Acupuncture Approaches to Decrease Disparities in Outcomes of Pain Treatment Two Arm Comparative Effectiveness Trial (AADDOPT-2)

Study Protocol

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RESEARCH STRATEGY

Part A. Background

Impact of the condition on the health of individuals and populations. (Criterion 1)

A.1. Prevalence and Impact of Chronic Pain and Disparities in Health Outcomes. Chronic pain is pain that has outlasted the healing of an acute injury by one month, continues or recurs frequently for three months, or is associated with a lesion that is not expected to resolve(1). Chronic pain disrupts the lives of millions of people worldwide. Minority populations in particular experience greater prevalence of chronic pain and worse outcomes. Estimates of the prevalence of chronic pain in the general U.S. population range from 10-40% in recent large surveys (2-7). Patients often do not bring such pain to the attention of physicians (8). Living with chronic pain is associated with impairment of physical and psychological functioning (3, 9, 10), lost productivity (11), and lower socioeconomic status (7). Established treatment guidelines for chronic pain are often not followed by clinicians (12-15). Under treatment is understood to be multifactorial, with causes that include limitations in the health care system, negative attitudes or lack of skill in clinicians, and specific attributes of the patient (16). Patient-level attributes often involve racial and ethnic differences (12, 14) as well as variation in attitudes, beliefs, and concerns, such as medical mistrust, culturally different expressions of pain symptoms and related behaviors, and culturally-based beliefs regarding the nature of illness and healing.

The prevalence and outcomes of chronic pain differ across groups of patients. Access to care is one key component in these differences. Hispanics (70%) are significantly less likely to have consulted a primary care practitioner for pain compared with Caucasians (84%) or African Americans (85%). Less frequent treatment seeking for pain is also associated with speaking Spanish, having limited education, and being unemployed. Hispanic ethnicity in particular appears to predict limited access. Others have examined the difference in treatment of pain in minority vs. non-minority populations and found similar disparities. For example, in a series of studies examining emergency room care for skeletal fractures Todd et al. found that Hispanics (17) and African-Americans (18) received appropriate analgesic treatment for fractures significantly less often than non-Hispanic whites. Others have reported similar rates of under-treatment of minority populations with post-operative and cancer pain (19).

A.2. Effectiveness of Acupuncture Therapy in Treatment of Chronic Pain. Extensive evidence now supports the use of acupuncture therapy in the treatment of chronic pain conditions (20-27), particularly in three common causes of chronic pain: osteoarthritis (28-32) neck pain (33, 34) and low back pain (35-38).

Osteoarthritis. Berman et al (28) examined the impact of acupuncture (23 sessions over 26 weeks) on pain and function in patients with osteoarthritis of the knee compared to sham acupuncture or education, and found significantly greater improvement at 26 weeks in both pain function and patient global assessment for acupuncture compared to the sham group. Witt et al (29) compared acupuncture (12 sessions over 8 weeks) vs. minimal acupuncture vs. no acupuncture in a randomized trial of patients with osteoarthritis of the knee**;** subjects in the acupuncture group showed significant improvement in pain and function compared to both minimal acupuncture and no acupuncture. Scharf et al (39) found that true acupuncture and sham acupuncture (10 treatments over 6 weeks) were effective for osteoarthritis of the knee (successful for 53.1% in the true acupuncture group, 51.0% for sham, and 29.1% for standard care).

Back and neck pain. A recent meta-analysis on treatment of low back pain with acupuncture showed it was significantly more effective than sham treatment (40). Other recent randomized trials of acupuncture for low back pain have found both real and sham acupuncture were significantly more effective than waitlist control(41, 42); investigators have found similar positive results for neck pain(34). Most studies demonstrate improvements in both pain and disability. Because effective interventions for chronic pain have utilized 10 or more acupuncture treatments weekly or more frequently, we will offer 12 treatments over 12 weeks.

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A.3. Previous Experience: Effectiveness of acupuncture in an ethnically diverse and medically underserved primary care patient population. Our previous NCCAM-funded acupuncture trial, ADDOPT (Acupuncture to Decrease Disparities in Outcomes of Pain Treatment) demonstrated the acceptability and effectiveness of acupuncture treatment for chronic pain in an ethnically diverse and medically underserved population at high risk for health disparities. The ADDOPT study, conducted in the urban primary care health centers of the NYC RING practice-based research network (PBRN), completed data collection in November 2011 and results have now been published (43,44). In this pragmatic effectiveness study, primary care physicians (PCPs) referred patients with chronic pain due to osteoarthritis, neck, or back pain to on-site acupuncture provided in weekly sessions staffed by student/faculty teams from the Acupuncture programs of Pacific College of Oriental Medicine and Swedish Institute (New York, NY). ADDOPT employed a quasi-experimental design, comparing primary outcomes of pain, pain free days, and quality of life for patients during a pre-acupuncture phase (during which patients received usual care only) to the period after acupuncture was provided. Repeated measures of pain (at two week intervals) were utilized to account for variability in patients' pain experience.

Table 1. Baseline Pain, Disability and Functional Status (n = 227)

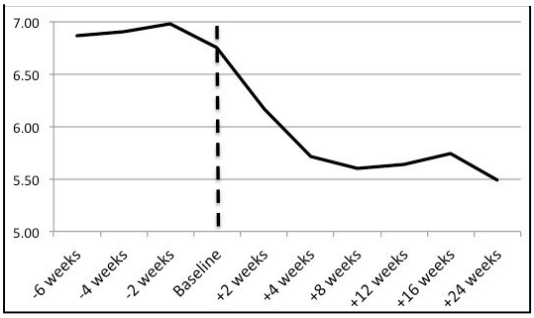
Chronic Pain Grading Scale (CPGS)	M	sd
Disability (0-100%)	66.9	30.8
Pain Intensity (0-100%)	77.3	15.9
Brief Pain Inventory (BPI)		
Pain Severity (0-10)	6.8	2.1
Pain Interference (0-10)	6.4	2.9
Pain Free Days (PFD)		
Days with pain last 2 weeks (0-14)	12.3	3.6
Pain Impact Questionnaire (PIQ-6)		
Pain score (40 - 78)	67.4	7.5
SF-12	M	sd
Physical health (0-100)	31.9	12.2
Mental health (0-100)	37.6	14.2
SF-12 Overall health rating	N	%
Poor	46	20.3
Fair	60	26.4

Participants. Back pain was the most common enrolled diagnosis (n=135; 59.5%), followed by osteoarthritis (n=37; 16.3%); many had multiple conditions (n=36, 15.9%). Participants were older (mean 54.3 years); low income (40.6% had household incomes less than $20,000) and 59% were on Medicaid. Over half were Hispanic (53.6%) and 27.1% primarily Spanish speaking. About a third (39.1%) were disabled. Table 1 describes the striking baseline characteristics, which indicate substantial disability, poorly controlled pain, and poor overall functional status of referred patients.

Feasibility. ADDOPT demonstrated the feasibility of integrating an acupuncture trial in the urban primary care setting, particularly regarding 1) success in referral (495 patients were referred over 2 years, with a large percentage of PCPs at each practice making referrals); 2) recruitment (47% initiated treatment - the most common reason for not initiating was schedule conflict/wait list); and 3) retention in care - of patients initiating treatment, 71% participated in ≥5 treatments [mean overall is 8.0 (SD 4.7)](43).

Outcomes. Repeated measures ANOVAs indicate that mean pain severity (BPI) and physical health scores (SF12) changed significantly over time during the course of the study. Pain severity improved from baseline (6.8 vs 5.7 at 12 wks and 5.8 at 24 wks) as did physical well-being (31.8 vs 35.4 at 12 wks and 35.2 at 24 wks). Using HLM methods, reduction in pain severity between baseline and treatment phase was significant ($p < .001$). Improvements in physical well being were significant at 12 and 24 weeks post-baseline ($p < .001$). Almost one-third (32.4%) experienced a 30% or greater improvement in pain.(61) Although this is slightly below the 40-50% response rate seen in many studies, given the constraints of the ADDOPT trial in delivering acupuncture using unpaid student acupuncturists—which could have easily led to decreased effectiveness –we feel this is strong evidence that a sizeable proportion will respond well to acupuncture. *The ADDOPT trial confirmed the feasibility of an acupuncture trial in this primary care population and indicates that many patients will experience what is typically considered to be a clinically meaningful reduction in pain (≥30%) with individual acupuncture.*

Figure 1: Mean Pain Severity Over Time



A.4. Evidence Gap. There is abundant evidence that individual acupuncture is effective for chronic pain and now evidence as well that it is feasible and effective specifically in an underserved and diverse population at risk for health

outcome disparities. Cost (including that most insurance plans do not cover acupuncture) and access to individual acupuncture treatment pose major barriers to widespread implementation in this patient population. To reduce cost, increase supply, and meet patient demand, a novel approach of group acupuncture is now being offered in some settings across the U.S. In the group approach, 6-8 patients are treated simultaneously by a single acupuncturist over a 60-90 minute period. In this approach patients are typically seated in a large room in comfortable chairs while receiving treatment; the acupuncturist takes a history and then treats each patient in turn, leaving the needles in place while moving on to treat the next person. Needles typically remain in place for 20-30 minutes as they would in an individual session, and participants have the potential added benefit of social interaction during the treatment session. Group acupuncture is now being offered in many settings, *but little or no evidence exists that acupuncture delivered in the group setting is as effective as individual acupuncture for chronic pain.* Between 2007 and 2010, membership in the Community Acupuncture Network tripled from 40 participating clinics in the U.S. to 120 (45). Qualitative studies to date show that treatment in the group setting is highly acceptable to patients (46,47) and that the group setting, community-based locations, and low cost of this model help eliminate some of the barriers to access to acupuncture (48). In terms of effectiveness, a recent study of patients (n=144) with osteoarthritis of the knee found significant improvements in pain and function after one month with benefits maintained up to two years in patients continuing treatment (49). A current NIH-funded study is evaluating the effectiveness of group acupuncture for painful diabetic neuropathy in an underserved population in California (50).

Controversy exists in the acupuncture and medical communities as to whether group acupuncture is as effective as individual treatment (51). In group acupuncture, since patients are typically seated rather than lying down and remain clothed, there is a greater emphasis on distal acupuncture points on the arms, legs, head and neck; some acupuncturists feel this decreases the effectiveness of the treatment. Because acupuncture therapy typically involves treatment of local and distal points together, a question of decreased effectiveness with distal treatment only remains unresolved. This important question needs to be addressed.

We propose the "Acupuncture Approaches to Decrease Disparities in Outcomes of Pain Treatment- A Two Arm Comparative Effectiveness Trial" (AADDOPT-2) to close this gap in the evidence, specifically to answer the important question of whether acupuncture for chronic pain delivered in a group setting is as effective as individual acupuncture in an underserved and ethnically diverse patient population at high risk for health disparities.

Part B. Significance

B.1. Potential for the study to improve healthcare and outcomes. (Criterion 2)

As discussed above, acupuncture is both safe and extremely effective in the management of chronic pain. Acupuncture is slowly being integrated into pain management in some conventional health care settings, yet cost and reimbursement are major obstacles to access. Despite the huge demand (we had 495 patients referred in ADDOPT and could only enroll half), and the demonstrated effectiveness, acupuncture is still rarely available to our patients. Group acupuncture can be offered for 17-33% of the cost of individual acupuncture (52, 53). Thus the primary aim of AADDOPT-2 will be **to evaluate whether acupuncture delivered in the group setting for patients with chronic pain is at least as effective as acupuncture delivered in the individual setting**. A second, more process-oriented objective of the project will be to **use qualitative analysis to understand and describe the patient experience of both acupuncture approaches, and to utilize this data to inform intervention delivery to better incorporate the patient perspective.** If the two approaches are equally effective for reducing pain and improving quality of life, **the findings from our first aim will facilitate increased access to acupuncture by reducing the cost of delivery in primary care and other pain management settings.** The experience in our second aim will allow us to disseminate a model for acupuncture delivery in a community setting for underserved patient populations that specifically incorporates the patient voice.

B.2. Patient-centeredness. (Criterion 4)

The symptom of chronic pain and its impact on function are outcomes of critical importance to patients. Patients need

more information regarding the range of treatment options available to them for management of chronic pain and the potential benefits and harms of those treatments. Safe and accessible treatment options for chronic pain are especially important now given the growing awareness among both patients and health care practitioners of the risks of side effects, dependence and addiction associated with many of the medications used to treat chronic pain. The availability of affordable acupuncture in an underserved community could help address not only the problem of pain treatment in that community but the problem of addiction and substance use as well. The main outcomes of this study (pain, pain-related disability, and quality of life) reflect outcomes of primary importance to individuals living with chronic pain.

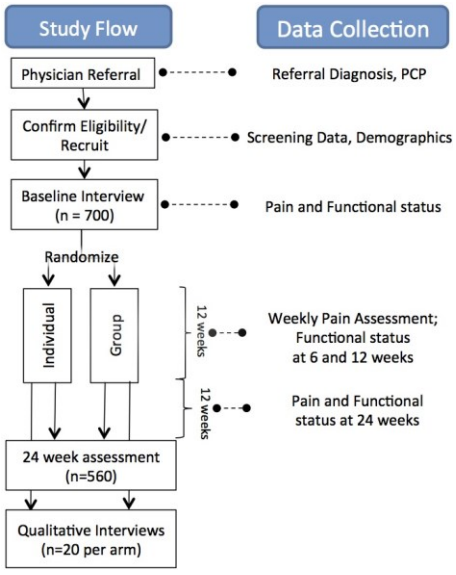
We will incorporate patients' voices throughout this project, from design, through implementation, interpretation of findings, and dissemination. The first step in this ongoing process started during the previous ADDOPT study. We carried out 37 in-depth interviews with ADDOPT participants. Although our analysis of this data is not yet published, this effort to understand patients' experiences has provided a wealth of information regarding such topics as facilitators and obstacles to participation, logistical challenges, the nature and importance of patients' relationship with the acupuncture practitioners, and patients' opinions regarding how acupuncture did or did not impact their pain and well-being. To further obtain input in the design of this study, we have recruited three former ADDOPT participants to serve as "Patient Partners" for this study. These patients participated in a preliminary advisory group meeting that further informed our approach, and will play a critical role throughout the study as Key Personnel on the project. Stakeholder engagement throughout the planned study is described in Section G.

Part C. Study Design and Approach

Demonstrate the study's technical merit. (Criterion 3)

C.1. Overview of Research Strategy. Our project, Acupuncture Approaches to Decrease Disparities in Outcomes of Pain Treatment: A Two Arm Comparative Effectiveness Study (AADDOPT-2), will be a randomized, comparative effectiveness trial evaluating acupuncture for treatment of chronic pain delivered either in individual or group visits in urban primary care health centers. After recruitment and baseline survey to assess pain and functional status, patients will be randomized to individual or group treatment. Randomization will be stratified by inclusion diagnosis, to ensure equal representation of neck pain, back pain, and osteoarthritis in each treatment group. After randomization, participants will be treated in weekly sessions for 12 weeks. Patient-centered outcomes of pain and quality of life will be assessed at 6, 12 and 24 weeks. Group and individual acupuncture sessions will be of similar duration and will be delivered by the same experienced study acupuncturists. Research associates gathering outcome data will be blinded to group assignment. We will carry out within-group and between group comparisons of pain and function outcomes.

Figure 2: Design Overview



In a patient-centered process to better understand participants' experience of the intervention, a subgroup of 20 participants in each arm will be invited for semi-structured interviews, after completing their 24-week outcome assessment. This data will be analyzed using qualitative techniques for themes which may prove important in facilitating the implementation of group or individual acupuncture in community health center practices. To maximize patient centeredness, our Patient Partners will assist with this process; findings will then be reviewed by all the Stakeholders and incorporated into 1) ongoing intervention delivery in this trial, and 2) dissemination efforts for future acupuncture delivery.

C.2. Specific Aims.

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1. To compare the effectiveness of group vs. individual acupuncture to reduce pain and improve function among primary care patients with chronic pain from an ethnically diverse, medically underserved population; and
2. To use qualitative methods to understand and incorporate the patient experience of acupuncture to maximize patient centeredness of the intervention and dissemination efforts.

Table 2: Participating Practices

Site	Unique Adult Patients	Patient Demographics	Medicaid	Uninsured	Neighborhood	FQHC
Family Health	8,893	Hisp (60%); Black (35%)	55.5%	11.5%	Fordham/Tremont	Yes
Grand Concourse	23,092	Hisp (40%); Black (35%)	15.2%	1.9%	Fordham/Tremont	No
Castle Hill	3,794	Hisp (58%); Black (26%)	48.6%	4.1%	Parkchester	Yes
Bronx East	31,534	Hisp (38%); Black (36%)	12.2%	3.4%	Parkchester	No
Williamsbridge	5,962	Hisp (21%); Black (75%)	43.2%	3.6%	Williamsbridge	Yes
Burke Ave	3,649	Hisp (25%); Black (77%)	24.8%	3.7%	Williamsbridge	No

C.3. Setting. The AADDOPT-2 project will take place in the health centers of the New York City Research and Improvement Networking Group (NYC RING), a practice-based research network dedicated to decreasing health disparities through primary care research in the urban safety net setting. Participating practices (listed in Table 2) are located in the Bronx, NY, a county comprised of a large proportion (85.5%) of ethnic minority residents of whom more than half (56.7%) are Hispanic. Nearly a third of the population lives below poverty level. These practices provide comprehensive primary care to patients with a variety of insurance coverage; FQHC sites see patients regardless of insurance status. Each practice has a clinical champion to support on-site acupuncture, and suitable sessions each week in which space is available. (See letters of support from Jon Swartz, MD and Don Raum, MD, Regional Medical Directors of Montefiore Medical Group).

C.4 Participants and Recruitment

Eligibility. Patients who receive primary care in 6 participating health centers will be eligible if they have a qualifying diagnosis of chronic (lasting 3 months or more) joint pain related to a diagnosis of osteoarthritis, or chronic neck or back pain related to non-cancer diagnoses. Participants will reflect typical health center patients, including many with multiple chronic diseases. To participate, they must be fluent in English or Spanish, able to provide home or cell phone numbers, and available for up to 24 weeks. Exclusions are limited to current anticoagulant use, and inability to provide informed consent due to mental illness or cognitive impairment.

Educational sessions. We will conduct brief educational sessions for practitioners and staff in the participating health centers,modeled after the module utilized for ADDOPT, to briefly introduce the philosophy of Chinese medicine and acupuncture therapy, safety and adverse effects and recent clinical evidence for effectiveness of acupuncture in chronic pain. The session will feature an acupuncture demonstration, since lack of personal experience with an "unconventional" modality can be a barrier to referral and utilization in practice.

Recruitment. All Primary Care Providers (PCPs) in each participating practice will be encouraged to refer appropriate adults (aged 21 and older) for acupuncture therapy. Employing procedures that worked well in ADDOPT, recruitment will be initiated when PCPs make referrals to the study team. At the clinician's discretion, acupuncture will be discussed as part of treatment planning during patient visits. For patients who meet eligibility criteria, PCPs will complete a study specific referral form. PCPs will obtain permission for a member of the study team to contact the patient, and obtain at least two current phone numbers to facilitate contact. Consent to participate in research will not be sought at this point. Clinicians will send referral forms to the practice's referral coordinator (as they would any other request for specialty consultation). The Study Coordinator will collect referrals, then contact patients by phone to verify eligibility, describe the study, and explain study procedures, including randomization (see Human Subjects for details of consent process).
We plan to enroll 700 patients over a 25 month year period, to allow us to reach our sample size target of 280 participants per arm assuming a 20% dropout rate.

We are confident in our team's ability to enroll the number of participants needed for this trial for several reasons. First, in our ADDOPT trial we recruited 495 patients in 18 months, from only four sites and with much more limited scheduling flexibility because we were using student acupuncturists. The two primary reasons roughly half did not receive acupuncture were the limitations of our acupuncture delivery capacity (which resulted in a long wait list) and scheduling

conflicts. Thus, in this project three capacity-expanding strategies will enable us to enroll a much higher proportion of referred patients: 1) staff acupuncturists rather than students will deliver acupuncture; this improves treatment time efficiency and therefore capacity; 2) evening and weekend hours will be available at an expanded number of sites, which enhances scheduling flexibility and 3) half of our participants will receive acupuncture in groups.

Randomization. Patients will b

Plan to ensure representativeness of participants. Our approach involves recruiting directly from practices that serve the urban underserved. Participants are limited to those who already receive their primary care in the participating health centers (demographics provided in Table 2, pg 5 of the proposal). Our referral approach in our pilot study resulted in a sample of patients with a high level of disability, multiple chronic diseases, and low SES reflecting the primary care population of interest. We are employing the same approach, including research staff who are bilingual in English and Spanish to ensure inclusion of primary Spanish speaking patients. We anticipate that using the same approach used in our first study will result in a similarly representative population in AADDOPT-2. To ensure this is the case, at three-month intervals we will carry out a systematic assessment of our study participants and our recruitment efforts to ensure that the procedures we followed in our pilot study are being equally effective in AADDOPT-2 and that our sample is representative. If we find any discrepancies in this analysis we will consult with our local stakeholders as well as with our participating practices to see what adjustments need to be made in our recruiting and enrollment efforts.

Plan to manage selection bias. Primary care providers will refer patients with chronic pain due to a qualifying condition. We have very few exclusionary conditions that might result in eliminating sicker patients. In addition to providing educational sessions with physicians and office staff, we will make information about acupuncture available in waiting areas and exam rooms so as to activate patients to inquire. We will offer convenient hours for data collection, and evening and weekend options for treatment. Offering the study intervention at the primary care site will also help facilitate ongoing participation from the participants with more disabling pain, since travel difficulties will be minimized, thus eliminating a potential selection bias toward patients with less severe pain.

Assessing adherence to enrollment practices. We anticipate that the quarterly assessments of recruiting and enrollment progress described above to ensure representativeness of our study participant population will also provide an opportunity to detect any substantive deviations from enrollment practices at our participating sites. If such deviations from the planned practices are detected, we will prepare and implement a process of remediation for the referring medical staff at the site(s) in question. Based on our experience in our pilot study we do not anticipate a major problem with this issue.

Plans to address population-unique issues for participant identification, recruitment, and retention. Our sample will include primarily individuals who have been historically underrepresented in health care research, including patients with multiple chronic diseases, low literacy, low SES, as well as racial and ethnic minority groups. As described above, many of the challenges of identifying such a population are minimized by working directly with primary care practices that serve this population, and offering the acupuncture interventions at the primary care practice. The task of identifying appropriate subjects will mainly reside with the medical and nursing staff at the community centers, who are already intimately involved in assessment and management of their patients' chronic pain. In our pilot study, we received almost 500 referrals from clinic staff, which significantly exceeded our treatment capacity in the trial.

Regarding retention, the REDCAP system will provide study staff with an automated screening, recruitment and tracking component to record all contacts with participants, implement a scheduling system, generate reminder emails and highlight all outstanding or upcoming follow up visits. Where needed, study staff will directly contact patients by telephone to help ensure follow-up and study retention. If we see specific patterns of loss to follow-up or problems in retention at certain sites, we will work with our stakeholders and with clinic staff to identify and address the site-specific issues.

C.5. Description of Interventions

Usual Care. Patients in both arms will continue to receive clinical services for management of chronic pain, as coordinated by primary care providers (PCPs). Usual care at these sites does not include alternative medicine services; it typically includes analgesic drug therapies and sometimes referral to specialist physicians or physical therapy. Based on

our ADDOPT experience, patients will vary substantially in the duration and other characteristics of the pain syndrome and in how it has been managed, and overall pain and related disability will be quite high.

Acupuncture therapy. Research on acupuncture therapy presents a unique challenge in terms of standardization of intervention dosage, frequency, and delivery, while allowing for the clinical responsivity of traditional East Asian medicine. We will use a pragmatic, real-world approach that allows for individualizing treatment from a pre-determined set of options (54), one to be used in the individual arm and one for the group arm. Acupuncturists will all use a common set of acupuncture points for either neck or back pain, and select from a set of additional optional points that address each individual's condition. Two nationally recognized acupuncturists, Dr. Nielsen (Director of Acupuncture Services at Beth Israel) and Dr. Anderson (Academic Dean and Research Director of Pacific College of Oriental Medicine, see biosketches), will develop the protocols for this trial based on the current literature, on our experience in the ADDOPT trial, and on their own extensive clinical experience. Two licensed acupuncturists with at least five years of practice experience will provide treatment once weekly for 12 weeks for each patient. We refer to our intervention as "acupuncture therapy" because the acupuncturists will be permitted to practice a range of different styles inclusive of both Traditional Chinese Medicine (TCM) and Classical Chinese Medicine. Patients will be evaluated based on their medical history, as well as on traditional Chinese Medicine physical examination including examination of the tongue (tongue diagnosis) and pulse (pulse diagnosis), and palpation of the channels. Based on this evaluation a diagnosis and treatment plan will be formulated. Individuals' progress will be evaluated and treatment adjusted as necessary. Acupuncture therapy will consist of needling body points with option of application of therapies often done in conjunction with acupuncture including: use of heat lamps, moxibustion, electrical stimulation of acupuncture points, needling auricular acupuncture points, adhesive application of ear seeds, and manual or instrument assisted stimulation of surface areas by palpation, massage (tui na) and/or Gua sha. All treatments will adhere to appropriate guidelines for safety and correct methodology (55). For needled points, treatment will consist of needle insertion and rotation to 'de qi' status (a sensory component felt by the patient, perceived by the practitioner as 'needle grasp') (56). Once 'de qi' has been felt, needles may be left in place to rest for a period of 10-30 minutes, or depending on the site, removed. The study coordinator (SC) will coordinate scheduling and make reminder calls to decrease missed visits.

Individual Treatment Arm. As in the ADDOPT trial, treatment in AADDOPT-2 will be offered once weekly for the individual acupuncture arm and delivered at the primary care health center. The average length of treatment will be approximately 45 minutes. We will take advantage of evening and Saturday hours where possible to enhance convenience for patients and exam room space availability.

Group Treatment Arm. Participants randomized to the group arm will receive their acupuncture treatment simultaneously in a group of 6-8 participants. Participants will be seated in comfortable chairs in a large room rather than in individual exam rooms. The length of time for treatment will be approximately 45 minutes, as in the individual arm, although the length of the entire group session will be longer (75-90 minutes) to allow adequate time for everyone to be treated. Based on feedback from our Patient Partners regarding patient privacy, each participant in the group arm will meet for a brief discussion in a private space with the acupuncturist prior to starting treatment.

Process and fidelity assessment: All acupuncturists will undergo training to become familiar with the study procedures, and for consistency in application of acupuncture and acupuncture therapies (as described above), and in interpersonal approach. Regarding this interpersonal dimension, which we seek to make as uniform as possible, this training will include video observation and feedback to standardize as much as possible the "non-specific" practitioner factors (empathy, communication style, etc), which might influence treatment outcomes. Acupuncturists will document treatments on standardized forms developed for the trial. To assess fidelity, on a monthly basis, Dr. Nielsen will examine all documentation of treatments in the context of the study protocol options. We will videotape 3-6 encounters (in acupuncture and attention control arms) for each acupuncturist and evaluate consistency in the interpersonal dimension. Feedback will be provided with retraining and reassessment when indicated.

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C.6. Quantitative Data Collection and Management (Aim 1): An overview of timing and approach of data collection is depicted in Table 3, below. For all data collection, questions will be administered in English or Spanish as preferred by the participant, in as neutral a manner as possible to avoid reporting bias. For data entry, we will use the state of the art, web-based data collection system available through the Einstein Institute for Clinical and Translational Research (ICTR) Research Informatics Core (RIC). Employing tablet computers, study staff will enter data directly via this platform whether by phone or in person at the participant's health centers. The initial research interview will take place after consent to participate in the trial has been obtained but *before randomization*, in most cases, within 1-2 weeks of referral. Evening and weekend hours will facilitate reaching working adults. Data at 6, 12, and 24 weeks will be collected by phone by a research assistant (RA) who will be blind to study group assignment. Participants will not receive an incentive to attend acupuncture treatments, but will receive modest incentives to complete the research interviews (see the Human Subjects section for details).

Table 3: Overview of Data Collection

Data	Content	Timepoint(s)	Location	Blinded
Screening	Eligibility/Demographics	At Referral	Phone	N/A
Baseline Survey	Pain Functional Status/QOL Medication Use	Pre-Randomization	Phone	N/A
Follow-up Assessments	Pain Functional Status/QOL & Medication Use	At 6,12 and 24 wks after treatment initiation 6,12, 24 weeks	Phone Phone	YES YES

Data will be entered and managed using the customized, secure, web-based platform, Research Electronic Data Capture, (REDCap). The system will generate de-identified study IDs and confirm consent before creating participant records. Automated measures of quality control such as out-of range and inconsistent data checks will be implemented to ensure data integrity and version control features will provide an audit trail that will track all data changes. This system will be supported by personnel from the RIC, and will provide study staff with an automated screening, recruitment and tracking component to record all contacts with participants, implement a scheduling system, generate reminder emails and highlight all outstanding or upcoming follow up visits. A Quality Assurance Protocol will be developed and documented for each phase, to flag deviations from protocol, highlight inconsistent or missing data and track data collection activities.

REDCap will generate status reports and basic descriptive analyses to spot anomalies in data over time. All reports will be reviewed by Dr. Fletcher, who will work directly with RIC staff to develop the study specific database, including tracking, reporting, and data checking functions. Reports will be reviewed at regular meetings of the Executive Committee.

C.6.1. Primary Outcome Measures. All instruments are established measures with good reliability; all have been validated for use in Spanish speaking populations. We will assess pain, pain interference with function, health status and pain-related disability at baseline, and then at 6, 12, and 24 weeks. Data may be collected from participants within a -4 and +6 week time interval for the 24-week data collection. Pain also will be assessed during four weekly telephone contacts during the four week run-in period prior to initiation of treatment.

*Brief Pain Inventory: Short Form (BPI)***.** The BPI (57) will serve as the primary outcome measure. It includes 4 pain scales, measuring "pain on average" during the past week, "pain at its worst" during the past week, "pain at its least" during the past week, and "pain right now". The primary outcome variable will be defined as a 30% or greater improvement on the BPI pain measure between baseline and week 12. The BPI also includes a validated 7-item scale measuring the extent to which pain interferes with function, including activity, mood, sleep, work and life enjoyment. For the weekly assessments, BPI scales for "pain on average" and "pain at its worst" will be used.

C.6.2. Secondary Outcome Measures.

PROMIS Quality of Life. The 10-item global Patient Reported Outcomes Measurement Information Systems (PROMIS) quality of life measure will be used as a secondary outcome measure. This scale is now being widely used to evaluate QOL and functional status outcomes in chronic pain as well as other conditions. It includes global ratings of the

five primary PROMIS domains (physical function, fatigue, pain, emotional distress, social health) as well as perceptions of general health that cut across domains (59), (http://www.nihpromis.org/software/assessmentcenter).

Patient Global Impression of Change (PGIC). Post intervention, patients will complete a short validated measure of global impression of change. The PGIC is a single question 7-point categorical scale. (58).

Medication use. We will track use of medications (opiates, non-steroidal anti-inflammatories [NSAIDS], and adjuvants) using two methods. Patients will be asked to report use of pain medications using a single question adapted from the Aberdeen Back Pain scale ("on the worst day in the past two weeks, how many painkilling tablets did you take"), assessed each time the BPI is administered (60). In addition, we will extract prescriptions written and refilled directly from the electronic medical record (EMR) using Clinical Looking Glass, a user interface to query Montefiore's electronic record that can be accessed for all participants with appropriate HIPAA consent.

C.6.3 Methods to Ensure Unbiased and Systematic Data Collection

Minimizing bias in data collection: We will keep all post-randomization data collection blind to study assignment. The RA will be blind to study assignment and will be solely responsible for post-randomization data collection. (The SC will know study assignment). The RA and SC will be trained by the PIs to conduct the interviews in as neutral a manner as possible. We will observe at least 5 interviews by each to confirm that additional training is not required. Our RA and SC will be bilingual in Spanish and English which should eliminate any potential for bias in data collection based on language issues. All data collection will be conducted as interviewer-directed, rather than self administered surveys, to facilitate involvement of patients with lower literacy.

Systematic data collection: Working with our NIH-funded Institute for Clinical and Translation Research (ICTR) Informatics Core, we will develop a robust study management database that includes reminders and reporting to alert study staff that a participant is due for data collection. The team will review reports that summarize data quality and missing data at weekly meetings and revise study procedures or provide additional training as needed.

C.6.4 Methods to Prevent and Monitor Missing Data. We will employ numerous strategies to ensure complete data. A Quality Assurance Protocol will be developed and documented for each phase, to flag deviations from protocol, highlight inconsistent or missing data and track data collection activities. Reviewing completeness of data will be a regular element of weekly staff meetings. We will obtain multiple contact numbers to ensure access throughout the follow-up period. When necessary, we will also take advantage of updated contact information available in the clinical information system. We are providing higher incentives for the 12- and 24-week data points to encourage participation. Many assessments will be completed by phone to encourage participation. All assessments are interviewer-directed, which should minimize incomplete survey data. Finally, we will make a concerted effort to maintain participants in follow-up even if they have chosen to discontinue acupuncture treatment.

C.6.5 Recording and Reporting Missing Data and Reasons for Dropout. As described above, we will make a concerted effort to obtain follow-up data from all patients, including those who choose to discontinue acupuncture. For all patients who opt to discontinue acupuncture treatment or who opt out of data collection, we will collect data to document the reason(s).

C.6.6 Assessing Data Source Adequacy. This project will not employ pre-existing data. Data sources for this project include: 1) primary survey data collected during run-in, at baseline and at follow-up; 2) interview material from patients participating in the qualitative interviews exploring the patient experience of receiving acupuncture in either the individual or group setting; and 3) prescribed medication use, obtained from the participants' electronic health record and self-report. We are employing validated patient-centered measures to assess the primary outcome of pain and secondary outcome of functional status. An additional secondary outcome, medication use, will be determined using a combination of self report and electronic health record (EHR). The design of this study is a randomized trial with an expected sample size of 350 subjects per group. To ensure equal representation of patients with different sources of pain (neck pain, back pain and osteoarthritis) in both treatment arms, randomization will be stratified by these categories. Given that a large number of subjects will be randomized to the two intervention arms of interest, we anticipate that any baseline patient characteristics that may be potential confounders will balance across the treatment groups. Baseline characteristics that will be evaluated

include level of disability, age, gender, marital status, socioeconomic status, and race/ethnicity among others. In the event that specific baseline variables are significantly different across groups by chance, we will adjust for these factors in the analysis using regression approaches.

C. 7 Qualitative Data Collection and Management (Aim 2)

Beginning in Year 1 of the study, we will conduct qualitative interviews with a subset of participants in both arms (n=40) who will serve as a "Patient Feedback Panel". These interviews will explore the patients' experience of receiving acupuncture in both the group and the individual setting. Working together with our three Patient Partners, we will develop a guide for semi-structured interviews to be used in this process and will recruit consecutive patients from those who are willing to be interviewed until we reach our desired sample size (anticipated at 20 per arm, depending on data saturation). The interview guide will be piloted with the first three patients and then modified as necessary. Participants will be offered an additional $50 incentive for completing the qualitative interview. Our Patient Partners will undergo training in qualitative interviewing (led by co-PI Dr. McKee, who has considerable experience teaching qualitative methods, including to staff of community-based organizations); the interviews will then be conducted by the Patient Partners and the Study Coordinator. Interviews will be conducted in either English or Spanish depending on patient preference, and can be done either in-person or by phone. Interviews will be audio-taped and transcribed verbatim prior to analysis. During the transcription, patient names will be removed to protect privacy and on the transcripts patients will be identified only by study ID number.

C.8. Quantitative Data Analysis Plan (Aim 1)

This study will evaluate whether group acupuncture is non-inferior to individual acupuncture in reducing pain and improving function in patients with chronic pain from an ethnically diverse, medically underserved population. All data analyses will be performed according to the intent-to-treat approach and will be preceded by extensive data checking and verification to identify and resolve the reasons for missing values, inconsistencies, and out-of-range values.

C.8.1. Primary Outcome. The primary outcome will be response to treatment, as defined by a 30% or greater improvement on the BPI pain measure between baseline and 12 weeks. The difference in response rates between the two acupuncture groups will be estimated along with corresponding two-sided 95% confidence intervals. Non-inferiority of the group approach relative to the individual approach will be declared if the upper limit of the 95% confidence interval for the true difference in response rates (individual therapy rate – group therapy rate) is less than δ, the margin of non-inferiority (defined to be $\delta = 10\%$).

Mean and median levels of other patient characteristics and outcomes measured at specific visits which are continuous variables, such as quality of life composite scores, pain scores, and pain-free days, will be estimated and compared between treatment groups using the two-sample T-test or Wilcoxon rank sum test depending on the distribution of the data. The chi-square or Fisher's exact test will be used to evaluate bivariate associations between categorical variables and treatment groups. General linear mixed models (GLMM) will also be fit to the data to analyze the repeated measures of pain and other outcome variables obtained during follow-up. This is a flexible statistical procedure that can easily accommodate missing values, irregular visit schedules, and within-subject correlation in the repeated measures. The model will include fixed effects for treatment arm (group versus individual acupuncture) and time, and a random subject effect to take into account the within-subject correlation between repeated measurements. Suitable transformations will be applied if data are non-normally distributed and an unstructured correlation matrix will be assumed for the within-subject correlation. Primary analyses will not be adjusted for covariates. To account for potential confounders, the relevant covariates will be included in the GLMM model. The Bonferroni approach will be used to adjust for the inflation in the Type I error rate due to the evaluation of multiple outcomes.

C.8.2. Heterogeneity of Treatment Effects. Additional analyses will be conducted to evaluate whether the treatment effect varies by source of pain (neck, back, OA), baseline level of disability (2 levels) and treatment compliance (3 levels). Initially, subgroups will be defined based on the above factors and estimates of treatment effect will be obtained separately in each subgroup using the methods described above. These analyses will be viewed as exploratory since

sample sizes may be limited. We will also formally test for the significance of any heterogeneous treatment effects across these factors by including main effects for the variables well as corresponding interaction terms with treatment group in the GLMM models.

C.8.3. Pre-specified and post-hoc analyses. Subgroup analyses will be conducted to evaluate whether the treatment effect varies by source of pain (neck, back, OA), baseline level of disability (2 levels) and treatment compliance (3 levels) for a total of 8 potential subgroup analyses. Initially, estimates of treatment effect will be obtained separately in each subgroup using the statistical methods described in the application. We will also formally test for the significance of any heterogeneous treatment effects across these factors by including main effects for the relevant variables well as corresponding interaction terms with treatment group in the proposed GLMM models. Since sample sizes and power may be limited for these analyses, they will be viewed as exploratory; formal multiple testing procedures will not be applied.

C.8.4. Missing data. In any clinical trial, some subjects will be lost to follow up or will miss study visits. Primary analysis will be based on available data at each time point. The advantage of the GLMM approach is that it can handle data which are missing at random and measurement times which are not evenly spaced. However, when the missingness mechanism depends on unobserved information, i.e., non-ignorable, parameter estimates and resulting tests on hypotheses will be biased without further adjustment. Different approaches for handling missing data will be performed in this study. Data will be stratified according to their missing pattern (e.g., early termination, late termination, and follow-up completers) and then variables based on these groups will be used as model covariates. Additionally, multiple imputation will be applied if missing data rates are observed to differ across observed covariates. Regardless of the technique, characteristics of patients who are lost to follow-up will be compared to those that remain in the study to assess the degree of any selection bias, and sensitivity analyses will be performed to evaluate robustness of conclusions to the different missing data approaches.

C.8.5. Sample size justification. The power of this non-inferiority trial was evaluated based on the primary outcome of response status, defined as a 30% or greater improvement on the BPI pain measure between baseline and 12 weeks. In addition, we define the margin of non-inferiority to be a difference in response rates (individual therapy rate – group therapy rate) of $\delta = 10\%$. With a sample size of 282 subjects per group, the study will have 80% power with a Type I error rate of 5% to conclude that group therapy is non-inferior to individual therapy under the alternative hypothesis that the true response rate in both groups is 35%. In this trial, we anticipate a slightly higher response rate than the 30% rate observed in the ADDOPT trial since we will be using experienced acupuncturists rather than students to administer the therapy. Moreover, the typical response rate in the literature for acupuncture for chronic pain is in the 40-50% range (40). Assuming a drop-out rate of 20%, we will enroll approximately 350 patients per group (700 total).

C.8.6. Sensitivity Analyses. Sensitivity analyses will be performed to evaluate whether the study results differ according to 1) varying assumptions about the correlation structure in the generalized linear mixed modeling approach (e.g. compound symmetry, auto-regressive, unstructured); 2) different transformations for non-normally distributed data (e.g. rank transform, log transform); 3) different approaches to modeling time in the repeated measures analysis (linear, categorical, polynomial); 4) unadjusted versus covariate adjusted estimates of treatment effects; 5) intent-to-treat versus per-protocol analysis; and 6) complete case analysis versus multiple imputation for handling missing data.

C.8.7. Assessing and Reporting Internal and External Validity. Our reports will follow the CONSORT approach for describing randomized clinical trials. Briefly, reporting will follow the CONSORT checklist, including a full description of enrollment, allocation, follow-up and analysis, and will include a diagram. To systematically characterize our acupuncture intervention, we will follow the approach laid out in the Standards for Reporting Interventions in Clinical Trials of Acupuncture[1], an extension of the CONSORT statement. STRICTA provides a checklist including elements such as acupuncture rationale, details of needling, specifics of the treatment regimen, and details of practitioner background.

[1] MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, Moher D; STRICTA Revision Group. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. PLoS Med. 2010;7(6):e1000261. PMID: 20543992

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These standards allow for consistency in reporting of acupuncture study interventions and for greater potential to allow future investigators to replicate a specific type of intervention approach.

C.9. Qualitative Data Analysis Plan (Aim 2). We believe it is critical to have the patient voice represented in analyzing the data on patient experience of acupuncture. Our Patient Partners will participate as members of the qualitative analysis team. The level at which each of our partners engages will vary based on their educational background, their level of commitment, and their interest in this part of the project. Analysis of interview data will begin with development of a simple descriptive coding scheme, using standard iterative approaches (61). The qualitative team (Kligler, McKee, the Study Coordinator, Patient Partners) will read through a selection of interviews and identify potential coding categories. These will be discussed in the group and then added to the code list and re-applied to new sub-sets of data. Coding differences are reconciled through discussion; the revised coding scheme will then be applied using standard iterative procedures. Once the coding scheme is determined to be sufficiently comprehensive and specific, it will be applied to the entire data set. Coded data will be uploaded into NVIVO^{tm}, a qualitative data analysis program that facilitates the rapid organization and retrieval of qualitative data. In a second step, we will examine themes in the interviews across the sample, and characterize participants' attitudes, and experiences regarding their experiences of acupuncture in the study. In a third confirmatory step, we will present our summary of themes describing the experience of acupuncture back to a subset of our Patient Feedback Panel to see if we have adequately captured our participants' voices. Following this step, a summary of the findings from this process will be provided to the study acupuncture team and Stakeholders by the Patient Partners with the goal of modifying the acupuncture procedures in a way that reflects the feedback from the participants.

Part D. Project Milestones and Timeline

To assure timely completion of our objectives, we have assembled an experienced multidisciplinary team and will engage a diverse group of stakeholders including patients, primary care physicians, acupuncture therapy providers, health care insurance payors and methodologists throughout the project. In order to effectively manage these activities, we will organize the following groups: **1) The Executive Committee** (Drs. McKee and Kligler as co-PIs, Dr. Nielson, Dr. Fletcher, and the Study Coordinator) who will meet weekly to oversee all aspects of study implementation; 2) **The AADDOPT-2 Project Team** (including the Executive Committee, plus the Study Coordinator, the acupuncturists, Dr. Anderson, Dr. Kim, and the Patient Partners), which will meet monthly throughout the study to provide interdisciplinary input on all aspects of the study design, implementation and analysis; and **3) the Stakeholder Advisory Panel,** which will include all stakeholders and the Executive Committee, and will meet quarterly.

YEAR 1		
MILESTONE	DELIVERABLE	PROJECTED COMPLETION DATE
1. Research preparation	Hire and train coordinator and RA	Month 1
	IRB Approvals obtained	Month 3
	Develop REDCap study management database	Month 2
	Baseline and outcomes assessment survey in REDCap and piloted for web-based data entry	Month 3
2. Primary care engagement	Conduct orientations at each practice	Month 2 and 3
	Referral tools available at sites	Month 2
3. Stakeholder consultation	Initial Stakeholder Retreat (in-person)	Month 3
	Convene Stakeholder Group quarterly (phone)	Month 6,9,12
4. Intervention delivery	Finalize acupuncture protocols	Month 1
	Hire and train acupuncturists	Month 2 and 3
	First acupuncture sessions begin	Month 4
	Begin supervision and fidelity assessment	Month 4 then ongoing

5. Data collection and quality assurance	Begin referrals and run-in data collection	Month 3
	Baseline data collection begins	Month 4
	Outcome assessment and data entry	Continuous
	Implement data quality checks/report at monthly Team meetings	Ongoing
	Qualitative Interviews (n=40) and analysis	Month 10-12
	Patient Feedback Group reviews interview findings	Month 12
6. Reporting	Deliver progress report to Stakeholders	Months 6,9 and 12
	Provide annual progress report to funder and Stakeholders	3 months after end of year
YEAR 2 and 3		
MILESTONE NAME	DESCRIPTION	PROJECTED COMPLETION DATE
1. Ongoing referrals	PCPs refer appropriate patients to acupuncture	Ongoing until month 27
2. Intervention delivery	Group and individual acupuncture at practices	Ongoing until month 30
3. Data collection and quality assurance	Baseline, 6, 12 and 24 week outcome assessments; Monthly data quality reports at Team meetings	Ongoing, last 24-wk assessments month 33
	Extract medication data from EMR	Month 12, 24, and 33
4. Stakeholder consultation	Convene Stakeholder Group quarterly (phone)	Month 15, 18, 21, 24, 27, 30, 33, and 36
5. Data Analysis	Baseline	Month 28-30
	Final Outcomes	Months 33-36
6. Dissemination	Develop dissemination plan with Stakeholders	Months 30-36

Part E. Patient Population

We anticipate that our patient population for this study will be very similar to the population in the ADDOPT trial. We will recruit from, and deliver acupuncture in primary care practices that participate in the NYC RING practice-based research network (see Part F below) in the Bronx. The specific practices are described in Table 2 (section C.2). Demographics, clinical and functional status of the patients as they presented in the ADDOPT study is provided in Table 4.

Part F. Research Team and Environment

Table 4. Demographics of participants who initiated treatment (n=226)		
	M	SD
Age (years)	54.3	14
Race/Ethnicity	N	%
Hispanic	121	53.5
Non-Hispanic Black	61	27
Non-Hispanic White	9	4
Non-Hispanic Other	34	15
Insurance	N	%
Fee for service Medicaid	7	3.1
Mgd Care Medicaid	129	57.1
Private Ins	52	23
No Insurance	13	5.8
Household Income	N	%
Less than $20,000	95	42
$20-$29,000	27	11.9
$30-$39,000	18	8
$40-49,000	6	2.7
Greater than $50,000	7	3.1
Don't Know/Refused	67	29.6

Research Environment. The New York City Research, Improvement and Networking Group (NYC RING) is a practice-based research network of practices that provide comprehensive primary care to large numbers of urban minority patients. NYC RING's mission is to conduct high quality urban primary care research with the goal of improving services and outcomes for disadvantaged populations. Dr. McKee (co-PI of this proposed project) is the director of NYC RING. The network consists of 35 community-based primary care practices affiliated with the Albert Einstein College of Medicine in the Bronx, lower Westchester County and Manhattan. NYC RING is one of only a few PBRNs in the US focused exclusively on the urban underserved. The network is founded on the premise that actively involving primary care providers in all phases of the research process will enhance the relevance of the questions, improve implementation of protocols, and significantly improve the translation of results into practice. A full time network coordinator (Ms. Lechuga) provides support for PBRN initiatives, and feedback of research results to practices. An aggregate profile of the NYC RING practices confirms that the patient population served reflects the communities in which the offices are located. About half of patients are Hispanic, about a third are Black, and Whites and Other comprise relatively equal proportions. Overall, 90% of patients are minorities. These practices also have substantial proportions of uninsured patients. Eight sites are federally-funded community health centers.

Research Team. The leadership team for this project has extensive experience collaborating over the past five years on the ADDOPT study as well as a number of other educational and research efforts. Key team members are listed below.

Co-Principal Investigator, M. Diane McKee, MD, MS. is Associate Professor of Family and Social Medicine, Co-Director of the Department of Family and Social Medicine Division of Research and the Director of the NYC RING practice-based research network. Dr. McKee is an experienced health services researcher who has led multiple primary care interventions. Most recently, she was PI of the ADDOPT trial, on which she worked closely with the other members of the team proposed for AADDOPT-2. As the Einstein-based co-PI, Dr. McKee will have primary responsibility for administrative and financial oversight and management of the project. Dr. McKee and Dr. Kligler will share responsibility for hiring, training, and supervising the Study Coordinator and Research Assistant, and for project implementation, report writing, evaluation and analysis. Dr. McKee will lead weekly Executive Team meetings and monthly meetings with the entire Project Team with Dr. Kligler. She will also share with Dr. Kligler responsibility for ensuring the ongoing involvement of the stakeholder panel in feedback and decision-making regarding the project. Dr. McKee will contribute her expertise in engaging primary care clinicians and office staff in adopting interventions; as such she will have primary responsibility for interfacing with the participating practices. She will also have primary responsibility for assuring adherence to the highest standards of human subjects protections including IRB reporting at Einstein. Dr. McKee and Dr. Kligler will jointly oversee the preparation of manuscripts and other dissemination activities.

Co-Principal Investigator, Benjamin Kligler, MD is Associate Professor of Family and Social Medicine at Albert Einstein and Vice Chair and Research Director of the Department of Integrative Medicine at Beth Israel. He is also a certified physician acupuncturist. Dr. Kligler is currently completing a Career Development Award from NCCAM focused on using qualitative methods to explore the patient factors that correlate with positive response to integrative medicine interventions. Dr. Kligler was a co-investigator with Dr. McKee on the ADDOPT trial. In addition to his NIH-funded experience, Dr. Kligler has served as PI on several privately funded studies over the past five years, including the recently published Urban Zen trial, which used a mixed methods design. Dr. Kligler also serves on the Pacific College of Oriental Medicine Board of Trustees. Dr. Kligler will participate in all aspects of study design, data collection and

analysis. He will co-lead the weekly Executive Team meetings and the monthly Project Team meetings with Dr. McKee. As the Beth Israel/PCOM-based co-PI, Dr. Kligler will have primary responsibility for working with Drs. Nielsen and Anderson to develop and implement the acupuncture intervention, and to hire, train and supervise the acupuncturists to ensure fidelity and quality in the intervention process. Dr. McKee and Dr. Kligler will jointly oversee the preparation of manuscripts and other dissemination activities.

Co-Investigator, Arya Nielsen, PhD, LAc is Director of Acupuncture Services at Beth Israel and also Director of the Beth Israel Acupuncture Fellowship program. Dr. Nielsen is an internationally known teacher and researcher on acupuncture, with a major focus in the area of gua sha, one of the "manual therapies" to be incorporated into the acupuncture protocols in this study. Her previous research has focused on understanding the biological mechanisms of this type of acupuncture therapy. She has also taught internationally on this topic and is the author of the premier textbook on gua sha. In addition, Dr. Nielsen has participated in developing manualization strategies for several acupuncture studies, experience which will provide important background for her work leading protocol development for this trial. Dr. Nielsen is currently PI of the Acupuncture for Spine Surgery study in progress at Beth Israel. Dr. Nielsen's role on the study will be to work with Dr. Anderson to develop the acupuncture protocol and ensure quality and fidelity in the acupuncture intervention, and provide ongoing supervision of the acupuncturists.

Co-Investigator, Belinda Anderson, PhD, LAc is the Academic Dean and Research Director at Pacific College of Oriental Medicine. Dr. Anderson has both a PhD in Molecular Biology and a Master's degree in Acupuncture and Oriental Medicine, with a license to practice acupuncture in the state of NY. She has extensive previous research experience having been a tenured academic with her own research group (supported by six consecutive years of government research funding), numerous publications in peer-reviewed journals and two patents for vaccine discoveries. In 2010 she was appointed as an Assistant Clinical Professor at Albert Einstein School of Medicine in the Department of Family and Social Medicine. In her current role at Pacific College of Oriental Medicine, she is leading the institution in developing a research curriculum. She is currently supported by a K-07 award from NCCAM. Dr. Anderson will be responsible for identifying and hiring acupuncturists for delivery of the intervention, conducting training, and with the assistance of Dr. Nielsen, developing the protocol and overseeing the ongoing fidelity evaluation for acupuncture delivery. She will be responsible for interfacing with the PCOM administration for all human subjects, grant accounting and reporting requirements.

Co-Investigator, Mimi Kim, ScD will be the lead study statistician for the project. She is Professor and Head of the Division of Biostatistics at the Albert Einstein College of Medicine and has over 20 years of experience designing and analyzing clinical and epidemiologic studies in many different disease areas. She has also directed the biostatistics cores of several large multicenter clinical trials. For this project, Dr. Kim has collaborated closely with investigators on the study designs and analytic plans. She will continue to provide statistical support on all aspects of the project including study conduct and monitoring, data analysis, and interpretation and reporting of results. She will directly supervise Dr. Fletcher who will assist in the data analysis

Consultant, Russell Portenoy, M.D. is former Chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Medical Center and Professor of Neurology and Anesthesia, Albert Einstein College of Medicine. Dr. Portenoy is an internationally recognized pain medicine expert with extensive research experience. He has participated in the development of several important quantitative pain and symptom measures which are currently in wide use in the field. Dr. Portenoy has collaborated with both Dr. McKee and Dr. Kligler on the ADDOPT study. For this project, he will contribute his expertise specifically advising on issues of pain measurement, instrument selection and analysis of pain data.

Consultant, Maria Chao, DrPH, is Assistant Professor of Medicine at the University of California San Francisco School of Medicine and is affiliated with the Osher Center for Integrative Medicine at UCSF. She has extensive research experience in evaluating innovative delivery models for acupuncture with a specific focus on strategies to improve access in underserved populations. Dr. Chao is currently funded on a K-01 award from NIH/NCCAM to study group acupuncture for painful diabetic neuropathy among underserved patients. For the AADDOPT-2 project, she will

contribute her expertise specifically advising on issues of intervention development and implementation as well as the qualitative evaluation of acceptability of group acupuncture.

Part G. Engagement Plan

Plan to engage patients and stakeholders meaningfully in the various phases of the proposed research. (Criterion 5)

G.1. Overview of Patient and Stakeholder Involvement. We are proposing three levels at which patients and other stakeholders will be actively involved with us in carrying out the AADDOPT-2 project. The first is a group of three **"Patient Partners"** who will play an integral role on the investigator team (see biosketches for details). The role of these Patient Partners is described in detail below. The second is a larger group of 40 patients **("Patient Feedback Group")** enrolled in the study during Year 1, who will choose to participate in our qualitative evaluation of the acupuncture intervention, giving feedback on the patient experience which will then be incorporated into the intervention going forward. The third is our **Stakeholder Advisory Panel,** which includes our Patient Partners but also several other members representing stakeholder interests relevant to our project. This larger panel will meet once in person at the start of the project and then quarterly by phone during the study. The specific involvement, roles and responsibilities of each of these groups are outlined below.

G.2. Stakeholder Involvement in Formulating the Research Questions and Study Design. We are very fortunate in that our engagement with patients in our community on the issue of acupuncture for pain began almost five years ago with the launch of the ADDOPT study, a rare example of NIH-funded community-based research in that the funder required that the research take place in a PBRN. As part of the ADDOPT study, we conducted in-depth qualitative interviews with 37 patients from our four participating health centers. Interviews were conducted in both English and Spanish and focused on understanding patients' experience of acupuncture treatment as well as their feelings about facilitators and obstacles to that treatment. A strong patient consensus emerged from that data that our patients want ongoing access to acupuncture treatment for their pain but that barriers of access and payment at this point made that impossible. From this patient voice arose the idea to try to examine a model of acupuncture delivery that could be more sustainable in our treatment environment, and the specific research question of whether group acupuncture would be as effective and acceptable to patients as our individual model in ADDOPT.

Our research question and study design have also been informed by another important stakeholder group: acupuncture practitioners and educators, as represented by Drs. Nielsen and Anderson on the study team. This group of stakeholders will ultimately be deeply involved if the model of group acupuncture for underserved communities proves to be an effective option. Drs. Nielsen and Anderson have collaborated in developing this proposal, and are specifically responsible for the description of the acupuncture interventions and how they will be delivered.

G.3. Role/Involvement of Patient Partners

Formulating the Study Design. We recruited three patient advisors (see letters of support) who participated in the ADDOPT study to help us create the intervention for AADDOPT-2, and identify our goals and outcomes. This group met and reviewed our study proposal prior to submission, and contributed several substantive changes to our strategy for delivering the group intervention. These three Patient Partners will continue to play key roles throughout the project, serving on our Steering Committee and fully in decision-making as we proceed. They will also be compensated financially as Key Personnel for their assistance.

Participating in and Monitoring the Conduct of the Project. Our Patient Partners will participate in project team monthly calls from the inception to the end of the study period. This regular contact will ensure that their perspective and feedback is integrated into all aspects of the study as it progresses. Our Patient Partners will participate in the quarterly Stakeholder Advisory Panel meetings throughout the study. In addition to these regular in person and phone meetings, our Patient Partners will be involved in numerous aspects of the process as the study evolves, many of which will take place outside of these regular calls. These roles will span planning the final details of the intervention, recruitment and data collection, and evaluation activities, as well as input into Stakeholder Advisory Panel meeting agendas.

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Intervention development.

1. In the first three months of the project, Patient Partners will work with our acupuncture team (Drs. Anderson and Nielsen) to develop details of the group acupuncture experience, such as how the intervention will be described to participants, how the rooms will be set up for group treatment to address modesty issues, and how to facilitate comfortable interaction between participants in the group arm. Patients will also share their experiences in the ADDOPT study with the acupuncture team to help inform study treatment protocol development, and then, at month three, participate in a pilot "group treatment" at one health center to generate additional feedback for the team. The present proposal already incorporates feedback from our Patient Partners on the issue of patient privacy based on our work with them prior to submission. Also, based on their input, we are opting for mixed-gender rather than single-gender groups, as they felt there was no need to offer single gender groups despite the fact that this has been mentioned in the literature to date.
2. Patient Partners will assist with developing the informed consent document for the study to make sure it is understandable to our study participants (both English and Spanish versions).
3. Patients will work with Drs. McKee and Kligler to develop the interview guide for the qualitative component, helping ensure that the questions accurately reflect true patient concerns and perspectives.

Recruitment and Data Collection.

1. Patient Partners will complete Human Subjects Training during the first three months of the project so as to be able to participate fully in all study-related activities.
2. They will be involved in developing fliers and other recruitment materials for use in the participating practices.
3. Patient Partners will assist in recruiting for the study from their own communities connected with the health centers and through other networks.
4. Interested Patient Partners will be trained in the qualitative interviewing process and will carry out interviews with study participants regarding their experience of acupuncture.

Data Analysis.

1. In the latter half of Year 1, interested Patient Partners will be offered a basic training in evaluating qualitative data and will then participate with Drs. McKee and Kligler in discussing results and extracting themes describing the study participants' experience.
2. Once these themes have been described and the qualitative team has had the opportunity to evaluate the material, they will discuss and comment on the conclusions drawn regarding the material.
3. In an engaged Continuous Quality Improvement (CQI) model, patient partners will participate in developing modifications to the intervention delivery based on feedback from the qualitative interviews and analysis.

Evaluation Activities.

The monthly phone calls with the project team will provide an opportunity for Drs. McKee and Kligler to "check-in" regularly with the Patient Partners to be sure that they are satisfied with their level of involvement in the study and that they feel their involvement is making an important contribution to the research. The project leaders will use this regular feedback to adjust the engagement as needed to ensure a real and meaningful partnership. In a similar process, other research team members will be invited on a regular basis to give feedback to the entire team regarding the patient involvement. To help ensure and promote open and honest communication even if there are disagreements, we will invite an outside facilitator to join the project team calls every third month to help with discussion of any sensitive or difficult issues that are confronting the project team.

G.4. Role/Involvement of Patient Feedback Group

In addition to the Patient Partners discussed above, we will engage a larger group of patients from our community who are actively participating in the study to give us feedback that will help us deliver the study intervention in the most patient-centered fashion possible. Twenty patients will be recruited from each arm of the study during Year 1 to be interviewed about their experience. These interviews will be conducted both by the Patient Partners and by our Research

Coordinator, depending on availability, in either English or Spanish as needed. Participants in this Patient Feedback Group will receive an additional honorarium of $50 for their participation in this 30-60 minute interview.

After the study team, including the Patient Partners, has reviewed and summarized the qualitative material, the members of the Patient Feedback Group will be asked to review a summary of the team's conclusions to check for accuracy and to be sure that the team is making the correct recommendations regarding how the intervention should be adjusted. As many of the members of the feedback group as are available will be invited to participate in a focus group to review the teams summary and recommendations; a Spanish translator will be present at this focus group and patients participating will receive an additional $50 honorarium for that participation.

Following this "confirmation" step, the Patient Partners and any of the feedback group who are interested in participating will meet with the study acupuncturists and the project leaders to discuss the feedback results and what specific changes should be made based on the patients' experience. As an example, there is some suggestion from the literature that same-sex groups may be more acceptable to patients than mixed groups; we will specifically explore this question with patients, along with other issues that may influence their experience.

G.5. Role/Involvement of Stakeholder Advisory Panel.

The stakeholder panel is meant to represent the interests of patients as well as those of other communities who may be interested in the outcomes of this project. The panel will meet once in person at the start of the project and then every three months by conference call for one hour during the three years of the project. Stakeholders' specific roles on the project will vary depending on their backgrounds; some will be involved more with intervention development, and others with dissemination. Although this is not all-inclusive, we have chosen to have the following groups represented on our stakeholder panel (number of members in parentheses, with a full list provided in Table 5): 1) patients from our community, as described in our "Patient Partners" role (3), 2) patients from the larger U.S. community, as represented by patient advocacy groups (1), 3) the acupuncture community at large, and specifically acupuncturists currently practicing in the group setting (2), 4) the interdisciplinary pain treatment community, at the intersection of conventional and CAM approaches, represented by the American Academy of Pain Management (1) and the Consortium of Academic Health Centers for Integrative Medicine (1), 5) payors/insurers (1), and 6) the primary care community (1).

Table 5. Stakeholder Advisory Panel

Stakeholder	Group represented	Specific Role
Carmen Suarez	Patients	See below
Linda Canales	Patients	See below
John MacDonald	Patients	See below
Robert Twillman	American Academy of Pain Management	Communication/Dissemination
Liza Goldblatt	National Acupuncture community	Communication/Dissemination
Dionetta Hudzinski	Patients and Patient advocates	Intervention development; Dissemination
Rob Benhuri	Community acupuncture clinicians	Intervention development; Dissemination
Urvashi Patel	Insurers/Payors	Dissemination; Policy advocacy
Tobi Fishel	Consortium of Academic Health Centers for Integrative Medicine	Communication/Dissemination
Ellen Tattelman	MMG Primary Care Clinician	Intervention development; Communication/Dissemination

G.5.1. Stakeholder Role in Planning Dissemination of the Study's Results. Stakeholders will have various roles in dissemination of the study results depending on the community they represent. Patient Partners will be involved in outreach to the local community both through the health centers and through their other community connections to make other patients in the community with chronic pain aware of the study findings and potential benefits of acupuncture. Patient Partners will also be invited to co-author articles describing the study findings for publication both in scholarly journals and in local press outlets. Stakeholder partners from national groups (AAPM, CAHCIM) will help with

dissemination of the findings to their membership through newsletters, website postings, and presentations at meetings. These roles are discussed in more detail in the Dissemination and Implementation section.

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DISSEMINATION AND IMPLEMENTATION POTENTIAL

A. Describe the potential for disseminating and implementing the results of this research in other settings.

In addition to the standard strategy of disseminating results through publication in academic journals and presentation at relevant meetings, we plan a range of other strategies to inform our stakeholder communities regarding the outcome of our research and hopefully to speed implementation of similar models around the country. We have envisioned the dissemination process as taking place in concentric circles involving our stakeholder groups.

1. Dissemination/Implementation in our local community: Patient Partners will be involved in outreach to the local community both through the health centers and through their other community connections to make other patients in the community with chronic pain aware of the potential benefits of acupuncture. Patient Partners will also be invited to co-author articles describing the study findings for publication in local press outlets. We also have a commitment from our department and from our medical group to explore the possibility of ongoing delivery of group acupuncture in our network if the treatment proves to be effective. The active implementation of individual acupuncture services in the NYC-RING clinics has been difficult due to cost issues, and our administration has expressed an interest in exploring group acupuncture further as a strategy to increase access.

2. Dissemination in the larger patient community: Through our stakeholder representative from the national patient advocacy perspective, we will pursue dissemination of our results to the community of pain patients across the country. This will be done through newsletters, web-site postings, and other meetings. Rapid dissemination to the patient advocacy network nationally will hopefully lead to pressure from patients on health systems and payors to provide group acupuncture in their communities, should it prove an effective approach.

3. Dissemination in the larger acupuncture community: Through Dr. Goldblatt, a nationally active member in the accreditation of acupuncture colleges, and through Dr. Anderson, the current Academic Dean at the largest acupuncture training program in the country (PCOM), we have excellent avenues for dissemination and implementation of our study findings in the larger acupuncture community. For example, Dr. Anderson is committed to developing additional training for acupuncturists within the three PCOM campuses on group acupuncture if our intervention proves to be as effective as individual acupuncture. The qualitative input from patients and lessons learned about implementation of acupuncture can also be easily translated into the treatment settings at PCOM and other training institutions.

4. Dissemination in the national pain treatment community: Stakeholder partners from national groups (AAPM, CAHCIM) will help with dissemination of the findings to their membership through newsletters, website postings, and presentations at meetings. The Clinical Working Group of CAHCIM, of which Dr. Fishel is former Chair, holds monthly webinars on clinical innovations attended by practitioners from around the country; this would be an ideal venue for dissemination of study results and discussion of strategies for implementation in other settings. The AAPM recently published a strong statement regarding the need for more education and clinical options for physicians in pain treatment and, thus, is primed to help disseminate the results of this project, as well as part of their training effort.

5. Dissemination in the research community: Dr. Kligler is a member of the Executive Committee of BraveNet, a 14-center practice-based research network. All of the centers in this network offer acupuncture. If the group acupuncture intervention is effective, many of the BraveNet centers will be very open to follow-up studies further defining how and for whom this intervention can be helpful. Our involvement with BraveNet provides an open avenue to a group of experienced researchers ready and willing to replicate and further elaborate on our approach in this project. We will, of course, also submit our findings for presentation at relevant meetings in the pain medicine, acupuncture, and integrative medicine communities, and publish our findings in the relevant journals. Finally, we will provide the outcomes data for peer review and then post it as a shared resource. Upon acceptance, we will post the data library and data set (HIPPA compliant for patient protection) to peer reviewed journals and include links to social media and our website.

B. Describe possible barriers to disseminating and implementing the results of this research in other settings.

We do not foresee any significant barriers to disseminating the results of our research, nor to the potential replication of our approach in other research settings. The most significant potential barriers are in the area of implementation, due to the fact that neither individual nor group acupuncture is currently reimbursed by most insurance plans. Thus, even though group acupuncture will offer a lower-cost approach to provide this service, patients with very limited financial resources and in areas where the health system has not committed to covering this treatment may still have difficulties with access. Two major factors will mitigate against this barrier, however. First, the fact that many large health systems are moving away from the fee-for-service model and towards the Accountable Care Organization (ACO) model will work in our favor. If group acupuncture proves to be effective, an ACO should be quite able and willing to offer this service to patients as a low-cost strategy for pain management, especially as it can potentially reduce costs in other areas. Since the ACO model is concerned with overall cost-containment and quality of care, rather than fees for specific services, it would seem that the group acupuncture approach could be very attractive to payors. Second, as mentioned above, Drs. Nielsen and Kligler have been working over the past year with the Joint Commission on the Accreditation of Hospital Organizations (JCAHO) on a classification of its directives on non-pharmacological options for pain treatment. It is quite clear--partially in response to the epidemic over-prescribing of addictive narcotic medications for pain-- that JCAHO is moving toward a higher-level expectation that hospitals provide more non-pharmacological options for pain treatment in the future. In fact, acupuncture is now specifically mentioned in the revised standards as one of these options. This movement on the part of the major hospital accreditation organization in the U.S. is certain to create additional pressure on hospitals to offer acupuncture as an option for pain treatment. Here again, group acupuncture, if shown to be effective, will be a very attractive option from a cost perspective. Thus, although there will be barriers to implementation, we are optimistic that there are also significant forces at play which will allow us to overcome those barriers easily.

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REPRODUCIBILITY AND TRANSPARENCY OF RESEARCH

A. Describe the ability to reproduce potentially important findings from this research in other data sets and populations.

Our replication plan consists of developing a web based archiving system housed in the REDCap platform with password protected access where we will provide a complete, final study protocol, describing the study population; primary and secondary hypotheses tested; sources and methods of measuring exposures, outcomes, and all covariates used in analyses, including data definitions, coding instructions, and the analysis plan. The IRB-approved protocol, along with the first 12-month progress report, will be made available within three months of the end of the each funding period. Descriptions of our study datasets, including code books, meta-data related to the datasets, and documented programming code used for creating the final study population, for creating variables, and for conducting all outcomes analyses will be provided within three months of the end of the final funding year. We agree to PCORI's right to share these materials with appropriate researchers, in consultation with the principal investigators of the study, Dr. M. Diane McKee and Dr. Ben Kligler.

B. Describe how you will make a complete, cleaned, de-identified copy of the final dataset used in conducting the final analyses available within nine months of the end of the final year of funding, or your data sharing plan, including the method by which you will make this dataset available, if requested.

The Research Informatics Core of the Albert Einstein College of Medicine, Institute for Clinical and Translational Research (ICTR) will store and secure our data. A copy of the complete, cleaned, de-identified final data set, code book, and the accompanying analytic methods will be available within nine months of the end of the final year of funding, or earlier by request, to PCORI and other relevant parties. Data may be shared electronically or via hard-data file transfer, and will be provided in the form of raw data excel spreadsheets for quantitative data, and original transcriptions for qualitative data obtained through interviews and focus groups. SPSS or equivalent syntax from the associated analyses can be made available as well.

C. Propose a budget to cover costs of your data sharing plan, if requested.

The budget for data sharing would depend on what data sharing entails. For our own proactive efforts to share data, no budget is requested. We also considered costs involved if we are approached by outside investigators wishing to collaborate on these data. If an investigator wants to work peripherally with us to reanalyze our data, costs would be similar to routine consulting ($500/hr for academic collaborator; $1500/hr for pharmaceutical). If the collaboration is more intensive, requiring on-going involvement from Drs. McKee, Kligler, or Kim, or other academic team members, it would likely involve % FTE of academic salary. If data sharing involves further hands on data- reduction or analysis on our end, additional staff time would need to be included. We would also welcome outside junior faculty, post-docs, and other students interested in conducting thesis research or other projects using these data. There would be no charge for trainee and student projects, as long as one of the study investigators is able to serve as a (co-)mentor or committee member.

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PROTECTION OF HUMAN SUBJECTS

Describe the protection of human subjects who will be involved in your research.

1. Risks to Subjects

The project team has extensive experience conducting research involving urban minority patients. Numerous safeguards have been considered to ensure protection of participants.

1.a. Human Subjects Involvement and Characteristics

Human Subjects Involvement.

Primary Care Providers (PCPs) in the participating practices will refer appropriate adult (aged 21 and older) patients for acupuncture therapy. Recruitment will take place continuously at the participating health centers. We plan to enroll 700 patients over a 25-month period, who will be randomly assigned to individual or group acupuncture. A subgroup of 20 patients from each arm will be recruited to participate in qualitative interviews, and will sign a separate consent form for that process. All patients seen will continue to receive clinical care as provided by their medical providers and office teams. Patients who consent to participate will contribute survey data to help evaluate the effectiveness of individual versus group acupuncture for pain.

Human Subjects Characteristics.

Participants will have chronic neck pain, back pain, or osteoarthritis, defined as pain for three months or more, and receive primary care in one of six participating health centers.

Inclusion Criteria. Individuals must:

1. have a diagnosis of chronic joint pain related to a diagnosis of osteoarthritis, or chronic neck or back pain related to non-cancer diagnoses
2. be fluent in English or Spanish,
3. be able to provide a home or cell phone number,
4. be available for up to 24 weeks.

Exclusion Criteria. Individuals will be excluded from participation if they:

1. are unable to provide informed consent due to mental illness or cognitive impairment,
2. lack fluency in English or Spanish,
3. do not have a phone,
4. will not be available for follow-up data in 6 months, or
5. are currently on anticoagulant medication.

1.b. Sources of Materials

The sources of data in this project include:

1) Primary survey data collected at baseline and follow-up,
2) Interview material from patients participating in the qualitative interviews exploring the patient experience of receiving acupuncture in either the individual or group setting, and
3) Prescribed medication use, obtained from the participants' electronic health record and self-report.

All participant interviews will be conducted in English or Spanish, as chosen by the participant.

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1.c. Potential Risks

This study presents minor risks to participants. The primary risks are: 1) possible discomfort discussing topics related to pain and disability; 2) breach of confidentiality of health information; 3) discomfort or bruising from acupuncture; 4) transient increase in pain during or after acupuncture; and 5) fear that refusal to participate in any part of the study might jeopardize their medical treatment at the health center. Special consideration and safeguards are integrated into the study methodology that we believe effectively limit these risks. These procedures are described below**.**

2. Adequacy of Protection Against Risks

2.a. Recruitment and Informed Consent

Procedures for recruitment, informed consent, and participant incentives are described below. Patients will be informed of their right to participate or discontinue participation at any time without jeopardizing the medical treatment they receive or any treatment they might request in the future. Incentives have been chosen based on prior experience demonstrating that the amounts are well received, and generous enough to demonstrate the teams' appreciation but not enough to be coercive.

Recruitment. All Primary Care Providers (PCPs) in each participating practice will be encouraged to refer appropriate adult (aged 21 and older) patients for acupuncture therapy. At the clinician's discretion, acupuncture will be discussed as part of treatment planning during patient visits. For patients who meet eligibility criteria, PCPs will complete a study specific referral form. PCPs will obtain permission for a member of the study team to contact the patient, and obtain at least two current phone numbers to facilitate contact. Consent to participate in research will not be sought at this point. Clinicians will send referral forms to the practice's referral coordinator (as would any other request for specialty consultation). The Study Coordinator will collect referrals, then contact patients by phone to verify eligibility, describe the study, and explain study procedures, including randomization. A subgroup of 20 patients from the each arm will be recruited after 24- week outcome data is collected to participate in qualitative interviews, and will sign a separate consent form for that process. After contacting the patient by phone the informed consent will be mailed or emailed to them.

Informed Consent. In a private location at the health center, study procedures will be explained in detail (in English or Spanish as preferred by the patient). Patients will be given opportunities to ask questions at any time during the enrollment and study, and informed that they can decline to participate or drop out of the study at any time. Patient will be asked to provide signed informed consent.

Incentives. Participants will not receive an incentive to attend acupuncture treatments, but will receive modest incentives to complete the research interviews. These incentives will be $5 for each of the baseline pain measurements, $25 for the pre-intervention baseline data collection, $10 for the 6-week follow-up assessment, $25 dollars for the 12-week assessment, and $30 for the 24-week assessment. Participants will be offered an additional $50 incentive for participating in the qualitative interview**.**

2.b. Protections Against Risks

Confidentiality Protections.

We will devote substantial effort and resources to protecting all participants from breaches of confidentiality. Strict procedures will be observed to offset any risks. All data will be identified only by a study number and kept in locked files. All data will be kept separate from identifying information used for subject follow-up (i.e., phone numbers) or to link data to subjects. No identifying information will be disclosed in reports, publications, or presentations. Patient interviews will be conducted in venues that allow the utmost privacy. Participants will be informed that they may refuse to talk about sensitive issues that may be upsetting to them, and that they can skip questions whenever they choose, or withdraw their participation in the study at any time.

All study personnel will complete required training in ethical procedures for the conduct of research**.**

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Data Protection
All electronic data (including all databases) will be protected using File Warden or equivalent encryption software. Electronic data will be anonymized by encoding direct and indirect identifiers. Sensitive data can only be accessed via the encryption code, (the "key") which is stored in a locked cabinet accessible only to the PIs and Dr. Fletcher. File Warden meets all HIPAA standards regarding privacy of health information. All electronic data will be stored on password protected PCs in the Division of Research. The information from the study will be used only in scientific papers and reports that will not contain individual names or identifying information.

HIPAA Compliance
Procedures described are in compliance with HIPAA requirements for maintaining the privacy and security of patient health information. The investigators have extensive experience conducting HIPAA-concordant research and are regularly trained in the most current HIPAA regulations and procedures.

Potential Benefits of the Proposed Research to the Subjects and Others
Subjects may experience the altruistic benefit of participating in a study that contributes to better health care services for patients with chronic pain. Subjects may experience an improvement in their pain and quality of life as a consequence of acupuncture treatment. If the study is positive, it may help improve access to acupuncture treatment for patients with pain by providing a strategy for delivering this treatment at a lower cost.

Importance of the Knowledge to be Gained
The new knowledge generated by this study may provide greater access to acupuncture as an effective treatment for chronic pain and an adjunct or alternative to medication management. While existing data from clinical trials suggests the efficacy of acupuncture for a variety of conditions, low income and minority patients rarely have access to complementary therapies. We hope to demonstrate the effectiveness of a new strategy to deliver acupuncture in the urban health center setting, and to further demonstrate that patient outcomes are improved.

Data Safety and Monitoring Plan
Serious adverse events are very unlikely given the known safety of acupuncture. Nevertheless we will track serious adverse events (deaths, illnesses leading to hospitalization) and more likely given the nature of the intervention, minor adverse events associated with acupuncture treatment occurring in the study participants. We will review these totals monthly. We anticipate that only zero, one, or two serious events will occur during the course of this small study. The number of minor adverse events may be slightly higher. Dr. Clyde Schechter (Professor of Epidemiology and Population Health at Einstein) has agreed to be the Data Safety Monitor for the study. All such events will be reported to him and to the Albert Einstein College of Medicine's Committee on Clinical Investigations (IRB). Should the numbers be unexpectedly high, the investigators will convene to discuss the nature of these events, and their distribution and decide whether the study should continue.

Targeted /Planned Enrollment:

	Sex/Gender		
Ethnic Category	Females	Males	Total
Hispanic or Latino	254	131	385
Not Hispanic or Latino	208	107	315
Ethnic Category: Total of All Subjects	462	238	700
Racial Categories			

American Indian/Alaska Native	5	2	7
Asian	5	2	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	125	64	189
White	18	10	28
Other/multiple/not indicated	297	172	469
Racial Categories: Total of All Subjects	450	250	700

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REFERENCES CITED

Each reference must include names of all authors (in the same sequence in which they appear in the publication); the article title; and journal or book title, volume number, page numbers, and year of publication. Include only bibliographic citations. Refer to the PCORI Application Guidelines, found on the PCORI Funding Center, for additional guidance. Use continuation pages as needed to provide the required information. Do not exceed 10 pages.

Following scholarly citation practice, list the source material cited in this Research Plan.

REFERENCES

1. Bonica's Management of Pain. 3rd ed. Loeser JD, Butler SH, Chapman RC, Turk DC, editors. Philadelphia: Lippincott Williams & Wilkins; 2001 January 15, 2001. 2178 pages p.
2. Elliott A, Smith B, Penny K, Smith W, Chambers W. The epidemiology of chronic pain in the community. Lancet. 1999;354(9186):1248-52. PubMed PMID: 10520633.
3. Gureje O, Von Korff M, Simon G, Gater R. Persistent pain and well-being: a World Health Organization Study in Primary Care. JAMA. 1998;280(2):147-51. PubMed PMID: 9669787.
4. Reyes-Gibby C, Aday L, Cleeland C. Impact of pain on self-rated health in the community-dwelling older adults. Pain. 2002;95(1-2):75-82. PubMed PMID: 11790469.
5. Von Korff M, Dworkin S, Le Resche L. Graded chronic pain status: an epidemiologic evaluation. Pain. 1990;40(3):279-91. PubMed PMID: 2326094.
6. Verhaak P, Kerssens J, Dekker J, Sorbi M, Bensing J. Prevalence of chronic benign pain disorder among adults: a review of the literature. Pain. 1998;77(3):231-9. PubMed PMID: 9808348.
7. Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: results of an internet-based survey. J Pain. 2010;11(11):1230-9. Epub 2010/08/28. doi: 10.1016/j.jpain.2010.07.002. PubMed PMID: 20797916.
8. Watkins E, Wollan P, Melton Lr, Yawn B. Silent pain sufferers. Mayo Clin Proc. 2006;81(2):167-71. PubMed PMID: 16471069.
9. Elliott A, Smith B, Hannaford P, Smith W, Chambers W. The course of chronic pain in the community: results of a 4-year follow-up study. Pain. 2002;99(1-2):299-307. PubMed PMID: 12237208.
10. Gureje O, Simon G, Von Korff M. A cross-national study of the course of persistent pain in primary care. Pain. 2001;92(1-2):195-200. PubMed PMID: 11323140.
11. Goetzel R, Hawkins K, Ozminkowski R, Wang S. The health and productivity cost burden of the "top 10" physical and mental health conditions affecting six large U.S. employers in 1999. J Occup Environ Med. 2003;45(1):5-14. PubMed PMID: 12553174.
12. Cleeland C, Gonin R, Hatfield A, Edmonson J, Blum R, Stewart J, et al. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med. 1994;330(9):592-6. PubMed PMID: 7508092.
13. Bernabei R, Gambassi G, Lapane K, Landi F, Gatsonis C, Dunlop R, et al. Management of pain in elderly patients with cancer. SAGE Study Group. Systematic Assessment of Geriatric Drug Use via Epidemiology. JAMA. 1998;279(23):1877-82. PubMed PMID: 9634258.
14. Breitbart W, Rosenfeld B, Passik S, McDonald M, Thaler H, Portenoy R. The undertreatment of pain in ambulatory AIDS patients. Pain. 1996;65(2-3):243-9. PubMed PMID: 8826513.
15. Phelan SM, van Ryn M, Wall M, Burgess D. Understanding Primary Care Physicians' Treatment of Chronic Low Back Pain: The Role of Physician and Practice Factors. Pain Medicine. 2009;10(7):1270-9. doi: 10.1111/j.1526-4637.2009.00717.x. PubMed PMID: ISI:000270589100012.
16. Pargeon K, Hailey B. Barriers to effective cancer pain management: a review of the literature. J Pain Symptom Manage. 1999;18(5):358-68. PubMed PMID: 10584460.

17. Todd K, Samaroo N, Hoffman J. Ethnicity as a risk factor for inadequate emergency department analgesia. JAMA. 1993;269(12):1537-9. PubMed PMID: 8445817.
18. Todd K, Deaton C, D'Adamo A, Goe L. Ethnicity and analgesic practice. Ann Emerg Med. 2000;35(1):11-6. PubMed PMID: 10613935.
19. Lin JG, Chen WL. Acupuncture analgesia: a review of its mechanisms of actions. Am J Chin Med. 2008;36(4):635-45. Epub 2008/08/20. PubMed PMID: 18711761.
20. Molsberger AF, Schneider T, Gotthardt H, Drabik A. German Randomized Acupuncture Trial for chronic shoulder pain (GRASP) - A pragmatic, controlled, patient-blinded, multi-centre trial in an outpatient care environment. Pain. 2010;151(1):146-54. doi: 10.1016/j.pain.2010.06.036. PubMed PMID: ISI:000281733300024.
21. Lathia AT, Jung SM, Chen LX. Efficacy of Acupuncture as a Treatment for Chronic Shoulder Pain. Journal of Alternative and Complementary Medicine. 2009;15(6):613-8. doi: 10.1089/acm.2008.0272. PubMed PMID: ISI:000267016200004.
22. Linde K, Gianni A, Benno B, Manheimer E, Vickers A, White A. Acupuncture for tension-type headache. Chichester, UK: 2009.
23. Noiman M, Garty A, Maimon Y, Miller U, Lev-Ari S. Acupuncture for Treating Temporomandibular Disorder: Retrospective Study on Safety and Efficacy. Journal of Acupuncture and Meridian Studies. 2010;3(4):260-6. doi: Doi: 10.1016/s2005-2901(10)60046-5.
24. Sun Y, Gan TJ. Acupuncture for the Management of Chronic Headache: A Systematic Review. Anesthesia and Analgesia. 2008;107(6):2038-47. doi: 10.1213/ane.0b013e318187c76a. PubMed PMID: ISI:000261196800044.
25. Tugcu V, Tas S, Eren G, Bedirhan B, Karadag S, Tasci A. Effectiveness of Acupuncture in Patients with Category IIIB Chronic Pelvic Pain Syndrome: A Report of 97 Patients. Pain Medicine. 2010;11(4):518-23. PubMed PMID: ISI:000276223500008.
26. Plank S, Goodard J. The Effectiveness of Acupuncture for Chronic Daily Headache: An Outcomes Study. Military Medicine. 2009;174(12):1276-81. PubMed PMID: ISI:000278061000023.
27. Fink M, Wolkenstein E, Karst M, Gehrke A. Acupuncture in chronic epicondylitis: a randomized controlled trial. Rheumatology. 2002;41(2):205-9. PubMed PMID: ISI:000174398100016.
28. Berman B, Lao L, Langenberg P, Lee W, Gilpin A, Hochberg M. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Ann Intern Med. 2004;141(12):901-10. PubMed PMID: 15611487.
29. Witt C, Brinkhaus B, Jena S, Linde K, Streng A, Wagenpfeil S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. Lancet. 2005;366(9480):136-43. PubMed PMID: 16005336.
30. Witt CM, Jena S, Brinkhaus B, Liecker B, Wegscheider K, Willich SN. Acupuncture in patients with osteoarthritis of the knee or hip: a randomized, controlled trial with an additional nonrandomized arm. Arthritis Rheum. 2006;54(11):3485-93.
31. Manheimer E, Linde K, Lao LX, Bouter LM, Berman BM. Meta-analysis: Acupuncture for osteoarthritis of the knee. Annals of Internal Medicine. 2007;146(12):868-77. PubMed PMID: ISI:000247347100005.
32. Kwon YD, Pittler MH, Ernst E. Acupuncture for peripheral joint osteoarthritis - A systematic review and meta-analysis. Rheumatology. 2006;45(11):1331-7. doi: 10.1093/rheumatology/ke1207. PubMed PMID: ISI:000241431000003.
33. Willich SN, Reinhold T, Selim D, Jena S, Brinkhaus B, Witt CM. Cost-effectiveness of acupuncture treatment in patients with chronic neck pain. Pain. 2006;125(1-2):107-13. Epub 2006/07/18. doi: 10.1016/j.pain.2006.06.006. PubMed PMID: 16842918.
34. Witt CM, Jena S, Brinkhaus B, Liecker B, Wegscheider K, Willich SN. Acupuncture for patients with chronic neck pain. Pain. 2006;125(1-2):98-106. Epub 2006/06/20. doi: 10.1016/j.pain.2006.05.013. PubMed PMID: 16781068.
35. Lee JH, Park HJ, Lee H, Shin IH, Song MY. Acupuncture for chronic low back pain: protocol for a multicenter, randomized, sham-controlled trial. BMC Musculoskeletal Disorders. 2010;11. doi: 118 10.1186/1471-2474-11-118. PubMed PMID: ISI:000279936400001.

36. McKee MD, Zayas LH, Fletcher J, Boyd RC, S.H. N. Effects of an intervention to reduce perinatal depression among low-income minority women in community primary care. Journal of Social Services Research. 2006.
37. Yuan J, Purepong N, Kerr DP, Park J, Bradbury I, McDonough S. Effectiveness of Acupuncture for Low Back Pain A Systematic Review. Spine. 2008;33(23):E887-E900. PubMed PMID: ISI:000260673300021.
38. Cherkin DC, Sherman KJ, Avins AL, Erro JH, Ichikawa L, Barlow WE, et al. A Randomized Trial Comparing Acupuncture, Simulated Acupuncture, and Usual Care for Chronic Low Back Pain. Archives of Internal Medicine. 2009;169(9):858-66. PubMed PMID: ISI:000265994000006.
39. Scharf H, Mansmann U, Streitberger K, Witte S, Krämer J, Maier C, et al. Acupuncture and knee osteoarthritis: a three-armed randomized trial. Ann Intern Med. 2006;145(1):12-20. PubMed PMID: 16818924.
40. Vickers AJ, Cronin AM, Maschino AC, Lewith G, MacPherson H, Foster NE, Sherman KJ, Witt CM, Linde K; Acupuncture Trialists' Collaboration. Acupuncture for chronic pain: individual patient data meta-analysis. Arch Intern Med. 2012 Oct 22;172(19):1444-53.
41. Brinkhaus B, Witt CM, Jena S, Linde K, Streng A, Wagenpfeil S, et al. Acupuncture in patients with chronic low back pain: a randomized controlled trial. ArchInternMed. 2006;166(4):450-7.
42. Haake M, Muller HH, Schade-Brittinger C, Basler HD, Schafer H, Maier C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. ArchInternMed. 2007;167(17):1892-8.
43. McKee MD, Kligler B, Blank AE, Fletcher J, Jeffres A, Casalaina W, et al. The ADDOPT study (Acupuncture to Decrease Disparities in Outcomes of Pain Treatment): feasibility of offering acupuncture in the community health center setting. J Altern Complement Med. 2012;18(9):839-43. doi: 10.1089/acm.2011.0193. PubMed PMID: 22867026; PubMed Central PMCID: PMC3429271.
44. McKee D, Kligler B, Fletcher J, Biryukov F, Casalaina W, Anderson B, et al. Outcomes of Acupuncture for Chronic Pain in Urban Primary Care. Journal of American Board of Family Medicine. 2013 In Press.
45. Lumiere KJM, Miller TK, and Miller CL. Community Acupuncture Patient Demographics: A Qualitative, Cross-sectional Pilot Study *American Acupuncturist* 53 (2010).
46. Asprey A, Paterson C; White A. 'All in the same boat': a qualitative study of patients' attitudes and experiences in group acupuncture clinics. Acupuncture in Medicine 2012 30(3):163-9
47. Simcock R, Fallowfield L, Jenkins V. Group acupuncture to relieve radiation induced xerostomia: a feasibility study. Acupuncture in Medicine 2009 Sep; 27 (3): 109-13.
48. Tippens, Kimberly M., et al. "Patient perspectives on care received at community acupuncture clinics: a qualitative thematic analysis." *BMC complementary and alternative medicine* 13.1 (2013): 293.
49. White A, Richardson M, Richmond P, Freedman J, Bevis M. Group acupuncture for knee pain: evaluation of a cost-saving initiative in the health service. Acupuncture in Medicine 2012 Sep; 30 (3): 170-5.
50. http://projectreporter.nih.gov/project_info_description.cfm?aid=8492046&icde=19909637&ddparam=&ddvalue=&ddsub=&cr=9&csb=default&cs=ASC, (Accessed 4/4/14)
51. Deadman P. Community acupuncture - making Ming vases from buckets: a reply. J Chinese Med 2012, 99:55–59.
52. Schnyer RN, Allen JJ. Bridging the gap in complementary and alternative medicine research: manualization as a means of promoting standardization and flexibility of treatment in clinical trials of acupuncture. J Altern Complement Med. 2002;8(5):623-34. Epub 2002/12/10. doi: 10.1089/107555302320825147. PubMed PMID: 12470444.
53. Chao MT, Tippens K, Connelly E. Utilization of group-based, community acupuncture clinics: A comparative study with a nationally representative sample of acupuncture users. Journal of Alternative and Complementary Medicine, 2012, 18(6):561-566.
54. Nahin RL, Barnes PM, Stussman BJ, Bloom B. Costs of complementary and alternative medicine (CAM) and frequency of visits to CAM practitioners: United States, 2007. Natl Health Stat Report 2009;18:1–14.
55. Given S, editor. Clean Needle Technique Manual for Acupuncturists: Guidelines and Standards for the Clean and Safe Practice of Acupuncture. 6th ed: National Acupucnture Foundation; 2009.

56. Langevin HM, Churchill DL, Wu J, Badger GJ, Yandow JA, Fox JR, et al. Evidence of connective tissue involvement in acupuncture. Faseb J. 2002;16(8):872-4. Epub 2002/04/23. doi: 10.1096/fj.01-0925fje. PubMed PMID: 11967233.
57. Badia X, Muriel C, Gracia A, Nunez-Olarte JM, Perulero N, Galvez R, et al. [Validation of the Spanish version of the Brief Pain Inventory in patients with oncological pain]. Med Clin (Barc). 2003;120(2):52-9. Epub 2003/02/07. PubMed PMID: 12570914.
58. Farrar J, Young JJ, LaMoreaux L, Werth J, Poole R. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001;94(2):149-58. PubMed PMID: 11690728.
59. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2009;18(7):873-80. doi: 10.1007/s11136-009-9496-9. PubMed PMID: 19543809; PubMed Central PMCID: PMC2724630.
60. Ruta DA, Garratt AM, Wardlaw D, Russell IT. Developing a valid and reliable measure of health outcome for patients with low back pain. *Spine.* Sep 1 1994;19(17):1887-1896.PMCH. PubMed PMID: 7997920
61. Miller WL, Crabtree BF. Qualitative analysis: how to begin making sense. The Family practice research journal. 1994;14(3):289-97. Epub 1994/09/01. PubMed PMID: 7976480.

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CONSORTIUM CONTRACTUAL ARRANGEMENTS

Use continuation pages as needed to provide the required information. Do not exceed 5 pages.

Describe the proposed research projects that will be performed by subcontracted organizations. Explain the strengths that these partners bring to the overall project.

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APPENDIX (Optional)

Use continuation pages as needed. You may provide an appendix of up to 10 pages to include additional materials, such as descriptions of survey instruments and interview guides. Note, however, that reviewers are not required to review the appendix when they assess your application.