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 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

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. It is the leading cause of disability worldwide. In the USA, low back pain accounts for nearly 4 million annual emergency department (ED) visits and more healthcare spending than any other health condition. Because the vast majority of low back pain is non-specific, emergency care for low back pain tends to focus on relieving patient suffering. Back pain is the most common reason opioids are prescribed from US EDs, with nearly half of all ED back pain visits receiving an opioid prescription in. 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.
Several randomised controlled trials have demonstrated that physical therapy interventions for low back pain are efficacious in the outpatient setting, where patients are referred to physical therapy after an initial clinical evaluation by a primary care physician. 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 across study arms. In a prior observational study we demonstrated that ED PT for low back pain is associated with improvements in pain-related functioning and lower utilisation of analgesic medications compared with usual care. 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.

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 complaint 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), 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), 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 comorbidities or 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 (e.g., 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.

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. Because we use physician-level covariates in the constrained randomisation procedure (e.g., 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 (e.g., 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) 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

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the US population, with a score of 50 representing the population mean and 10 points representing 1 SD. 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.

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, 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.

Patient-reported opioid use will be collected via a medication use survey instrument from our previous work. 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.

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. GROC is a single-item survey widely used by clinicians and researchers to evaluate the overall effectiveness of therapy in low back pain.

PCS measures the degree to which an individual catastrophises in response to pain; higher scores are associated with progression from acute to chronic pain. PSEQ measures the belief that one can perform tasks or activities despite pain. We will use the 4-item versions of PCS and PSEQ to minimise respondent burden.

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.

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), 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-physician interaction and known influential predictor effects (age, sex, Keele StarT score). Inference will focus on treatment effects 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.

**Contributors**

HK and JDC conceived and designed the study, obtained funding and drafted the manuscript. KMM, ILF, JMS, ALS, KJS, BL, MV and DM substantially contributed to the design of the study and critically revised the manuscript. HK had full access to all study materials and takes responsibility for the integrity of the proposed trial.

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**Competing interests**

None declared.

**Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication**

Not applicable.

**Provenance and peer review**

Not commissioned; peer reviewed for ethical and funding approval prior to submission.

**Supplemental material**

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**REFERENCES**


28 Calculating total daily dose of opioids for safer dosage 2016.

29 Opioid morphine equivalent conversion factors 2015.


