Study Protocol

Official Title: Targeted Interventions to Prevent Chronic Low Back Pain in High Risk Patients: A Multi-Site Pragmatic Cluster Randomized Controlled Trial

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Targeted Interventions to Prevent Chronic Low Back Pain in High Risk Patients: A Multi-Site Pragmatic RCT (TARGET Trial)

Protocol

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Synopsis

Study title: Targeted Interventions to Prevent Chronic Low Back Pain in High Risk Patients: A Multi-Site Pragmatic RCT (TARGET Trial)

Objectives:

Low back pain (LBP) is one of the most prevalent and potentially disabling conditions for which people seek health care. Patients, providers, and payers are in agreement that greater effort needs to be directed toward prevention of the transition from acute to chronic LBP. Chronic LBP is painful, disabling and expensive (from a patient's perspective), extremely difficult to manage (from a provider's perspective), fraught with inefficiencies including unnecessary exposure to expensive tests and risky procedures (from a payer's perspective), and may contribute to opioid dependence and abuse (from society's perspective). With the majority of patients who experience acute LBP seeking care from their primary care physician (PCP), this study will compare common, pragmatic, evidence-based, and patient-centered approaches emanating from the PCP environment to reduce the proportion of people with acute LBP who transition to chronic LBP and improve functional abilities.

The research question to be addressed with the present study is:

> **For patients with acute LBP deemed high risk to transition to chronic LBP, does prompt referral to psychologically informed physical therapy (PIPT) reduce the rate of transition to chronic LBP and improve functional abilities?**

To answer this question, we will compare:

1. A Guideline-Based Care (GBC) arm (comparator arm) in which management decisions are made between PCPs and patients with the guidance of best evidence but with no specific directives; and
2. A Guideline-Based Care plus Psychologically Informed Physical Therapy (GBC+PIPT) arm (intervention arm) in which PCP care is enhanced with a prompt referral to physical therapy (PT) that includes psychologically informed coaching directed towards education and reduced fear of movement.

Specific aims:

Primary Aims: For patients with acute LBP deemed high risk to transition to chronic LBP, determine the effect of prompt referral to PIPT in (1) preventing transition to chronic LBP and (2) improving functional abilities.

Secondary Aims: (1) Measure use of medical resources for treatment of LBP for those patients categorized as high risk at presentation; and (2) Describe rates of transition from acute to chronic LBP, functional ability, and use of medical resources for patients categorized as low or medium risk at presentation to their PCP.

Hypotheses: The combined GBC+PIPT intervention arm for high risk patients will be more effective than the GBC comparator arm alone in (1) preventing patients with acute LBP from developing chronic LBP, (2) improving functional outcomes, and (3) reducing medical resource utilization for the treatment of LBP.

Design and outcomes:

The primary randomized controlled trial (RCT) cohort study is a multi-site cluster RCT comparing GBC versus GBC+PIPT for patients with acute LBP at high risk for transition to chronic LBP, as determined by the STarT Back Screening Tool. A secondary, prospective, observational cohort study will be conducted for those patients presenting with acute LBP who are at low or medium risk for chronic LBP as measured with the STarT Back Tool.

The STarT Back Tool is a 9-item, validated questionnaire for use in the PCP setting to screen patients with acute LBP for prognostic indicators of transition to chronic LBP. The tool groups patients into low, medium, and high risk categories. Though the tool was developed and tested with European samples, there is emerging evidence to support its use in the US. Recruitment will include a minimum of 12 PCP clinics within each of five geographical areas (Pittsburgh, PA; Boston, MA; Baltimore, MD; Charleston, SC; Salt Lake City, UT). Each PCP clinic will be cluster randomized to one of two arms of the trial.

The primary outcome measures of the study are the presence or absence of chronic LBP and functional ability, determined by the Oswestry Low Back Pain Disability Index (Oswestry), at 6 months in the high risk group. A secondary outcome measure is medical resource utilization related to LBP (e.g., imaging, epidural steroid injections, prescribed medications, surgery) determined through electronic medical record (EMR) data.

Interventions and duration:

This research study is built upon a quality improvement (QI) initiative that includes 1) collection of patient-reported outcomes in all primary care settings and 2) prompt referral to PIPT for patients with high risk acute LBP in the intervention settings. All PCPs part of the initiative will receive a primer on current evidence-based clinical care guidelines for the treatment of acute LBP. All PCP practices will receive QI instruction on how to collect data for the Chronic LBP Questionnaire, the Oswestry LBP Questionnaire, and the STarT Back Tool, which will be given to clinicians and PCPs through the EMR. Clinicians in the intervention settings will also receive QI instruction and EMR tools to refer patients with high risk acute LBP to a PT practice where physical therapists have been trained in PIPT methods. Patients in the GBC comparator arm will receive care from their PCP based on best evidence but with no specific directives or prompts for referrals. Recruiting for participation in the research study will occur at each of the five sites for 15-26 months.

Sample size and population:

Plans are to enroll 1,860 high risk patients for the RCT. The observational cohort will consist of 6,900 low and medium risk patients. Both groups will be followed for 12 months.

1 Study objectives

The target population for this study is adult patients who present to PCPs (i.e., internal medicine, family practice, and geriatric medicine physicians) to receive care for back pain during the primary care clinic visit. To distinguish “acute” versus “chronic” LBP, a 2-question screen based on criteria developed by the NIH Research Task Force on Chronic Low Back Pain will be used: 1) How long has low back pain interfered with your ability to do regular daily activities? 2) Think only about the past 6 months. How often has low back pain interfered with your ability to do regular daily activities? A response of “more than three months” to question 1, and a response of “half the days or more than half the days” to question 2 will define chronic LBP. By definition, all other patients will be defined as having acute LBP. Patients will be excluded who have medical contraindications to PT (“red flags”) based on the judgement of the PCP as documented in the EMR.

1.1 Primary objective

The primary aims (PA1 and PA2) of this pragmatic clustered RCT and the primary hypotheses (H1 and H2) are:

1.1.1 **PA1**: In patients with acute LBP who are deemed “high risk” for transition to chronic (RCT cohort), two study arm treatments will be compared, 1) GBC and 2) GBC+PIPT, and the proportion of this cohort that transition to chronic LBP at the 6-month assessment.

1.1.2 **H1**: GBC+PIPT will be more effective than GBC alone for preventing patients with high risk acute LBP from developing chronic LBP.

1.1.3 **PA2**: Compare between the two study arms LBP-related function (e.g., lifting, walking, sleeping) for high risk patients using the Oswestry at 6 months.

1.1.4 **H2**: GBC+PIPT will be more effective than GBC alone for improving functional outcomes for patients with high risk acute LBP.

1.2 Secondary objectives

Secondary aims (SA) and relevant hypotheses are:

1.2.1 **SA3**: Compare between the two study arms acute LBP-related medical resource utilization (e.g., imaging, epidural steroid injections, opioids) for high risk patients.

1.2.2 **H3**: GBC+PIPT will be more effective than GBC alone for reducing LBP-related medical resource utilization for patients with high risk acute LBP.

1.2.3 **SA4**: Follow patients with acute LBP who are deemed “low and medium risk” in an observational cohort to determine the proportion that transitions to chronic LBP at 6 months, assess functional outcomes at 6 months, and measure LBP-related medical resource utilization at 12 months.

1.2.4 **SA5**: Conduct subgroup analyses for PA1-2 and SA3-4 on patients with lower socioeconomic status (using Medicaid or no insurance as a proxy) and the co-morbid conditions of smoking, depression, and obesity.

1.2.5 **H5**: GBC+PIPT will have lower transition to chronic LBP and will be more effective than GBC alone for improving functional outcomes and reducing LBP-related medical resource utilization for the subgroup of patients with depression or low socioeconomic status. Because the interventions being studied do not specifically target obesity and smoking, and the influence of smoking and obesity on the progression of acute to chronic LBP is uncertain, group x obesity or smoking interactions are not expected.

2 Background

2.1 Background on acute LBP

2.1.1 **LBP is highly prevalent**. Low back pain (LBP) is the most common type of pain and the second most common reason for doctor visits in the United States.[1] More than 26 million Americans age 20-64 have frequent LBP[2] and nearly 2.5 million Americans are disabled by LBP, 1.2 million permanently.[3] Up to 80% of United States adults will experience at least one episode of LBP in their lifetime[4,5] and approximately 25% report experiencing an episode of LBP during the previous month.[6] Chronic LBP affects an estimated 5-10% of United States adults.[7]

2.1.2 **Acute LBP frequently transitions to chronic LBP.** The prognosis of acute LBP is generally considered good, with a prevailing view that spontaneous recovery occurs within six weeks.[8] However, epidemiologic studies in primary care settings report that only 60% to 75% of patients improve within one month,[9] and at three months, 27% are completely better, 28% improved, 30% have no change, and 14% are worse or much worse.[10] Additionally, recurrences are common (up to 54% in first 6 months) and 19% of patients can still be symptomatic at 2 years.[11] Patients, providers, and payers are in agreement that greater effort needs to be directed toward preventing the transition from acute to chronic LBP. Once LBP becomes a chronic condition, it is painful, disabling, expensive, extremely difficult to manage, and fraught with health system inefficiencies.

2.1.3 **LBP significantly reduces quality of life**. LBP is associated with limitations in physical function, work, and school activities.[12] It can impact the ability and desire to engage in social activities, resulting in social isolation, marital conflict, and feelings of resentment and dejection in friends or family members.[13] Over 50% of adults with chronic LBP report difficulties with basic functions such as movement or cognition, and 55% report difficulties with complex actions such as self-care or work activities.[1] LBP is also the most common cause of lost work productivity and is second only to upper respiratory complaints as a reason for lost work time.[12]

2.1.4 **LBP results in high medical resource utilization**. LBP accounts for 34 million office visits annually to family physicians and primary care internists.[14] Annual direct costs for LBP care in the US are more than $50 billion.[15] Indirect costs for chronic LBP (predominantly change in work productivity in most populations)[16] are large and estimated to be greater than direct costs.[17-22] Back pain patients incur up to 75% more medical expenditures than patients without back pain.[23,24] Back injury is the leading and most expensive cause of workers' compensation claims.[25,26]

2.1.5 **Opioid prescribing for LBP is contributing to the opioid abuse problem**. Opioids are increasingly prescribed by PCPs for patients with LBP. The

evidence for opioid treatment for chronic LBP is weak but suggests modest clinical improvement in pain control as compared to controls, with no evidence of functional or quality of life improvement.[27,28] There are numerous concerns associated with the increased prescribing of these medications, including addiction and opioid-induced overdose. Since the 1980s, opioid prescribing and unintentional opioid overdose deaths have increased four-fold, and substance abuse treatment admissions for prescription opioid addiction have increased five-fold.[29,30] In 2010, opioids were the leading cause of prescription drug overdose death in the US, responsible for 16,651 deaths.[31]

2.1.6 **Health disparities are associated with LBP**. LBP disproportionately impacts racial and ethnic minorities.[7,32,33] Medical expenditures for LBP in minorities are 30% lower than for whites.[15] Minorities with LBP receive less patient education,[14] analgesic prescriptions,[14,34] back surgery,[35] specialty referrals,[36] and intensive rehabilitation for occupational back injuries.[37]

2.2 Gaps in evidence

2.2.1 **Effective patient-centered strategies to prevent acute LBP from becoming chronic are unknown.** The most comprehensive systematic review of practice guidelines to date, issued in 2007 by the American College of Physicians and the American Pain Society in *Annals of Internal Medicine,* found there were insufficient data to support any specific approach to prevent the transition from acute to chronic LBP.[38] An exhaustive review of the literature published after 11/1/2006 (search terms clinical trials, back pain, chronic, acute, prospective, prognosis) was conducted that yielded 96 citations. The titles and abstracts were reviewed to identify 59 papers that were reviewed more thoroughly. Of these, 23 attempted to either predict the transition from acute to chronic pain and/or follow patients through the transition. However, no definitive prospective clinical trials were identified comparing different patient-oriented interventions with sufficient long-term follow-up to determine effectiveness for the prevention of the transition from acute to chronic LBP.

2.2.2 **The rate of transition from acute to chronic LBP is not well characterized.** The societal burden of chronic LBP, which is attributed to a small minority of patients with LBP, is well supported.[39] Despite numerous studies documenting epidemiological features of LBP, there is little discrete information about chronic LBP and its relationship to acute LBP,[26] including more precise data concerning the rate of transition from acute to chronic. Estimated rates of transition vary widely from 5-33%.[8-11,40] European studies[41] of a stratified approach similar to our proposed intervention demonstrated improvement in patient-centered outcomes, such as back pain-related function (e.g., improvements in walking, climbing stairs, carrying groceries, sexual function), pain intensity, patient satisfaction, sleep, and mood. Reduced patient exposure to expensive and possibly risky tests and procedures was also found. However,

the European studies did not assess the potential for reducing the transition from acute to chronic.

2.2.3 **There is a historical lack of a consensus definition of chronic LBP.** A contributor to the lack of strategies to prevent chronic LBP and characterization of chronic LBP is the lack of definition of chronic LBP, ranging from 7-12 weeks.[42] However, the 2014 NIH Research Task Force on Chronic Low Back Pain addressed this issue by developing a straightforward two-question approach to distinguish chronic from acute LBP.[42]

2.2.4 **Deficiency of LBP guideline implementation at the PCP level.** Various clinical practice guidelines for the management of LBP have been developed with the goal of enhancing the effectiveness and efficiency of care.[8,43] The aforementioned 2007 *Annals of Internal Medicine* review recommended patients with acute nonspecific LBP should be provided with generic treatment that emphasizes spontaneous recovery facilitated through low-impact exercise and a prompt return to normal activity, at the same time discouraging early diagnostic (e.g., MRI) and intervention (e.g., epidural steroid injections, surgery) procedures.[44] However, systematic reviews of adherence to guidelines suggest that, in general, adherence is incomplete and slow[45] and only minimally influenced by printed educational materials and other passive diffusion techniques.[46]

2.2.5 **Primary care LBP clinical guidelines do not always align with psychosocial factors related to LBP.** All LBP guidelines promote early activation (e.g., encouragement to quickly return to normal activities). Yet some patients overtly avoid physical activity during an episode of LBP because of fear of aggravating their condition ("fear avoidance"), a disproportionately pessimistic outlook ("catastrophizing"), and depression.[47] Fear avoidance, catastrophizing, and depression are generally recognized as major obstacles to recovery.[48] Recent work largely carried out in European countries has demonstrated that a *stratified approach* using prognostic screening tools to assess both physical and psychosocial factors, coupled with matched intervention pathways, can have important implications for better managing acute LBP in primary care settings.[41,49,50]

2.2.6 **Deficiency of LBP guideline implementation in PT care.** Guideline adherence in PT environments remains at a persistently low level and variation is poorly understood,[51-55] despite the existence of accepted guidelines and reasonable evidence for effectiveness of LBP treatments.[56] Of particular relevance to the proposed study is the emerging evidence in PT that supports the use of psychologically informed physical therapy for patients with psychosocial characteristics associated with transition to chronic LBP. Combined therapies for those individuals, who can be identified via a brief screening procedure, are recommended in current PT guidelines.[56]

2.2.7 **Patient preferences do not always align with LBP guidelines**. A systematic review of qualitative and quantitative studies[57] verified that patients with LBP expect: 1) a physical exam, 2) a diagnosis and explanation of the cause of their pain, 3) information and instructions on self-care, and 4) pain relief. Patients also expect health care providers to confirm that their pain is real, listen to and respect their views and treatment preferences, and include them in decision making. Patients can become impatient with “wait and see” approaches, which are common in guideline recommendations, and will instead request more biomedical explanations for their symptoms.[58] In response to patient desires and demands, PCPs will commonly order expensive diagnostic tests,[57] invasive therapies, or referrals to specialists that include significant out-of-pocket expense or expose patients to unnecessary risk. For example, between 2000 and 2002, almost 61% of Pennsylvania Medicare cases received an MRI for nonspecific LBP even though there were no indicators for the procedure, as specified by the U.S. Department of Health and Human Services Agency for Health Care Policy and Research guidelines for LBP.[59] Opioid analgesics, epidural steroid injections, and spine surgery referrals are also commonly recommended by PCPs for nonspecific LBP despite lack of strong evidence supporting effectiveness.[60]

2.2.8 **PCP constraints do not align with LBP guidelines**, Though guideline-based approaches to LBP do not appear to be uniformly embraced by PCPs,[61] the non-adherence to guidelines may have less to do with PCP knowledge gaps and be more related to time constraints. Stakeholder engagement discussions with PCPs, confirmed by the literature,[62] identify time constraints common to PCP practice in the US as the major barrier in addressing patient concerns. Given the prevalence of LBP in primary care settings, the cumulative time for communication and education - specifically inquiring about patients' expectations, providing opportunities to correct misperceptions, explaining the natural history of LBP and the rationale for test and treatment decisions - quickly becomes overburdening in a busy PCP clinic. A quote heard in more than one PCP stakeholder engagement session was, “It’s far easier to just order the MRI and prescribe medications.” Our own patient stakeholders uniformly comment that they also are frustrated by the lack of time their PCP has to address their LBP, especially when it is above and beyond multiple other chronic issues, such as diabetes and hypertension, that all need to be addressed in a 15-minute visit. Patients also expressed dissatisfaction with a medication-only approach. A common sentiment of our patients was, “All the doctor wants to do is prescribe drugs.”

2.3 Study rationale

This study will assess whether the stratified approach using PIPT matched to acute LBP patients at high risk for poor outcomes 1) is effective in the US; 2) has the potential to prevent patients from transitioning to chronic LBP; and 3) reduces patient exposure to unnecessary, expensive, and potentially harmful tests (e.g., MRIs),

medications (e.g., opioids), and procedures (e.g., epidural steroid injections). The research will provide guidance to patients, primary care providers, clinics, hospital systems, insurers, payers, and professional organizations responsible for clinical practice guidelines and dissemination regarding the following health decision: *Should prompt referral to evidence-based psychologically informed physical therapy be strongly recommended for high risk patients presenting with acute LBP?*

2.3.1 **Pragmatic clinical trial design**: This study is focused on whether the stratified approach with PIPT is feasible and effective in a primary care clinical setting. Consequently, based on the work of Thorpe et al[64] and Loudon et al,[63] the study intentionally incorporates the Pragmatic Explanatory Continuum Indicator Summary tool, version 2 (PRECIS-2), nine domains to achieve a pragmatic approach. The nine domains are eligibility criteria, recruitment, setting, organization, delivery, adherence, follow-up, primary outcome, and primary analysis. These domains will be referenced in the remainder of the document as specifics of the design, interventions, and analysis are presented.

2.3.2 **Subjects are patients with acute LBP that present at primary care practices**: Subjects for this study will be adult patients who present to PCPs (i.e., internal medicine, family practice, and geriatric medicine physicians) to receive care for back pain during a primary care clinic visit. Testing this approach in primary care environments was chosen because many patients in the US prefer accessing their PCP for the majority of their health problems, including LBP. This setting is consistent with the PRECIS-2 pragmatic setting domain. Subjects will then be identified as acute or chronic using a modified version of the chronic LBP definition recently created by the NIH Research Task Force on Chronic Low Back Pain.[42]

2.3.3 **Acute LBP interventions based on a stratified approach**: After identification as an acute LBP patient, the STarT Back Tool will be administered, and the resulting scores will stratify patients as low, medium, or high risk for transition to chronic LBP. Patients identified as high risk are patients who would likely benefit from increased education and attention due to greater perceived pain, poor physical functioning, maladaptive coping behaviors (catastrophizing, fear avoidance), and comorbid depression and anxiety.[65] PCPs can then efficiently target interventions for these patients.

This stratified approach to treating LBP in the primary care environment is largely based on compelling effectiveness data from European investigators.[41] Foster's study in UK family practices used the STarT Back Tool to stratify acute LBP patients into 3 risk categories: high, medium, low.[50] In the development of the STarT Back Tool, patients were a significant part of a clinical advisory panel that reviewed the list of potential constructs and chose the final ones. Patient acceptability of the tool was also assessed using a sample of back pain patients consulting primary care. Patients need 2-3 minutes to answer the 9 patient-centered, yes/no questions. Those patients determined by the STarT

Back Tool as being high risk had higher levels of fear avoidance, catastrophizing, mood disturbance, and perceived pain. They were deemed high risk for worse outcomes and were referred to psychologically informed PT to address physical symptoms and function, and also psychosocial obstacles to recovery.[41,49,50] Compared to usual care, the high risk group referred to PT experienced significantly improved back function, less time off work, and less expensive care.[41,49,50] Though the stratified approach with targeted intervention is beginning to be evaluated in the US, published studies based in US healthcare systems have thus far been limited in scope, observational in nature, and have not prospectively measured the transition from acute to chronic LBP.

2.3.4 **Pragmatic RCT comparing GBC and GBC+PIPT interventions**: This pragmatic RCT will have two study arms for treating patients identified as high risk for transitioning to chronic LBP: 1) GBC arm in which management decisions are made between PCPs and patients with the guidance of best evidence but with no specific directives, and 2) GBC+PIPT in which the PCP care includes directives for an immediate referral of high risk patients to a standardized regime of PIPT directed towards education and reduced fear of movement. By assessing the comparative effectiveness of GBC versus GBC+PIPT in an RCT conducted in the US, patients and their PCPs will be better able to judge the potential effectiveness of prompt referral to PIPT in reducing the risk of acute LBP leading to persistent disability from chronic LBP. Based on stakeholder feedback, an RCT design was chosen because its results will be more compelling and definitive, more generalizable with a greater degree of certainty that could lead to changes in provider behavior and payers' benefit design. This study's primary outcome (PRECIS-2 domain) of rate of transition from acute LBP to chronic LBP for high risk patients receiving PIPT is directly relevant to high risk acute LBP patients because it will address their specific psychosocial conditions and improve outcomes. Furthermore, it will provide PCPs with specific techniques for caring for these patients.

2.3.5 **Rationale for GBC comparator arm**: Based on guidance from Thompson and Schoenfeld,[66] a comparator arm (GBC in this case) is justified because: 1) the research question is to compare an evidence-based "strategy" against guideline-informed care and 2) both approaches are considered prudent and good care for the target population. The "strategy" (GBC+PIPT) is an approach designed to match patients with LBP stratified to high risk to the PIPT regimen, which has been shown to be effective.[41,49,50] In the GBC arm, PCPs will be given a primer on guidelines for LBP and have available through the EMR information about the patients' chronic versus acute status, functional limitations (Oswestry), and risk level (STarT Back). However, a PT referral will not be automatically generated and the PCP will have the freedom to treat high risk patients according to their individual clinical judgment.

Furthermore, there are pragmatic reasons to include the GBC arm. Primary care for low back pain is highly variable with little evidence thus far of adequate translation of evidence-based practice (EBP) guidelines to routine clinical care. Until recently, most approaches to EBP uptake in primary care have relied solely on passive diffusion (e.g., “publish it and they will come”) approaches. With health care reform and increasing emphasis on quality, however, there are other factors that may accelerate clinicians’ adoption of EBP approaches. At the University of Pittsburgh Medical Center (UPMC), Intermountain Healthcare, and Boston Medical Center, shared savings programs and other system-wide quality initiatives have been implemented, all of which may result in better uptake of best care standards. Provider stakeholders interviewed all agreed that LBP represents an area of concern within their systems and predicted that it will be a target of such initiatives. Given these probable initiatives within the study sites, it is essential to have a comparator arm to the study as an accurate comparator of real-life primary care for LBP. In addition, a number of the primary care stakeholders interviewed do not routinely refer to physical therapists. However, they are willing to go along with the randomization assignment and will comply with either arm of the trial. Although some degree of crossover is anticipated (i.e., patients assigned to GBC will be referred to PT), it is highly likely to be less than patients from GBC+PIPT sites. Moreover, this crossover will be tracked through the EMR.

2.3.6 **Rationale for GBC+PIPT intervention:** When familiarized with the studies from Europe on the STarT Back approach, stakeholders and investigators were intrigued with its sensibility and, most importantly, its positive results with regard to outcomes, such as less pain, improved back function, and reduced exposure to tests and measures. The probability of transitioning to chronic LBP relative to GBC will be measured, which was not measured by the European studies. Though all interviewed stakeholders agreed and understood the lack of generalizability to the US health care system, all were confident that the approach could be easily replicated in the US with some caveats. Although PT is a covered benefit common to virtually all US payers, the size, scope, and cost of US PT benefits are often distinctly different than in Europe (i.e., less care with greater co-payments). These concerns were quickly brought forth for discussion by patient stakeholders and PCP providers whose clientele are under-served populations.

2.3.7 **Quality improvement initiatives**: This study is dependent on the implementation of two QI initiatives. First, all sites and PCP clinics involved in this study will implement tools (e.g., patient portals, tablet computers, EMR upgrades) for the collection of patient-reported outcomes. They will also put in place QI training programs for staff and clinicians to learn how to collect patient-reported outcomes into the EMR. Finally, they will create monitoring reports that track performance of the PCP clinics in capturing patient-reported outcomes. Second, all intervention sites will implement tools (e.g., EMR

notifications, order sets, electronic orders, letters) to alert clinicians and PCPs of patients with high risk acute LBP. They will also conduct QI training programs on when and how to refer patients to PIPT. Monitoring reports for referral to PIPT will also be implemented to track performance on this QI initiative.

2.3.8 **Generalizability of subject eligibility**: This study will use broad inclusion criteria (age 18 or older, primary complaint of back pain) and limited exclusion criteria ("red flag" signs and symptoms of medical contraindications to physical therapy based on the judgement of the PCP as documented in the EMR). The study will exclude patients less than 18 years of age based on feedback from primary care stakeholders who stated that patients younger than 18 commonly have their care managed by pediatricians, and LBP in adolescents is typically managed differently than adult LBP. Selection of the exclusion criteria was determined based on concerns for patient safety. In keeping with the pragmatic nature of the trial and the PRECIS-2 domain of eligibility, it will: 1) have no upper age limit; 2) include women who are pregnant; and 3) include people with non-severe compressive nerve root signs, all of which are typical exclusion criteria in studies of acute LBP.

2.3.9 **Rationale for patient-reported outcomes**: This study will also measure patient-reported outcomes with the Oswestry questionnaire. Since 1994, there has been a growing recognition in the treatment of back pain that patient perspectives are essential in judging the results of treatment. In fact, many experts argue that improving the patient's "quality of life" is often the main goal of therapy. Consequently, research in LBP has shifted dramatically from physiologic outcomes (e.g., range of motion, muscle strength, neurologic deficits) to rigorous measurement of patient-reported outcomes such as pain, functional status, medication use, role function, quality of life, satisfaction with treatment, and work status. In many cases, functional outcomes can be measured with a high level of reproducibility. Because symptoms and functional outcomes are sometimes only loosely associated with physiologic phenomena in LBP research, the functional outcomes should be measured directly. Modern questionnaires for measuring patient quality of life combine the expertise of social scientists, clinicians, and patients to result in excellent reliability and validity.

Through qualitative interviews with patients with LBP who were familiar with PT, several accepted LBP-specific instruments designed to measure health-related quality of life were reviewed. Patients were asked for candid judgments of whether the items on the outcome instruments adequately represented what was important to them. Surprisingly, some items were uniformly rejected by the patients, such as numeric pain ratings and global ratings of change, both of which are considered essential and widely accepted in the LBP literature. Instead, questionnaires that dealt with functional ability (e.g., Oswestry) were uniformly endorsed, with patients confirming the relevance of the items to their

problem and even going as far to say the instrument helped them to articulate how their problem was affecting their everyday life. Consequently, patients also stated that any study that demonstrated improvement in the items listed on outcome assessment forms, such as the Oswestry, would be relevant to them.

2.3.10 **Non-reliance on clinician expertise**: Other than providing updates to existing guidelines through standard continuing education courses, this study does not require additional expertise on the part of PCPs or physical therapists in either arm. In both study arms, high risk patients will be identified in the EMR at the PCP office. In the GBC arm, the high risk patients will be identified for the PCPs, and the PCP will be given the freedom to treat the patient according to their individual clinical judgment. Matched interventions (advice to stay active, cognitive behavioral approaches, education, etc.) will be recommended through the EMR. In the intervention GBC+PIPT arm of the study, high risk patients will be identified and PIPT will be recommended. To keep the trial pragmatic, the treatments will be made available with an explanation of potential benefits to patients in their respective study arms as well as referrals when applicable. There will be no undue pressure to comply with the treatments in either arm of the study. This is consistent with the PRECIS-2 domain of flexibility (delivery).

PIPT training will be provided to physical therapists to whom patients are commonly referred by the PCP offices. The continuing education courses for physical therapists will be limited to 8 hours, far less than the licensure requirements in the states participating, and physical therapists will not be restricted due to expertise. Continuing education will be focused on reviewing the principles of PIPT and not dictating to physical therapists exactly how the interventions are to be carried out.

2.3.11 **Potential risks**: Due to the highly pragmatic nature of this study, the risks of either of these interventions are minimal. All aspects of patient care are within normal clinical practice and under the control of clinic-based practitioners. Any risks would be subject to the PCP or PT sites' normal patient safety procedures.

3 Study design

3.1 Primary, secondary and additional study designs

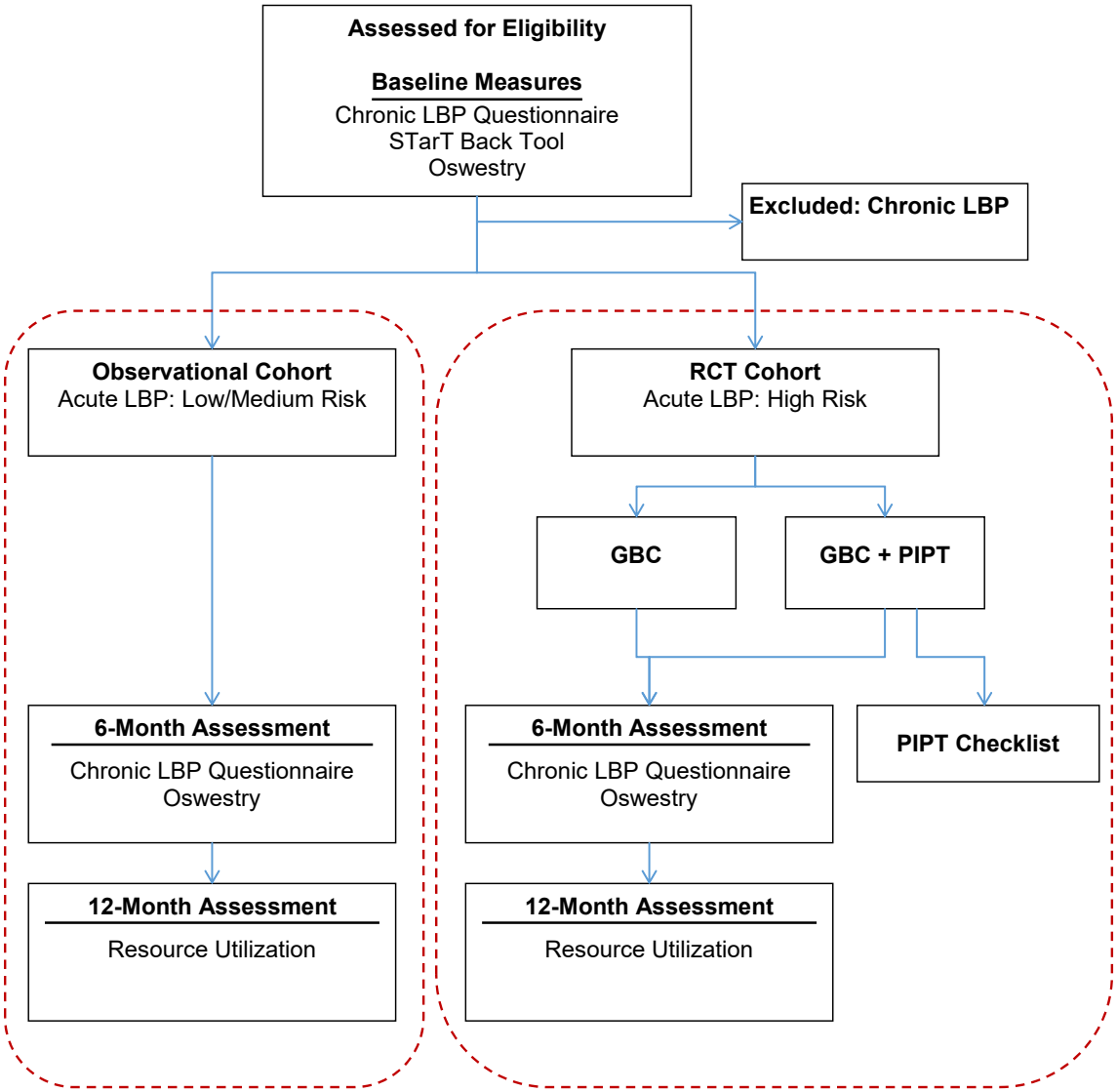

Figure 1. Diagram of sample size by cohort and study arm

3.1.1 **Primary study (PA1-2, SA3, SA5)**: The primary study is a multi-site cluster RCT comparing GBC with GBC+PIPT for patients with acute LBP deemed to be high risk for transition to chronic LBP (RCT cohort). Data collection will be conducted at baseline, 6 months, and 12 months. Resource use, determined with EMR data, will be evaluated in a subset of patients.

3.1.2 **Secondary study (SA4-5)**: A secondary ancillary prospective, observational cohort study will be conducted for those patients presenting with acute LBP

deemed to be low or medium risk. Patients with acute LBP who do not meet criteria for high risk will be identified for the prospective observational cohort. These patients will receive GBC and not be targeted with any specific study interventions, such as PIPT. Data collection will also occur at baseline, 6 months, and 12 months. The objective of this ancillary observational study is to precisely determine the rates of transition from acute to chronic LBP and resource use in the treatment of LBP.

3.2 Randomization

The study will be conducted in five distinct US geographical areas in each of which a minimum of 12 primary care clinics will be participating and enrolling patients. The unit of cluster randomization will be the primary care clinic site. Thus, in one geographical area, six PCP clinics will be randomized to the GBC arm and six to the GBC+PIPT arm. The unit of randomization and analysis is a cluster because the intention is to enhance the application of a stratified approach to treating LBP in primary care environments as a whole while minimizing contamination.[67] When randomization at the individual level was considered, it was found to be impractical and susceptible to selection bias and contamination.

The randomization for each study site will be conducted by the study biostatistician and will be stratified by two factors: Total Back Pain Encounters (Factor 1) and % Medicaid/Self-Pay (Factor 2). First, the clinics will be ordered by Factor 1 and divided into subgroups (blocks). Clinics in each block will then be further ordered by Factor 2, and randomly assigned to either group A or group B, making sure that the two groups would be balanced in terms of both Factor 1 and Factor 2.

3.3 Primary, secondary, and additional study outcomes

3.3.1 **The first primary outcome of the study (PA1) is the presence or absence of chronic LBP**. This is determined through the patients' answers to a two-item Chronic LBP Questionnaire based on criteria developed by the NIH Task Force on research standards for chronic LBP.[42] The questions are: 1) How long has low back pain interfered with your ability to do regular daily activities? 2) Think only about the past 6 months. How often has low back pain interfered with your ability to do regular daily activities? Chronic LBP is defined as a response of "more than three months" to question 1, and a response of "half the days or more than half the days" in the past 6 months to question 2.

3.3.2 **The second primary outcome of the study (PA2) is the Oswestry Disability Index**.[68] Originally described by Fairbanks et al,[68] the Oswestry LBP Questionnaire is a reliable, well-validated, easily-administered, disease-specific measure that results in an index of a patient's perceived level of function due to LBP and is based on ten areas of performance. Items include how the back pain impacts the patient's ability to care for themselves (washing, dressing, etc.), lift, walk, sit, stand, and sleep. It also assesses the effect of the pain on the patient's sex life (if applicable), social life, and ability to travel. Patient

stakeholders unanimously find this type of instrument more patient-centered than the standard pain numerical rating scale and believe that the Oswestry represents functional activities that can become impaired when they experience back issues and are important to them to overcome. Each area is scored from 0 - 5 with zero representing no limitation and five representing maximal limitation. The ten areas, which include an assessment of pain intensity, are added together, resulting in a maximum score of 50. This score is doubled and interpreted as a percentage of patient-perceived disability, with higher scores representing greater disability.

3.3.3 **A secondary outcome (SA3-5) is LBP-related medical resource utilization**, including 1) referrals to specialists (e.g., orthopedists, spine surgeons, physiatrists) and other health care providers, 2) tests (e.g., MRIs), surgical procedures (e.g., epidural steroid injections, laminectomy), and 3) prescription analgesics including opioids.

3.4 Study population and sites

The target population for this study will be adult patients who present to primary care physicians (i.e., internal medicine, family practice, and geriatric medicine physicians) with a primary complaint of LBP. Patients will be recruited from health systems in five regional areas that surround: 1) Pittsburgh, PA (UPMC); 2) Boston, MA (Boston Medical Center); 3) Baltimore, MD (Johns Hopkins Medicine); 4) Charleston, SC (Medical University of South Carolina); and 5) Salt Lake City, UT (Intermountain Healthcare). Within the individual regional areas, primary care clinics have been identified that represent community-based PCP clinics. In all instances, there are more potential sites than are required for successful completion of the trial, which will allow flexibility in the randomization scheme and alternatives should there be individual PCP-clinic recruitment shortfalls. This large, nation-wide group of clinics across five different health systems provides a high level of pragmatism for the PRECIS-2 organizational domain because the systems will be variable with regards to provider expertise, resources, and organizational structure.

Certain patient subgroups are of particular interest **(SA5)** given greater risk for poorer LBP outcomes as demonstrated in observational cohort studies. Adequate enrollment will be assured to have statistical power to conduct subgroup analyses of patients with lower socioeconomic status (using insurance as a proxy) and the comorbid conditions of smoking, depression, and obesity.[11,69-71] Identification of subgroups will be based on information obtainable in the EMR. The participating primary care clinics will be sampled to reflect gender, race, and ethnicity proportions of the population being served at the recruitment sites.

4 Selection and enrollment of participants

4.1 Inclusion criteria

Inclusion criteria for the study are:

1) 18 years of age or older, and
2) Receiving care for acute low back pain (i.e., does not meet the criteria for chronic LBP) during a primary care clinic visit.

An even distribution of age from 20-60 years of age is expected with a slight drop off after age 60, due to LBP becoming more of a chronic problem with aging. The lower age limit on recruitment of 18 years was included based on stakeholder feedback from internal medicine and family medicine colleagues that pointed out the different nature of LBP in adolescents. Gender is expected to be 50% male and race/ethnicity will closely match those in the geographical location of the sites. English language proficiency will not be an inclusion criterion because it is assumed that clinics with a significant non-English population will have translation capabilities for that population.

4.2 Exclusion criteria

Exclusion criteria are limited to medical contraindications to physical therapy based on the judgement of the PCP as documented in the EMR (i.e., “red flag” signs and symptoms of a potentially serious condition such as cauda equina syndrome, major or rapidly progressing neurological deficit, cancer, spinal infection or fracture).[72]

4.3 Study enrollment procedures

4.3.1 **Subjects will be enrolled** at all of the PCP clinics selected for the trial. In keeping with the pragmatic nature of the trial, all patients will be admitted into the trial who present with a complaint of acute back pain. Recruitment (PRECIS-2 domain) is highly pragmatic being solely based on patients presenting to the clinic with back pain.

4.3.2 **Randomization:** The study is a cluster RCT; randomization of treatment arm assignment is at the clinic level, not the individual patient. Enrollment will be the same for both arms of the study.

4.3.3 **Screening procedures:** Using patient portals, clinic-based tablets, or manual questionnaires, administrative staff or clinicians at the PCP sites will administer a baseline assessment with three components that will be included in the patients’ EMR. At all sites, the EMR will be modified to accept these data elements:

1) The 2-item Chronic LBP Questionnaire (Appendix 1),[42]
2) The 9-item STarT Back Tool to stratify risk for transition to chronic LBP and identify high risk patients (Appendix 2),[41]
3) The 10-item Oswestry LBP Questionnaire (Appendix 3).

4.3.4 **Ineligibility and non-participation**: Patients with chronic LBP will be documented as not eligible and will not be enrolled for intervention or subsequent assessments. Patients refusing to complete the baseline assessments will be documented as refusing screening and not included in the enrollment for intervention or subsequent assessments.

5 Study interventions

Table 1: Study intervention components by study arms

Intervention components	GBC	GBC+PIPT
Training of non-clinical and clinical staff at PCP offices on patient identification and data collection (QI)	✓	✓
PCP primer of LBP guidelines (QI)	✓	✓
PCP and clinical staff instruction on stratification and referral to PIPT (QI)		✓
Training for physical therapists on PIPT (QI)		✓
Identification of LBP patients upon scheduling appointments or arrival in clinic (QI)	✓	✓
LBP patient completion of questionnaires (Chronic LBP, STarT Back, Oswestry) (QI)	✓	✓
Patient questionnaire results given to PCPs in EMR (QI)	✓	✓
Acute LBP patient informed consent and enrollment in study for assessments at 6 months and review of medical record data (Research)	✓	✓
Acute LBP high risk patients referred to PIPT (QI)		✓
Acute LBP high risk patients attend PIPT session (QI)		✓
PT performs PIPT for acute LBP high risk patients (QI)		✓
PT completes checklist and returns to PCP for acute LBP high risk patients (QI)		✓
6-month assessment for all acute LBP patients (Research)	✓	✓
12-month EMR resource use assessment for all acute LBP patients*(Research)	✓	✓
**EMR data for UPMC, BMC, JHM, IH*		

5.1 Interventions, administration, and duration

5.1.1 **Referral to PIPT**: As a result of the QI initiative, all patients in the intervention arm identified as high risk will be referred to PIPT. PCPs will have the results of the screening questionnaires in the EMR to identify the high risk acute LBP patients and refer them to PIPT. PCPs will provide patient education materials as appropriate, including materials about musculoskeletal injury, PT, and pain management. Referrals will occur through automatic electronic referral, manual electronic referral, written prescription, fax, or verbal means.

5.1.2 **Delivery of PIPT**: Upon referral to PIPT, trained physical therapists will use the PIPT approach with the high risk patients. The number of PT sessions recommended by the physical therapist will be based on their clinical judgment. Physical therapists will complete a checklist based on PT standards of care (see Appendix 4 based on Guide to Physical Therapy Practice http://guidetoptpractice.apta.org/) that will reflect the elements of the treatment provided. This checklist will be sent to the PCP and entered into the EMR. This

checklist will allow tracking of how many patients have received the prescribed physical therapy (i.e., a completed checklist, number of PT sessions).

5.1.3 **Patient-centered PIPT discharge instructions**: Community discussions with patients emphasized the desire to have a home exercise program in place after physical therapy that is feasible, effective, and sustainable. As an adjunct to the PIPT program, physical therapists can provide patients at discharge printed instructions for home practice exercises and a list of recommended community-based exercise classes and resources appropriate for the patient.

5.1.4 **Patient-reported outcomes**: At 6 months for all sites, lists of eligible patients will be generated from the EMR and patients will be contacted by research assistants by phone, email, or postal mail. This procedure is a modest departure from the pragmatic approach (PRECIS-2 follow-up domain); however, stakeholders indicated that 6-month assessments of this nature were not normal practice for the PCP clinics. These assessments will be for the Chronic LBP Questionnaire and Oswestry.

5.2 Handling of study interventions

5.2.1 **PCP clinic instruction**: As part of the QI initiative, all PCP clinic sites will receive instruction on how to identify and collect patient-reported outcomes for patients with back pain. QI staff will work with physician champions at each practice site and their staff to ensure smooth processes for administering the screening tools. They will also receive an educational presentation, including a primer on guidelines for LBP, an overview of the Chronic LBP Questionnaire, the STarT Back Tool, and the Oswestry. Sites included in the GBC arm will not be instructed to alter their normal clinical procedures beyond data collection while those in the intervention arm will be coached by QI staff on referral to PIPT.

5.2.2 **PIPT physical therapist education**: To educate physical therapists in the referral areas for the intervention arm, a PT continuing education program will be provided for physical therapists that includes PT guidelines, principles of PIPT, clinical application, and adherence. Initial training of physical therapists will consist of a 1-day (8-hour) course that offers:

1) A condensed and focused summary of the principles of pain neuroscience and cognitive behavioral therapy (CBT),
2) Case examples of using PIPT principles with back pain patients,
3) Basic training in specific communication skills and styles that can enhance patient motivation for attitudinal and behavioral change, and
4) Interactive, experiential training in delivering brief educational and PIPT approaches.

Ongoing training to promote adherence to the PIPT skills in clinical treatment will be provided through telephone and email access to trainers/mentors, online

discussion groups, and an adherence checklist for use during treatment of high risk patients. The intervention is designed to be a practical, patient-centered, and activity-based treatment, and will utilize American Physical Therapy Association (APTA) Orthopaedic Section Clinical Practice Guidelines.[56]

5.3 Concomitant interventions

In keeping with the pragmatic nature of the trial, there will be no restrictions on patients taking part in other clinical trials.

5.4 Adherence assessment

5.4.1 **Patient adherence**: Patients will be compensated for their participation in data collection: one payment of $15 will be mailed after the completion of the 6-month assessment. All care will be paid for through existing health insurance benefit structures, established programs for underserved patients, or will be self-pay.

5.4.2 **Provider adherence**: Approaches will be implemented to enhance provider adherence within the context of the EMR. PCP stakeholders strongly believed that time restrictions would not permit them to enter into the EMR the data necessary to identify baseline characteristics (2-item chronic questionnaire, STarT Back Tool, and Oswestry LBP Questionnaire). As a result, the portal or tablet-based approaches programmed within the EMR environment would be the first line of data collection utilized uniformly throughout the study sites. Portal and tablet-based approaches are becoming increasingly implemented in PCP environments, supporting generalizability. The study team will not dictate treatment fidelity approaches for PT provider adherence, but will implement a “checklist” that includes reference guidelines for the PIPT approach. This checklist will be included in the routine communication that occurs between the physical therapist and a referring PCP.

6 Study procedures

6.1 Schedule of evaluations

Table 2: Schedule of evaluations

Assessment	Screening and Enrollment	6-Months	12-Months
Chronic LBP Questionnaire	✓	✓	
STarT Back Tool	✓		
Oswestry LBP Disability Index	✓	✓	
EMR Medical Resource Use*			✓
**EMR data for UPMC, BMC, JHM, IH*			

A detailed flow diagram for each regional site is provided in Appendix 5.

6.2 Description of evaluations

6.2.1 **Screening evaluation**: Patients receiving care for acute back pain will be given the three-part assessment during the PCP visit scheduling process (up to seven days prior) or upon arrival at the clinical site. Candidates will be deemed eligible for the study if they are identified as an acute LBP patient. Those in the high risk STarT Back group will be identified for enrollment in the RCT for the primary and secondary outcomes, and those in the low or medium risk STarT Back groups will be identified for enrollment in the observational cohort for secondary outcomes. The screening evaluations are part of normal practice, and results for all screened patients will be available for clinical staff to use in the EMR.

6.2.2 **Consent process**: The University of Pittsburgh Institutional Review Board (IRB) has approved a waiver of informed consent/HIPAA authorization to access, record, and use protected patient health information/patient medical record information for review and analysis of medical recorddata for the conduct of this study at UPMC clinics and Intermountain Healthcare clinics. It has also approved a waiver for the requirement to obtain a written informed consent for completion of questionnaires and interviews at those sites. Verbal consent will be obtained by telephone or electronic consent by email prior to the 6-month assessment by research staff from the University of Pittsburgh. A letter will be mailed from the Healthsystem prior to the contact by research personnel to inform the patients about the research study and provide them an option of opting out of receiving any additional follow up by calling a project office telephone number or sending an email message to the project email address. Participants will be given the option of completing the 6-month assessment as a hard copy self-report, which will be mailed to the project office with a consent template with their name recorded for tracking. The research involves no more than minimal risk to the participant, the waivers will not

adversely affect the rights and welfare of the participant, and the research could not practicably be carried out without the waivers.

Specifically,

- The study is comparing two standard-of-care treatments that patients could receive regardless of participation in the study,
- These standard clinical approaches do not require consent outside of the research context,
- A total sample size of at least 8,760 participants is needed from these sites to meet the aims of the study,
- The study needs to be conducted within the clinical setting (i.e., a pragmatic trial), which typically allows <15 minutes per patient visit; the consent/authorization procedures would disrupt the clinical setting and potentially impact patient care.

6.2.3 **Enrollment and baseline evaluation**: Upon determination of eligibility, patients will be enrolled in the QI initiative of the study. Baseline data will be contained in the EMR and extracted for study purposes, including screening results, demographic information, billing information, and clinical data (e.g., diagnoses, referrals to specialists). Patients identified as high risk, acute LBP patients in the intervention arm will be referred to PIPT, and this referral will also be captured in the EMR. The list of baseline variables to be extracted from the EMR is provided in Appendix 6.

6.2.4 **Randomization**: As a cluster RCT, randomization will occur at the clinic level and not the patient level; therefore, randomization is not a factor in the enrollment or baseline evaluation.

6.2.5 **Follow-up**: Follow-up to the initial screening and QI enrollment visit will occur through three mechanisms:

1) **Referral to PIPT**: For eligible patients referred to PIPT, follow up at PT will be evaluated through the checklist completed at the PT visit and returned to the PCP site. This checklist will indicate use of the PIPT approach and number of PT sessions.
2) **Six-month assessment**: Research staff will contact all enrolled patients 6 months after their initial visit at all sites and conduct the Chronic LBP Questionnaire and the Oswestry to assess the primary outcomes.
3) **Medical resource utilization**: Researchers will also extract data from the EMR at select sites to determine the secondary outcome of LBP-related medical resource utilization of tests, procedures, and pharmaceuticals by enrolled patients for 12 months after the initial visit.

The list of variables for medical resource utilization is provided in Appendix 6.

7 Safety assessments

All clinical activities related to this trial will be performed in accordance with normal clinical practice. Safety concerns and adverse events arising from clinical operations within the PCP or PT settings will also follow normal clinical procedures. Adverse events related to the research study would be limited to a data breach of confidentiality. This would not require patient report but would require study report, following Office of Information Security protocols at the University of Pittsburgh for reporting and resolution.

8 Intervention discontinuation

Enrollees who do not follow the clinical practices contemplated within this trial or do not respond to the follow-up calls will be documented but not discontinued.

9 Statistical considerations

9.1 General design issues

9.1.1 **A primary aim (PA1)** is to determine in patients with acute LBP who are deemed high risk for transition to chronic, what is the proportion of patients transitioning to chronic LBP by the time of the 6-month assessment who are treated with 1) GBC compared to 2) GBC+PIPT.

9.1.2 **H1**: GBC+PIPT will be more effective than GBC alone for preventing patients with high risk acute LBP from transitioning to chronic LBP.

9.1.3 The primary outcome will be determined by patients' responses to the Chronic LBP Questionnaire at 6 months. The proportion of patients that have transitioned will be compared across the two study arms.

9.1.4 **PA2** is to compare patient-centered outcomes of LBP-related function (e.g., lifting, walking, sleeping) for high risk patients between the two study arms at the 6-month assessment.

9.1.5 **H2**: GBC+PIPT will be more effective than GBC alone for improving functional outcomes for patients with high risk acute LBP.

9.1.6 This primary outcome will be measured using patients' responses to the Oswestry LBP Questionnaire at baseline versus at 6 months to determine changes in the score.

9.1.7 **SA3** is to compare acute LBP-related medical resource utilization (e.g., imaging, epidural steroid injections, opioids) for high risk patients between the two study arms.

9.1.8 **H3**: GBC+PIPT will be more effective than GBC alone for reducing LBP-related medical resource utilization for patients with high risk acute LBP.

9.1.9 This secondary outcome will be measured by retrieving patient medical resource utilization data from the EMR for LBP-related tests, procedures, specialty visits, and pharmaceuticals for 12 months after the initial visit.

9.1.10 **SA4** is related to PA1-2 and SA3 but will determine the proportion of medium and low risk patients that transitions to chronic LBP; patient-centered outcomes (e.g., functional impact); and LBP-related medical resource utilization.

9.1.11 Outcomes for this aim will utilize the same measures and sources as PA1-2 and SA3 for the medium and low risk patients.

9.1.12 **SA5** is to conduct subgroup analyses for PA1-2 and SA3 on patients with lower socioeconomic status (using insurance as a proxy) and the co-morbid conditions of smoking, depression, and obesity.

9.1.13 **H5**: GBC+PIPT will have less transition to chronic LBP and will be more effective than GBC alone for improving functional outcomes and reducing LBP-related medical resource utilization for the subgroup of patients who are underserved or with depression. Because the interventions being studied do not specifically target obesity and smoking, and the relationship of these variables to transition to chronic are unclear, group x obesity interactions are not expected.

9.1.14 Outcomes for this aim will utilize the same measures and sources as PA1-2, SA3 but will also include EMR data on patient co-morbidities, smoking status, and socioeconomic status.

9.1.15 **Missing data**: Baseline characteristics, such as age, gender, and health insurance status, will be compared between patients with complete assessment data to those with missing data by treatment group in order to assess potential biases that may exist in the complete case analysis. Sensitivity analyses for the primary and secondary outcomes will be conducted using several methods, which have different missing data assumptions.[73]

1) Complete case analyses, which assumes missing data are completely at random,
2) Multiple imputation using M=10 imputations, which assumes missing at random, and
3) Assigning poor scores and good scores for missing values differentially by treatment group, which aligns with non-ignorable missingness (the data missingness is nonrandom and related to the actual value).

9.2 Randomization, sample size and power – RCT cohort

9.2.1 **Randomization** will occur at the clinic level, which was chosen for the pragmatic reason that randomizing patients within a clinic would result in cross contamination of the interventions within the same clinic. The biostatisticians and the individuals conducting the 6-month assessments will be blinded to the randomization assignment to avoid bias in analyses and data capture.

9.2.2 **Sample size** is based on the first primary outcome of the transition rate to chronic LBP at month 6. We propose to enroll N=1860 high risk acute LBP patients. We are targeting an average of n=31 enrolled high risk patients per clinic (60*31=1860) to account for the variation in cluster sizes (assuming coefficient of variation=0.65) and 40% non-response rate at 6 months.

9.2.3 **Power**: With a total of 60 PCP clinics for randomization, m=30 clinics per intervention strategy and fixed n=10-14 completers per clinic for the 6-month assessment, we will have just over 80% power to detect a 40% reduction in transition to chronic LBP assuming the control arm has a transition rate of 25%-30% and the intraclass correlation is 0.05, which is an upper bound for what has been observed in other cluster randomized trials with respect to either pain of LBP. Assuming that low and medium risk subjects with acute LBP have an expected 20% transition to chronic and using data on obesity and smoking rates based on national surveys, depression rates based on prevalence rates reported in primary care, and proportions of underserved patients estimated from patient registries at each of the five regional sites, the planned sample size for the observational cohort is sufficient to detect at least a 30% relative difference (6% absolute difference) from 20% with powers ranging from 79% to 87%. The study would have 65% power to detect a 40% relative or 8% absolute difference (hypothesized increased rate of transition) for the depression subgroup.

9.2.4 **Treatment assignment procedures**: Detecting an interaction effect the same size as the overall intervention effect would require a four-fold increase in the effective sample size (more clinics and patients accounting for clustering), which is not feasible.[82] There will be sufficient power to detect stronger intervention effects in some *a priori* defined subgroups at the participant level (smoking, depression, obesity, lower SES) if the cohort is evenly split.

9.2.5 **Analysis of randomization**: Distributions of baseline characteristics for clinics and patients will be compared between the study arms to assess effectiveness of the randomization, and statistical or clinical differences will be adjusted for in sensitivity analyses. All analyses for treatment group comparisons will use an intention-to-treat approach and results will be reported using the CONSORT extension to cluster randomized trials.[83] This approach is highly pragmatic per the PRECIS-2 primary analysis domain.

9.3 Randomization, sample size and power – observational cohort

9.3.1 **Randomization** is not applicable to the observational cohort because moderate and low risk patients will not receive the PIPT intervention.

9.3.2 **Sample size** is again based on a total of 60 PCP clinics. An average of n=115 patients will be enrolled per clinic, for a total sample of N=6,900 low or medium risk acute LBP patients.

9.3.3 **Power**: The sample size will allow precise determination of 1) the transition rates for low risk and medium risk acute LBP who receive GBC; 2) differences between low/medium risk patients receiving GBC in the observational cohort and high risk patients receiving GBC in the intervention group; and most importantly, 3) differences among low/medium risk patients due to specific subgroup characteristics, in particular patients who are underserved, obese, depressed, or smokers. Of the three objectives, the subgroup analyses require the greatest sample size, and therefore will be described in detail here.

For the purposes of the calculations, from the literature it is assumed that low and medium risk subjects with acute LBP have an expected 20% transition to chronic. Data on obesity and smoking rates are based on national surveys. Depression rates are based on prevalence rates reported in primary care. Proportions of underserved patients are estimated from patient registries at each of the five regional sites. For the underserved, obesity, and smoking subgroups, the given sample sizes in Table 3 would be ample enough to detect at least a 30% relative difference (6% absolute difference) from 20% with powers ranging from 79% to 87%. The study would have 65% power to detect a 40% relative or 8% absolute difference (hypothesized increased rate of transition) for the depression subgroup.

Table 3: Power *at a significance level of 0.05 to detect the specified % absolute and relative differences from a 20% chronic transition rate based on a two-sided Z-test adjusted for clustering within clinic (ICC=0.01) among 60 clinics, N=6900 enrolled and conservatively 60% response rate at 6 months in the low or medium risk population (adjusting for design effect and nonresponse N=2464).*

Subgroups (N)	25% relative difference (5% absolute difference)	30% relative difference (6% absolute difference)	35% relative difference (7% absolute difference)	40% relative difference (8% absolute difference)
Underserved (n=665 of 2464)	74	87	95	98
Obesity (n=640 of 2464)	73	86	94	98
Depression (n=184 of 2464)	33	44	54	65
Smoking (n=493 of 2464)	64	79	89	95

9.4 Outcomes

9.4.1 **Primary outcome 1**: To test the effect of the intervention on preventing the transition from acute to chronic LBP (**PA1**), the study team will compare the rates of transition to chronic LBP at 6 months, based on the results of the 6 month Chronic LBP Questionnaire, between enrolled patients at intervention clinics and enrolled patients at comparator clinics. This comparison will be conducted for high risk patients at 6 months (**PA1**) as well as low and medium risk patients (**SA4**) and specific subgroups (**SA5**).

9.4.2 **Primary outcome 2:** To test the effect of the intervention on improving patient-centered outcomes of back-related function (**PA2**), the study team will compare changes in the Oswestry scores from baseline to 6-month assessment between enrolled patients at intervention clinics and enrolled patients at comparator clinics. This comparison will be conducted for high risk patients at 6 months (**PA2**) as well as low and medium risk patients (**SA4**) and specific subgroups (**SA5**).

9.4.3 **Secondary outcomes**: To test the effects of the intervention on reducing medical resource utilization (**SA3**) the study team will compare LBP-related medical resource utilization data for enrolled patients at intervention clinics and enrolled patients at comparator clinics for a period of 12 months. This comparison will be conducted for high risk patients (**SA3**) as well as low and medium risk patients (**SA4**) and specific subgroups (**SA5**). The medical resource utilization data will be identified and categorized using Healthcare Common Procedure Coding System (HCPCS) Level 1 (CPT-4) and 2, and ICD-10 codes. These data will be used to evaluate the frequency, intensity and composition of services received within the participating PCP/PT practices as well as care delivered in other community practices and facilities. The study team will investigate evaluation & management services (PCP & specialist), diagnostic testing, rehabilitation services, and medical procedures. Furthermore, the study team will also capture prescribing patterns for key drug classes commonly used for LBP management such as non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen (Tylenol), opioid analgesics, skeletal muscle relaxants, antidepressants (e.g., tricyclic antidepressants and duloxetine), and drugs for neuropathic pain (e.g., gabapentin).[38]

9.5 Data analyses

9.5.1 **Primary outcome 1**: This initial analysis (**PA1**) will use a generalized linear mixed model with a logit link controlling for block set (see Randomization) and a fixed effect for intervention accounting for the cluster RCT design with a random clinic effect. Primary analyses will also adjust for patient characteristics (maladaptive pain coping behaviors such as catastrophizing and fear avoidance, functional impairment as measured by the Oswestry, and presence

of psychiatric comorbidities), as these have been associated with higher transition to chronic LBP.[69] The intraclass correlation coefficients will also be estimated and reported for all outcome measures to assess the assumptions for sample size analyses and also for future investigations using similar designs and outcomes. Analysis for the secondary aims (**SA4** and **SA5**) will be largely descriptive assessing the proportion of patients who transition to chronic LBP among the low and moderate risk observational cohort. The proportion and confidence interval will be estimated using generalized linear models adjusting for clustering.

9.5.2 **Primary outcome 2**: This aim (**PA1**) will be analyzed using contrasts from a linear mixed models analysis for 6-month back-related function (Oswestry) controlling for baseline Oswestry and the block set (see Randomization). The intervention will first be explored by time interaction, and then proceed to a main effects model with only group and time. For the secondary aims (**SA4** and **SA5**) patient-centered outcomes, such as functional status, would use general linear models if deemed appropriate based on normality assumptions. If normality is hugely violated, a cutpoint for 'response' will be applied.

9.5.3 **Secondary outcome**: Analyses of health care utilization data (**SA3**) will use generalized linear mixed models with the distribution determined by the type of data but still controlling for the cluster randomized trial design by having random effects for clinics. Logit link (binary distribution) will be used for health care outcomes, such as surgery, that are dichotomous (Yes/No) variables. For outcomes resulting in count data over the time frame such as number of outpatient visits for back pain, hospitalizations or ER visits, Poisson or negative binomial distribution with log link will be used to compare the event rates controlling for the period of follow up. The secondary aims (**SA4** and **SA5**) would use a similar approach.

10 Data collection and quality assurance

10.1 Data collection

10.1.1 **Baseline data**: Data collection for the three baseline patient questionnaires (Chronic LBP Questionnaire, STarT Back, and Oswestry) will be self-report via an internet-based form in a patient portal, a tablet-based form, or a paper questionnaire. The forms via patient portal or tablet will be loaded into the EMR. For paper questionnaires, the medical assistant will enter the data directly into the EMR. The PT checklist will be completed either electronically or on paper, and will also be loaded into the EMR.

10.1.2 **Follow-up data**: The study team will extract data from the EMR to determine 6-month assessment dates for enrolled patients. These data will be collected by the study team via telephone or e-mail, or as participant hard copy self-report returned to the project office, entered into a database, and matched with the EMR data.

10.1.3 **Medical resource utilization data**: Data for LBP-related use of medical resources during the 12-month assessment period will be collected for four of the five regional sites (Pittsburgh, Boston, Baltimore, and Salt Lake City). All four regional study sites participate in robust clinical research data networks (CRDNs). Boston Medical Center has access to the Clinical Data Warehouse of Boston University Medical Campus and Boston HealthNet, a partnership between Boston Medical Center, Boston University School of Medicine, and 15 community health centers that are participating in the study. Data from these resources will allow the capture of comprehensive information regarding the LBP-related medical resource utilization (e.g., office visits, specialty visits, tests, procedures, prescriptions, surgeries).

10.1.4 **Data sweeps**: The EMR administrators and programmers at each site have agreed to work with the study team to provide all necessary data. Reporting needed for the aims are related to data that need to be regularly pulled from the EMR and provided to practice managers and study personnel. These include:

1) Total numbers of subjects with LBP ICD-10 codes or who received care for back pain during the primary care clinic visit,
2) Total numbers of subjects with completed data elements that include:
    - Chronic LBP Questionnaire
    - STarT Back Questionnaire
    - Oswestry LBP Questionnaire

All sites have agreed to program into the EMR the data elements above. They also agreed to program:

1) Bi-weekly sweeps of the EMR with a report that documents the ratio of completed data sets to total patients enrolled with LBP by clinic. These

will be used to assure appropriate recruitment levels at all sites. Reports will be directed to PCP champions and staff responsible for the clinic.

2) Regular reports from all of the EMRs of the data elements as well as the common data elements. These will be de-identified and sent to the coordinating site (Pittsburgh), where the Data Integrity Committee will work to harmonize all of the data integral to the primary aims of the study from the 5 sites.

10.2 Data management

10.2.1 **Data coordination and quality monitoring**: The University of Pittsburgh will manage data from the 5 regional sites' EMR teams. Monitoring of the trial will be facilitated through regular reports provided to the PIs and the Steering Committee. University of Pittsburgh staff have experience regularly running reports for other trials to monitor recruitment, enrollment, protocol implementation, attrition, and safety. They are also experienced with generating Data and Safety Monitoring Reports in both open and closed formats.

10.2.2 **Data source adequacy**: In choosing sites, major criteria were an established EMR linked with networked PCP clinics. All of the sites fit this criterion. One of the criteria for eligible PCP clinics was past volume of patients with LBP, identified by the ICD-9 code list. All sites conducted a data sweep representing calendar year 2013. In order to be an acceptable clinic site for the study, clinics needed to have a minimum of 400 patients with LBP diagnoses. Most of the selected clinics were far above that number. The conservative estimate is that that 10% of the 400 (40 per clinic) would be acute and high risk and therefore eligible, based on past literature for chronic rates, which range from 8-10%.[4,88] In addition, a payer stakeholder, OPTUM, shared data with us based on first-time visits at primary care clinics across the country. Their analysis of chronicity (defined as 2 or more subsequent visits six months after the initial visit) verified a chronicity rate of <20%. Given the literature on chronic LBP and the STarT Back Tool, and data from OPTUM, 10% is a conservative estimate for a yearly yield of 31 patients per clinic.

10.3 Quality assurance

10.3.1 **Methods used to ensure unbiased and systematic data collection from all participants**: The major sources of potential bias in data collection with a cluster-RCT design lie in 1) the selection of sites and 2) missing or incomplete data collection once subjects are enrolled within a site. EMRs of all participating PCP clinics will be analyzed every two weeks for data completion rates (# completed data sets/total number of possible data sets). De-identified aggregate data completion rates will be provided to the site PI and feedback will be given to individual PCP clinics through the PCP site champion on a biweekly basis. The site PI for each city and the PCP clinic champions will meet regularly, using in person and teleconference visits as needed. During

these meetings recruitment, enrollment, retention, and data collection rates for the previous month and cumulative-to-date will be reviewed for each clinic and the city as a whole. Successes and challenges will be discussed in a spirit of quality improvement. This approach will allow sharing of best practices, successes, and challenges; rapid identification of potential barriers to optimal recruitment, retention, and data collection strategies; and rapid Plan-Do-Study-Act (PDSA) cycling to address barriers.

11 Participants rights and confidentiality

11.1 Institutional Review Board (IRB) review

This protocol and any subsequent modifications will be reviewed and approved by the relevant IRB for each study site. The University of Pittsburgh IRB as the IRB of Record for the UPMC and Intermountain Healthcare study sites has approved a waiver of informed consent/HIPAA authorization to access, record and use protected patient health information/patient medical record information for review and analysis of medical record data. It has also approved a waiver for the requirement to obtain a written informed consent for completion of questionnaires and interviews. Separate review and oversight will be conducted by the Boston University Medical Center IRB, Johns Hopkins University IRB, and Medical University of South Carolina IRB.

11.2 Informed consent scripts

The letter to be mailed to QI participants informing them of the research data collection and scripts to be used for obtaining verbal consent are provided in Appendix 7 (6--month assessments).

11.3 Participant confidentiality

Any data, forms, reports, and other records in the study database will be identified only by a unique participant identification number (Participant ID or PID) to maintain confidentiality. All hardcopy records will be kept in a locked file cabinet. All computer entry and networking programs will be done using PIDs only.

11.4 Study discontinuation

The study may be discontinued at any time by the IRB or PCORI as part of their duties to ensure that research participants are protected.

12 Committees

The following committees will guide the work of this project:

- **Steering Committee**: made up of the project PI and Co-PI, site PIs, and patient co-investigators who will participate in monitoring the conduct of the project from its inception to the dissemination of the study results. Additional key co-investigators and staff from each of the study sites will also participate in Steering Committee conference calls and meetings.
- **Advisory Board**: this board is made up of a team of patient, provider, payer and purchaser representatives. The Advisory Board will provide a “safe harbor” for the Steering Committee members to review study options and provide input from their respective stakeholder perspective. The board will meet face-to-face as well as on conference calls and engage in meaningful and inclusive discussions of key issues as they emerge, particularly during the formative stages early in the granting period. Specifically, it will engage and advise the Steering Committee, be active ambassadors for the study, help with organization and planning, and directly participate in the dissemination phases the study.
- **Dissemination and Publications Committee**: this committee will promote, facilitate, and monitor TARGET Trial dissemination products and ensure compliance with PCORI dissemination policies.
- **Data Integrity Committee**: this committee will work to harmonize all of the data integral to the primary and secondary aims of the study from the five sites. This includes creating data dictionaries; data extraction templates, policies, and timelines; ensuring secure data housing; and working with the study statisticians to ensure the data is ready for analysis.

13 Publication of research findings

Publication of the results of this trial will be governed by the policies and procedures developed by the Steering and Dissemination Committees.

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15 Appendix 1: Chronic LBP Questionnaire

Screening for Chronic Low Back Pain
1. How long has low back pain interfered with your ability to do **regular** daily activities? ☐ Less than 1 month ☐ 1 – 3 months ☐ More than 3 months 2. Think only about **the past 6 months**. How often has low back pain interfered with your ability to do **regular** daily activities? ☐ Less than half the days ☐ Half the days or more than half the days

Definition and questionnaire rules:

- "Chronic" = greater than 3 months (Q1c) + at least half the days (Q2b)
- "Acute" = all else Q1a, Q1b, or Q1c+Q2a
- If patient answers 1a or 1b, stop and patient is acute
- If patient answers 1c, proceed to question 2
- If patient answers 2a, patient is acute
- If patient answers 2b, patient is chronic

16 Appendix 2: STarT Back Tool

STarT Back Screening Tool for Risk Stratification

Thinking about the **last 2 weeks**, check your response to the following questions:

	Disagree 0	Agree 1
1. My back pain has **spread down my leg(s)** at some time in the last 2 weeks	☐	☐
2. I have had pain in the **shoulder** or **neck** at some time in the last 2 weeks	☐	☐
3. I have only **walked short distances** because of my back pain	☐	☐
4. In the last 2 weeks, I have **dressed more slowly** than usual because of my back pain	☐	☐
5. It's not really safe for a person with a condition like mine to be physically active	☐	☐
6. **Worrying thoughts** have been going through my mind a lot of the time	☐	☐
7. I feel that **my back pain is terrible** and **it's never going to get any better**	☐	☐
8. In general I have **not enjoyed** all the things I used to enjoy	☐	☐

9. Overall, how **bothersome** has your back pain been in the **last 2 weeks**?

Not at all	Slightly	Moderately	Very much	Extremely
☐	☐	☐	☐	☐
0	0	0	1	1

Total Score (all 9):	Sub Score (Q5–9):

Scoring System

Low Risk:	Total Score = 3 or less
Medium Risk:	Total Score = 4 or more + Sub Score Q5–9 = 3 or less
High Risk:	Total Score = 4 or more + Sub Score Q5–9 = 4 or more

17 Appendix 3: Oswestry LBP Questionnaire

Oswestry LBP Questionnaire

This questionnaire is designed to give us information as to how your back (or leg) trouble affects your ability to manage in everyday life. Please answer every section. Mark one box only in each section that most closely describes you today.

Section 1 – Pain Intensity
- ☐ I have no pain at the moment.
- ☐ The pain is very mild at the moment.
- ☐ The pain is moderate at the moment.
- ☐ The pain is fairly severe at the moment.
- ☐ The pain is very severe at the moment.
- ☐ The pain is the worst imaginable at the moment.

Section 2 – Personal Care (washing, dressing, etc.)
- ☐ I can look after myself normally without causing additional pain.
- ☐ I can look after myself normally but it is very painful.
- ☐ It is painful to look after myself and I am slow and careful.
- ☐ I need some help but manage most of my personal care.
- ☐ I need help every day in most aspects of self care.
- ☐ I do not get dressed, I wash with difficulty and stay in bed.

Section 3 – Lifting
- ☐ I can lift heavy weights without additional pain.
- ☐ I can lift heavy weights but it gives additional pain.
- ☐ Pain prevents me from lifting heavy weights off the floor but I can manage if they are conveniently positioned, e.g. on a table.
- ☐ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned.
- ☐ I can only lift very light weights.
- ☐ I cannot lift or carry anything at all.

Section 4 – Walking
- ☐ Pain does not prevent me from walking any distance.
- ☐ Pain prevents me from walking more than one mile.
- ☐ Pain prevents me from walking more than a quarter of a mile.
- ☐ Pain prevents me from walking more than 100 yards.
- ☐ I can only walk using a cane or crutches.
- ☐ I am in bed most of the time and have to crawl to the toilet.

Section 5 – Sitting
- ☐ I can sit in any chair as long as I like.
- ☐ I can sit in my favorite chair as long as I like.
- ☐ Pain prevents me from sitting for more than 1 hour.
- ☐ Pain prevents me from sitting for more than half an hour.
- ☐ Pain prevents me from sitting for more than 10 minutes.
- ☐ Pain prevents me from sitting at all.

Section 6 – Standing
- ☐ I can stand as long as I want without additional pain.
- ☐ I can stand as long as I want but it gives me additional pain.
- ☐ Pain prevents me from standing for more than 1 hour.
- ☐ Pain prevents me from standing for more than half an hour.
- ☐ Pain prevents me from standing for more than 10 minutes.
- ☐ Pain prevents me from standing at all.

Section 7 – Sleeping
- ☐ My sleep is never interrupted by pain.
- ☐ My sleep is occasionally interrupted by pain.
- ☐ Because of pain I have less than 6 hours sleep.
- ☐ Because of pain I have less than 4 hours sleep.
- ☐ Because of pain I have less than 2 hours sleep.
- ☐ Pain prevents me from sleeping at all.

Section 8 – Sex Life (if applicable)
- ☐ My sex life is normal and causes no additional pain.
- ☐ My sex life is normal but causes some additional pain.
- ☐ My sex life is nearly normal but is very painful.
- ☐ My sex life is severely restricted by pain.
- ☐ My sex life is nearly non-existent because of pain.
- ☐ Pain prevents me from having any sex life at all.

Section 9 – Social Life
- ☐ My social life is normal and causes me no additional pain.
- ☐ My social life is normal but increases the degree of pain.
- ☐ Pain has no significant effect on my social life apart from limiting my more energetic interests, e.g., sport, etc.
- ☐ Pain has restricted my social life and I do not go out as often.
- ☐ Pain has restricted my social life to home.
- ☐ I have no social life because of pain.

Section 10 – Traveling
- ☐ I can travel anywhere without pain.
- ☐ I can travel anywhere but it gives me additional pain.
- ☐ Pain is bad but I am able to manage trips over two hours.
- ☐ Pain restricts me to trips of less than one hour.
- ☐ Pain restricts me to short necessary trips of under 30 minutes.
- ☐ Pain prevents me from traveling except to receive treatment.

18 Appendix 4: Physical Therapist Checklist

Thank you for this referral to *(Insert Clinic Name)* . The following is a summary of content areas covered (indicated by checked boxes) with this patient during treatment for their acute low back pain, based on your initial referral of / / .

Patient Information:

Patient Name: _____ **HICN:** _____ **DOB:** / /

Diagnosis Indicating Therapy: _____ **ICD-10 Code:** _____

Referring Physician: _____ **Start of Care Date:** / /

Progress Content Areas:

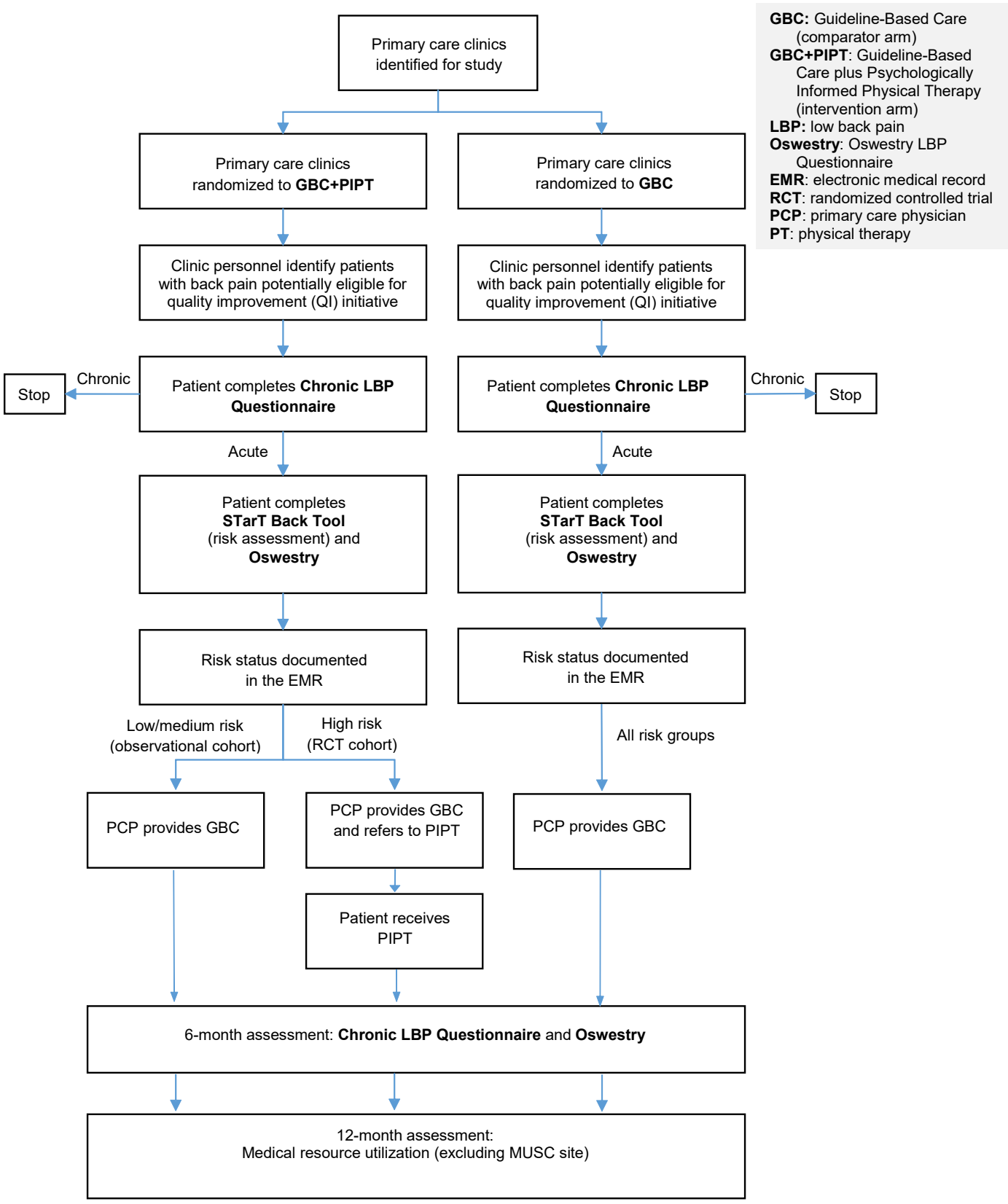
- **Communication**
  - ☐ Active listening (eye contact, paraphrase/repeat back what patient says)
  - ☐ Facilitation of self-disclosure, activation philosophy (elicit patient's concerns, discuss and reassure RE: activity)
  - ☐ Patient centered goal-setting / motivational interviewing (connect with patient RE: shared goals)
- **Pain coping skills taught and reinforced**
  - ☐ Relaxed breathing
  - ☐ Adaptive distraction skills (e.g., pleasant place imagery)
  - ☐ Balanced statements to counteract unhelpful thinking styles (e.g., pain catastrophizing, all-or-nothing thinking)
- **Activity-based treatment**
  - ☐ Graded activity (to reduce pain-related activity avoidance)
  - ☐ Graded exposure (to reduce fear-related motion avoidance)
- **Physical impairment component – most appropriate classification (from APTA clinical practice guidelines):**
  - ☐ Acute/subacute LBP with mobility deficits
  - ☐ Acute/subacute LBP with movement coordination impairments
  - ☐ Acute LBP with related (referred) lower extremity pain
  - ☐ Acute/subacute LBP with radiating pain
- **Home exercise program:**
  - ☐ Specific activities integrating pain coping skills (as described above)
  - ☐ Specific education (e.g., web-based format)
- **Treatment monitoring completed:** **Yes** ☐ **No** ☐

Additional comments:

Therapist's Name: _____ **Date:** / /

(Completed checklist is to be forwarded to office of referring PCP via electronic scan or fax.)

19 Appendix 5: Flow diagram for each regional site



20 Appendix 6: Data from electronic medical record

Contact information (for 6- and 12-month assessments)

- Name
- Street address
- Electronic mail address
- Telephone number

Baseline sociodemographic variables

- Sex
- Race
- Hispanic ethnicity
- Date of birth
- Height
- Weight
- Body mass index
- Tobacco use
- Comorbid conditions
- Insurance status

Encounters and procedures

- Name of providers
- Primary care visits
- Referrals to specialists (orthopedists, spine surgeons, physiatrists)
- Rehabilitation procedures (physical therapy, occupational therapy, osteopathic manipulation, chiropractic manipulation, acupuncture)
- Imaging of spine (radiologic , computed tomography, magnetic resonance)
- Surgical procedures (epidural steroid injections, laminectomy)
- Emergency department visits
- Observation unit stays
- Hospitalizations

Medications prescribed/dispensed

- Non-steroidal anti-inflammatory drugs
- Antidepressants
- Antiepileptic drugs
- Skeletal muscle relaxants
- Opioid analgesics

21 Appendix 7: Letters from health system to eligible patients (30 days)

Aiming to Improve Low Back Treatment **Insert Site-Specific Logo**

Study Site Project Office
Return Address

<<Date>>

«First_Name» «Last_Name»
«ADD_LINE_1» «ADD_LINE_2»
«CITY», «STATE» «ZIP»

Dear «First_Name» <<Last_Name>>:

Your primary care doctor's office, «DEPARTMENT», is participating in a **research study about back pain** (the TARGET Trial) to find out how people like you are doing 6 months after a doctor visit for back pain. Because you were recently seen at <DEPARTMENT> for back pain, you are eligible for this study.

In about 5 months, researchers from the University of Pittsburgh will get in touch with you by phone or email and ask if you would be willing to complete a short survey (about 5-10 minutes long) asking if you have any back pain and, if so, how it affects your daily activities.

- **You will be paid $15 for completing the survey.**
- **You do not have to join this research study. Whether or not you decide to complete the surveys will not affect your medical care at [insert Study Site] now or in the future.**

If you do <u>not</u> want to be contacted for this research study, please call (xxx) xxx-xxxx or email targettrial@pitt.edu**.**

Dr. [Site PI] is the main person in charge of this research study. If you have any questions or concerns about this letter or the study, please call the study team at the number listed above or Dr. [Site PI] at xxx-xxx-xxxx.

Thank you for your consideration.

Sincerely,

Site-specific signature

Title

Appendix 7 (continued): Letters from health system to eligible patients (90 days)

TARGETTRIAL

Aiming to Improve Low Back Treatment **Site-Specific Med Center Logo**

Study Site Project Office
Return Address

<<Date>>

«First_Name» «Last_Name»
«ADD_LINE_1» «ADD_LINE_2»
«CITY», «STATE» «ZIP»

Greetings from the **TARGET Trial Study Team**.

This is a reminder that **researchers from <Site Name> will be contacting you in about 3 months** (by phone or email) **to complete a brief (5-10 minutes) survey**.

The purpose of the survey is to see how you are doing since your visit to <DEPARTMENT> on <DATE> for back pain. We are interested in learning if you still have any back pain and if it affects your daily activities.

You will receive $15 after completing the survey.

Please note that **you do not have to join this study. Whether or not you choose to take part in the study will not affect your medical care at <Site Name> now or in the future.**

TARGET Trial Project Office

Phone: xxx-xxx-xxxx Email: targettrial@xxx.edu

(*) options: University of Pittsburgh for UPMC, Boston Medical Center, Johns Hopkins, Intermountain Healthcare, Medical University of South Carolina

Appendix 7 (continued): Letters from health system to eligible patients (150 days)

Aiming to Improve Low Back Treatment **Site-Specific Medical Center Logo**

Study Site Project Office
Return Address

<<Date>>

«First_Name» «Last_Name»
«ADD_LINE_1» «ADD_LINE_2»
«CITY», «STATE» «ZIP»

Dear «First_Name» <<Last_Name>>:

Your primary care doctor's office, «DEPARTMENT», is participating in a **research study about back pain (the TARGET Trial)**. According to your records, you mentioned having back pain when you saw <<Dr. Name>> about 5-6 months ago.

Researchers from the <<Site Name>> (area code xxx) will be contacting you by phone or email in about 2-4 weeks **to invite you to complete a 5-10 minute survey**. **We have included a copy of the survey with this letter.** The survey will ask if you have any back pain and, if so, how it affects your daily activities.

- **We are very interested in learning how you are feeling now, even if you no longer have any back pain.**
- **You will be paid $15 for completing the survey.**
- **You do not have to join this research study. Whether or not you choose to participate or complete the study will not affect your medical care at <<Site-specific medical center>> now or in the future.**

Before you complete the survey, you will need to agree (consent) to take part in this study. If you would like to fill out the enclosed survey now, please check the consent box at the top of the survey, complete the survey, and mail it back in the enclosed, self-addressed, stamped envelope. You can also use the following link <<xxxxxx>> and complete the questions online.

If we do not get a mailed survey or online survey from you within the next two weeks, we will contact you by phone or email to complete the survey.

Dr. <<Site PI Name>> is the main person in charge of this research study. If you have any questions or concerns about this letter, the survey, or the study, please call the study team at <<xxx-xxx-xxxx>> or send an email to targettrial@xxx.edu. Thank you for your consideration.

Sincerely,*Site-specific signature from Medical Center*

Title

22 Appendix 8: Consent for 6-month assessment

TARGET Trial Verbal / Electronic Consent at 6 Months

Your doctor's office is participating in the TARGET Trial, a research study about back pain, to find out how well people like you are doing 6 months after a visit to their doctor. You are being asked to join this research study because you reported having back pain several months ago when you saw your doctor. At that time, you were asked some questions about how pain interferes with your everyday life. If you agree to be in this study, you will be asked the same questions now. A letter about the study, including the survey questions, was mailed to your home recently.

The questions will take about 5-10 minutes to answer. The study will not directly benefit you, but it may help doctors improve care for patients with back pain in the future. There is no cost to you to participate and you will be mailed a $15 debit card in appreciation for your participation after completing the survey. It is your choice whether or not to participate. If you do participate, you do not need to answer any questions you don't want to.

This study is classified as minimal risk. There is an unlikely risk that the information you provide could be seen by people outside the research study, but every effort will be made to keep your information confidential. Dr. [PI Name] at [Study Site Name] is the main person in charge of the study. If you have any questions, he can be reached at [PI phone #]. If you have any questions about your rights as a research subject or wish to talk to someone other than the research team, you may call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2268.

Do you give your consent to participate in this research?

Yes [ ] _→ (Provide web-based link for electronic survey, or proceed with interview)

No [ ] → Thank you for your time today.

If returning survey in enclosed
envelope, please print name here: _____

23 Appendix 9: Participating study sites and investigators

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