSMB Charter can be amended as needed during the course of this study. Information to be included as amendments will be any updates to the DSMB member roster, meeting formats / frequency, or any specific DSMB duties. All amendments will be documented via version control and dated, and they will be recorded in the minutes of the relevant DSMB meeting. Each revision will be reviewed and agreed upon by the NEED-PT Study Team and the DSMB Members. All versions of the charter will be stored in the trial master file and in secure locations at Northwestern University, along with meeting minutes and open / closed reports.

Attachments

Attachment 1: DSMB Members, Investigators, key personnel
Attachment 2: Data and Safety Monitoring Plan (DSMP)

DSMB Charter Signature Page

A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

April 27, 2021

Version 1.0

My signature indicates my agreement with the above named version of the NEED-PT DSMB Charter. I agree to keep all reports, meeting discussions, and minutes as confidential. I confirm that:
☐ I have no conflicts of interest.
☐ I have the following potential conflict(s) of interest:

Signed,

Signature, date

Printed name

Kim HS, *et al. BMJ Open* 2022; 12:e061283. doi: 10.1136/bmjopen-2022-061283

ATTACHMENT 1: CONTACT INFORMATION

DSMB Chair

Dr. Timothy F. Platts-Mills, MD, MSc
Senior Director
Healthcare and Life Sciences
Quantworks, Inc.

DSMB Members

Dr. Rogelio Coronado, PT, MPT, PhD
Assistant Professor
Department of Orthopedic Surgery
Vanderbilt University Medical Center

Dr. Janel Fedler, PhD
Assistant Professor
Director of Biostatistics and Data Sharing
Clinical Trial Statistical and Data Management Center

Dr. Dave Lu, MD, MSCI, MBE
Associate Professor
Department of Emergency Medicine
University of Washington School of Medicine

Dr. Diana Wilkie, PhD, RN
Earl and Margo Powers Endowed Professor
Department of Biobehavioral Nursing Science
University of Florida College of Nursing

Kim HS, *et al. BMJ Open* 2022; 12:e061283. doi: 10.1136/bmjopen-2022-061283

NEED-PT Investigators and Study Team

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Department of Preventive Medicine - Biostatistics
Northwestern University Feinberg School of Medicine

Bruce L. Lambert, PhD
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Department of Communication Studies
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Northwestern University Feinberg School of Medicine

Kim HS, *et al. BMJ Open* 2022; 12:e061283. doi: 10.1136/bmjopen-2022-061283

Confidential

Physician Consent for NEED-PT (PI: Howard Kim) Study

The following is a study consent document.

After completing, you will be asked to complete a short survey on your demographic information.

NEED-PT Physician Consent Form

Title of Research Study: A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain

Investigator: Howard S. Kim, MD MS

Supported By: Agency for Healthcare Research and Quality (R01HS027426)

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you are an attending emergency physician at Northwestern Memorial Hospital.

What should I know about a research study?

Someone will explain this research study to you. Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you. You can ask all the questions you want before you decide.

Why is this research being done?

We are studying how patients respond to different treatments for low back pain. Low back pain is a major source of pain and disability for many people, and we don't know the best way to treat low back pain. Some have suggested that physical therapy can be helpful for low back pain, so we are studying patients who saw a physical therapist in the emergency room to see how they compare to people who did not see a physical therapist in the emergency room. By conducting this research, we hope to find a better way to treat low back pain in the future for other patients that might come in to the emergency room with similar problems. We are asking for your participation in this study because we will randomly assign a physical therapist to work with emergency physicians as a member of their team.

How long will the research last and what will I need to do?

We expect that you will be in this research study for up to one year. In this study, physicians will be randomized to have a physical therapist paired with them (or not have a physical therapist paired with them) during their emergency department (ED) shifts. This study uses a randomization method called "cluster randomization," whereby the intervention being studied (i.e., physical therapy) is randomized to physicians rather than individual patients themselves.

If you are randomized to have a physical therapist, you will be asked to allow a physical therapist to be positioned on your treatment team when you are working shifts during normal business hours (Monday-Friday, 8am-5pm). You will conduct your usual clinical duties as you normally would, however, we will ask you to allow this physical therapist to see and evaluate all your patients with low back pain automatically (ie, similar to how the ED pharmacist automatically performs a medication reconciliation for admitted patients).

If you are randomized to usual care (i.e., not have a physical therapist on your treatment team), you will conduct your usual clinical duties as you normally would. If you feel that a physical therapist consult is necessary for your patient, you may still consult the physical therapist.

More detailed information about the study procedures can be found under the section What happens if I say "Yes, I want to be in this research"?

Is there any way being in this study could be bad for me?

We do not foresee any risks to having a physical therapist work with you in the emergency room. We will collect basic demographic information about you for the study. We will not ask you for any personal health information. We will ask you some questions about your treatment decisions for patients with low back pain and your involvement of the physical therapist. There is a minimal risk of unintentional disclosure of this information to individuals outside of the research team.

More detailed information about the risks of this study can be found under Is there any way being in this study could be bad for me? (Detailed Risks)

Will being in this study help me any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include increased efficiency and expertise in patient care by having a physical therapist work with half of the volunteer physicians. Future patients may also benefit from your research participation if findings from this research show that a physical therapist on the treatment team may influence and even improve care of patients with complaint of low back pain.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate.

Whom can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at:

Howard S. Kim, MD MS
Principal Investigator
312-926-0591
howard.kim@northwestern.edu

Kayla Muschong
Research Coordinator
312-926-0591
kayla.muschong@northwestern.edu

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

Your questions, concerns, or complaints are not being answered by the research team. You cannot reach the research team. You want to talk to someone besides the research team. You have questions about your rights as a research participant. You want to get information or provide input about this research.

How many people will be studied?

We expect about 40 physicians will be in this research study.

What happens if I say “Yes, I want to be in this research”?

We will randomly assign you to either have a physical therapist work you or not have a physical therapist work with you (i.e., usual care). The group you are assigned to will be chosen by chance, like flipping a coin. Neither you nor the study investigator will choose your group assignment. You will have an equal chance of being assigned to either the physical therapist on your treatment team for up to one year or to usual care (i.e., no physical therapist on your treatment team) for the evaluation of patients with low back pain. We will collect basic background information about you at the beginning of the study, such as your gender, age, years in clinical practice, and average number of shifts worked per month. This data is used collectively to summarize the characteristics of physicians who participated in the study. You will answer these questions only once at the beginning of the study.

If you are assigned to the physical therapy group, we will ask you about your work schedule and find suitable days to assign the physical therapist to work with you. The physical therapist will only be assigned to your ED shifts that occur during normal business hours (Monday-Friday, 8am-5pm) due to limited staffing. While the physical therapist is on your treatment team, you will conduct clnical care as per your usual practice, which includes incorporating input from multiple team members (e.g., nurses, technicians, pharmacists, and specialists) in the management of any given patient. In this case, the physical therapist will evaluate all your patients who present with a chief complaint of low back pain without you specifically consulting the physical therapist to do so. You may choose to incorporate or disregard the physical therapist’s assessment at your own discretion. However, the physical therapist consultation note will appear in the patient’s medical record and the patient will be billed for the evaluation, just as it is in current clinical practice.

A research assistant with also work with you and the physical therapist to determine whether the patient would be eligible for longitudinal data collection as part of the research study. If the patient is deemed not eligible (ie, due to chronic low back pain), or does not want to participate in the study, the physical therapist would still evaluate the patient and provide you with their treatment recommendations. If you believe the patient has red-flag symptoms (eg, bowel or bladder incontinence) that necessitate timely diagnosis and intervention, you will retain the ability to have the physical therapist not evaluate the patient such that you can pursue these emergent diagnoses. If the physical therapist becomes aware of any red-flag symptoms during the course of their assessment, they will stop their assessment and inform you immediately. Finally, patients would retain the ability to refuse the physical therapy assessment, just as they have the ability to refuse any individual clinical service provided in the ED (eg, electrocardiogram, urine pregnancy test, blood tests, x-rays, pharmacist evaluation, medical student evaluation).

If you are assigned to the usual care group, you will not have a physical therapist assigned to work with you. You will conduct clinical care as per your usual practice, which may include consulting physical therapy at your own discretion

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

Accept your assignment to either the physical therapy or usual care group. If assigned to physical therapy, allow the physical therapist to be present on your treatment team and evaluate patients with low back pain. What happens if I say “Yes”, but I change my mind later?

You can leave the research at any time; it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can ensure that you do not receive any further e-mails or other notifications. If you were assigned to the physical therapy group, we will make sure that the physical therapist no longer joins your treatment team.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment or your present or future employment (for employees at NU or its affiliates).

Detailed Risks: Is there any way being in this study could be bad for me?

We do not foresee any risks to having a physical therapist work with you in the emergency room.

Although we will collect basic background information about you (e.g., age, gender, years in practice) we will de-identify this information by giving you a unique study number (e.g. Physician 1, Physician 2). If this background data is included in any publication, it will be presented collectively for all study participants rather than for individual participants (i.e., “The average years in clinical practice for physician participants was 8.6 years.”). This background information helps readers to understand whether a study population might be applicable to their own practice setting. During the conduct of this research study, there is a chance that a loss of confidentiality of this information could occur, however, we expect this risk to be a minimal risk. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: What happens to the information collected for the research?.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you. There is a minimal risk that the physical therapist assigned to your treatment team impacts your clinical efficiency. However in a recent evaluation of Northwestern ED visits for low back pain, we found that the overall length of stay between patients receiving physical therapy and usual care were similar (223 vs 225 minutes, respectively).

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include: increased efficiency and expertise in patient care by having a physical therapist work with you. Your patients may also benefit from your research participation by having a physical therapist work with them to improve their care.

Data Collection, Sharing, and Additional Details

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including study records and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

Your data relating to this study will be stored on a password-protected, access-limited drive on the Northwestern University Feinberg School of Medicine server. Only the research team will have access to this securely stored data. The data will be stored for a period of three years following the completion of the study.

The sponsor, monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), and the US Food and Drug Administration (FDA) may be granted direct access to the medical records of your patients to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena. Identifiable information that could still be disclosed beyond the research team: The Certificate does not stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations. Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Data Sharing

De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

What else do I need to know?

You will not receive any direct compensation for your participation in this study.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire on 08/31/25. You may revoke consent to participation in this research at any time and in any format.

Confidential

Consent Authorization

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

Participant Name: _____

Date: _____

Participant Signature: _____

Confidential

Research Study Consent

Please review and complete the study consent below.

Let the study team know if you have any questions.

Title of Research Study: A Cluster-Randomized Trial of the Northwestern Embedded Emergency Department Physical Therapy (NEED-PT) Protocol for Acute Low Back Pain (also known as "the Northwestern back pain study").

Investigator: Howard S. Kim, MD MS

Supported By: Agency for Healthcare Research and Quality (R01HS027426)

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you came to the emergency room for low back pain.

What should I know about a research study?

Someone will explain this research study to you. Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you. You can ask all the questions you want before you decide.

Why is this research being done?

We are studying how patients respond to different treatments for low back pain. Low back pain is a major source of pain and disability for many people, and we don't know the best way to treat low back pain. Some have suggested that physical therapy can be helpful for low back pain, so we are studying patients who saw a physical therapist in the emergency room to see how they compare to people who did not see a physical therapist in the emergency room. By conducting this research, we hope to find out if this study will show a difference in patients with low back pain who see a physical therapist in the emergency room compared to those patients who do not see a physical therapist in the emergency room. This research may lead to improvements in future emergency care for patients with low back pain.

How long will the research last and what will I need to do?

If you agree to participate, we expect that you will be in this research study for up to one year. In this study, the emergency room doctors have already been assigned (by random chance) to either have a physical therapist paired with them or not have a physical therapist paired with them. This assignment happened before your emergency room visit today and is part of a common research design called "cluster randomization." As a result, you may or may not see a physical therapist in the emergency room today.

As part of the research study, you will receive seven electronic surveys over the next year asking about your low back pain symptoms and whether you have used any medications for pain. These surveys will be sent to you by secure email link or secure text message (or over the phone, if you do not have email or text messaging) at one week, one month, two months, three months, six months, and one year after your emergency room visit.

If you saw a physical therapist in the emergency room today, you will be asked to perform three home exercises that have been personally selected for you by the physical therapist (eg, supine lower trunk rotation). You will also be referred to follow-up with an outpatient physical therapist. If you did not see a physical therapist in the emergency room today, we will refer you to see an outpatient physical therapist.

More detailed information about the study procedures can be found under the section. What happens if I say "Yes, I want to be in this research"?

Is there any way being in this study could be bad for me?

There is a small risk of accidental disclosure of your private information to others that are not involved in research. Additionally, we will ask you to perform some home exercises after you leave the emergency room today. These

exercises will involve movement, so there is a small risk that these activities may temporarily make your pain worse.

More detailed information about the risks of this study can be found under “Is there any way being in this study could be bad for me? (Detailed Risks)”

Will being in this study help me any way?

We cannot promise any benefits to you or others from your taking part in this research. However, performing home exercises may ultimately improve your low back pain and allow you to recover from an injury more quickly. We also hope that your participation in this research study will allow us to learn more about physical therapy for low back pain and help other patients in the future.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate. If you choose not to participate in this study, you will still receive all of the usual components of medical care determined to be necessary by the emergency room physician. This could include advice from the physician, medications, laboratory or imaging tests, or an evaluation by a physical therapist.

Detailed Information:

The rest of this document includes detailed information about this study (in addition to the information listed above).

Whom can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at:

Howard S. Kim, MD MS
Principal Investigator
312-926-0591
howard.kim@northwestern.edu

Kayla Muschong
Research Coordinator
312-926-8117
kayla.muschong@northwestern.edu

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

Your questions, concerns, or complaints are not being answered by the research team. You cannot reach the research team. You want to talk to someone besides the research team. You have questions about your rights as a research participant. You want to get information or provide input about this research.
How many people will be studied?

We expect about 360 people will be in this research study.

What happens if I say “Yes, I want to be in this research”?

If you saw a physical therapist in the emergency room today, they will have provided you with some recommended exercises to perform at home. As part of the research study, we will ask you to tell us how frequently you performed these exercises. We would also like to know how your symptoms are doing at home in the year following your emergency room visit. You will receive an e-mail or text message survey containing several questions about your low back pain symptoms and medications you have taken for low back pain at one week, one month, two months, three months, six months, and year following your emergency room visit (see below for full list of surveys). These surveys can be completed at home and should take about 15 minutes to complete. Finally, we will collect some basic information about your emergency room visit from the medical record, such as the total time spent in the emergency room, any medications received or prescribed, any imaging studies obtained, and your visit diagnosis.

If you saw a physical therapist in the emergency room today, the physical therapist evaluation is part of your standard medical care and you and your insurance company will be billed as you would for any clinical care received, such as blood or urine tests, x-rays, medications received, or procedures such as stitches. The follow-up surveys are part of the research study.

The follow-up surveys will be sent to you seven times over the course of the next year. The surveys will contain questions from the following questionnaires:

PROMIS-Pain Interference Oswestry Disability Index Pain Medication Use Survey Numeric Pain Rating Scale Global Rating of Change Scale Pain Self-Efficacy Questionnaire Pain Catastrophizing Scale Keele STarT Back Screening Tool
What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

Answer seven surveys about your symptoms and medication use over the next year.
If you saw a physical therapist today in the emergency room, tell us how frequently you performed the home exercises shown to you. You would tell us this information during the seven surveys mentioned above.

What happens if I say “Yes”, but I change my mind later?

You can leave the research at any time; it will not be held against you. If you decide to leave the research, contact the investigator so that the investigator can remove you from any future e-mails or phone calls about further study participation.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

If you ask to withdraw from the study, we will ask you what you would like us to do with the data already collected in the past. You can either choose to allow us to use the previously collected data or you can ask us to delete it.

Detailed Risks: Is there any way being in this study could be bad for me?

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. Although the researchers have procedures in place to lessen the possibility of this happening, we cannot guarantee against unintentional disclosure of your information. This may result in loss of privacy or reputational harm.

If you saw a physical therapist today, they will have recommended that you perform some exercises at home. Performing recommended exercises will involve movement, so there is a risk that these activities may temporarily make your pain worse. We will not ask you to go through any movements that are unsafe or contraindicated, so we expect the risk for worse pain to be low and that care is taken to minimize such risk.

At each of the seven follow-up surveys, there will be an option to let us know about any worsening symptoms. We will monitor your comments weekly and contact you if needed. If you experience severe or debilitating pain, please contact the study staff sooner using the telephone or email address on the previous page. If you experience any of the following symptoms, please go directly to the nearest emergency room: loss of sensation to your legs or buttocks, weakness in your legs, or loss of control of your bladder or bowels. These could be signs of a more serious cause of your low back pain than what was originally diagnosed in the emergency room.

See the section below titled: “What happens to the information collected for the research?”.

Will it cost me anything to participate in this research study?

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay (i.e., costs associated with your emergency room visit), such as the doctor’s evaluation, physical therapist evaluation, bloodwork, X-rays, or medications given. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include: improvement in low back pain as a result of participating in physical therapy after your emergency room visit.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution. An exception to our promise of confidentiality is when we in good faith are permitted by law or policy to report evidence of child [or elder] abuse or neglect.

Your data relating to this study will be stored on a password-protected, access-limited drive on the Northwestern University Feinberg School of Medicine server. Only the research team will have access to this securely stored data. The data will be stored for a period of three years following the completion of the study.

The sponsor, monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), and the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

Identifiable information that could still be disclosed beyond the research team: The Certificate does not stop

reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Data Sharing and Final Details

Data Sharing

De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

What else do I need to know?

If you agree to take part in this research study, we will pay you up to $70 for your time and effort. This breaks down as follows: You would receive a $10 Visa gift card after completing each follow-up survey (at the original emergency room visit, then at one week, one month, two months, three months, six months, and one year following your emergency room visit). These gift cards will have an expiration date but will not have any fees for use and will not have restrictions on use. These gift cards will be provided in electronic format and delivered to you by e-mail.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

Results of physical examinations in the emergency room Medical history Lab tests or radiology tests obtained in the emergency room Records about study medication or drugs Billing information The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office].

The following entities may receive your health information:

Authorized members of the Northwestern University and the Shirley Ryan AbilityLab" workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board. Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers. Clinical affiliates, including but not limited to Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities. Other University research centers and University contractors who are also working on the study, Study monitors and auditors who make sure that the study is being done properly, Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate

permission.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire on 08/31/25.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

PI's Name: Howard S. Kim, MD MS
Institution: Northwestern University Feinberg School of Medicine
Department: Department of Emergency Medicine
Address: 211 E. Ontario St, Ste 200, Chicago IL 60611.

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

Consent Authorization

◯ I consent to participate in this study
◯ I do NOT consent to participate in this study

A copy of this signed consent document, information about this study, and the results of any test or procedure done may be included in your medical records and may be seen by your insurance company.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

Patient first name: _____

Patient last name: _____

Today's Date: _____

Patient Signature: _____