

**Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study (ACUITY)**

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## Tool Revision History

Version Number: 1

Version Date: 03/11/2021

Summary of Revisions Made: NA

Version Number 2:

Version Date: 04/19/2021

Summary of Revisions Made:

- Protocol: Updated needle sizes; Added more info/clarification about ear seeds; Added information about topical Arnica cream to prevent bruising, for muscle pain, or in event of hematoma; Updated Inclusion/Exclusion criteria; Updated randomization process (REDCap OR Envelopes); Added a screening bubble in work flow diagram; Updated window for follow-ups from +/- 2 days to +/- 4 days; Added that acupuncturist will share Acupuncture After Care summary with AQ patients (with ear seeds and arnica info); Updated platform used for remote interviews from Zoom to “the audio only function of a HIPAA-compliant commercial tele-health platform (e.g. Zoom Health Professional or Doxy.me)”
- RCT Consent: Language about personal phone use/Twilio possibly/possibly not being available while in the ER; Updated ED to ER; Updated platform used for remote interviews from Zoom to “the audio only function of a HIPAA-compliant commercial tele-health platform (e.g. Zoom Health Professional or Doxy.me)”
- Study Information Sheet for both Provider and Patient: Updated platform used for remote interviews from Zoom to “the audio only function of a HIPAA-compliant commercial tele-health platform (e.g. Zoom Health Professional or Doxy.me).”; Updated ED to ER for patients

Version Number 3:

Version Date: 05/12/2021

Summary of Revisions Made:

- RCT Consent: Language about use of personal phones and Twilio messaging while in the ER has been removed from the protocol
- Updated the Co-investigators to include Dr. Vago.

Version Number 4

Version Date: 05/21/2021

Summary of Revision Made:

- Study Design: included additional 15 pilot patients (5 per site) into the Sample Size and Population
- Protocol: removed UH specific research credentialing to allow study staff at Einstein Coordinating Center to be research credentialed at all three sites
- Outcomes: updated language for Primary Outcomes measures and Secondary Outcomes measures
- Inclusion Criteria: removed the 3V acuity level as this designation may not be standard at all sites, replaced with the standard 3 acuity level

- Exclusion Criteria: removal of 'Patient arriving via ambulance or skipping triage' exclusion criteria
- Study Enrollment Procedures: added language describing the patient's refusal to provide their phone number and email address as being a declination of participation in the study; added procedural language for distributing remuneration for completing the Qualitative Interview; added documentation language for tracking Qualitative Interview and number of phone call attempts
- RCT Consent: included the updated version of the Informed Consent that reflects the changes to the protocol listed above
- Provider Qualitative Interview Study Information Sheet: included the updated version of the provider information sheet that reflects the changes to the protocol listed above
- Patient Qualitative Interview Study Information Sheet: included the updated version of the patient information sheet that reflects the changes to the protocol listed above
- Updated the Executive, Steering and ED Physician and Site PI committees.
- Quality Assurance: added ACUITY QA Monthly Consent and Eligibility Data Review Tool and timing for review and completion of Eligibility Checklist

Version Number 5

Version Date: 11/15/2021

Summary of Revision Made:

- Study Enrollment Procedure: added the use of a pre-treatment flyer to the recruiting procedure
- Study Interventions: Arnica removed from the Acupuncture After Care sheet
- Study Procedures: the addition of satisfaction questions asked during the Post-Treatment assessment was noted in the Schedule of Evaluations with a detailed listing in the Follow-Up Visits section
- Study Enrollment Procedures: added study staff assessment of patient capacity to understand and sign documents prior to informed consent process and the addition of instruction to only continue with study activity after written consent is obtained to Recruitment Methods and Consent Process sections; and removal of clinical consent procedure
- Description of evaluation: added study staff assessment of patient capacity to understand and sign documents prior to informed consent process and the addition of instruction to only continue with study activity after written consent is obtained to Consenting Procedure section; and removal of clinical consent procedure
- Supplement/Appendices: replaced informed consents and information sheets with current documents
- Safety Assessment: removal of clinical consent procedure
- Data Management: added paper collection of PRO at 1-week and 4-week follow-ups

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**PRÉCIS**

**Study Title**

Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study (ACUITY)

**Objectives**

The objectives of this study are to: conduct a feasibility randomized control trial (RCT), to examine the feasibility of data collection in the RCT, develop a responsive acupuncture intervention and assess implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. (UH Cleveland Medical Center ED (site 1), the Vanderbilt University Medical Center (VUMC) ED (site 2) and the Hillcrest University of California San Diego (UCSD) ED (site 3)). This study will include qualitative interviews and structured observation to assess feasibility of implementation.

## Design and Outcomes

This is a multi-site single visit, un-blinded, feasibility randomized control trial of acupuncture in the ED.

### Interventions and Duration

Acupuncture for pain management in the Emergency Department (ED) will be compared to usual care. The interventions will be administered during the ED visit. During that time, pre-, post- and discharge assessments will be administered. Follow up assessments will take place at one and four weeks post ED visit.

### Sample Size and Population

The target population are adults presenting to the ED with acute non-emergent (musculoskeletal, back, pelvic, non-cardiac chest, abdominal, flank or head) pain  $\geq 4$  on a 0-10-point Numeric Rating Scale (NRS) due to non-penetrating injury. A total of 150 patients (50 patients per recruiting site) plus 15 pilot (5 per recruiting site) will be recruited study-wide.

Additionally, 30 (10/site) ED stakeholders, including providers (physicians, nurse practitioners, physician assistants, and registered nurses) and ED staff employed for at least one year including the study period, as well as acupuncturists who are employed or credentialed by one of the participating institutions to perform acupuncture in the emergency department as part of the study will be interviewed about their perspectives and experiences related to implementation of the acupuncture study in the ED.

Patients who are randomized to the acupuncture group will be contacted to participate in a brief qualitative interview about 3 weeks after their ED visit. The expectation is that 15 patient participants per site (n=45 total) will consent to the qualitative interviews about their experience of receiving acupuncture as part of the RCT.

## STUDY OBJECTIVES

### 1.1 Primary Objective

The primary objective is to refine procedures for conducting a future fully powered multi-site RCT in 3 EDs.

### 1.2 Secondary Objectives

The secondary objectives of this study are to: examine the feasibility of data collection in the RCT, develop a responsive acupuncture intervention and assess implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. This study will include qualitative interviews and structured observation to assess feasibility of implementation.

## 2. BACKGROUND AND RATIONALE

### 2.1 Background on Condition, Disease, or Other Primary Study Focus

**Pain Burden in the United States:** Pain affects an estimated 100 million adults in the United States.<sup>1</sup> The annual cost related to pain in the U.S.—including costs due to lost productivity, as well as medical care—is estimated to be between \$560 to \$635 billion.<sup>1,2</sup> The burden of pain extends beyond costs. Pain is a public health problem, a major driver of health care seeking and for taking medications, a major cause of disability, and a key factor in quality of life and productivity.<sup>1</sup> Unrelieved pain can negatively impact every area of an individual’s life, including

employment, personal relationships, and social activities, and may induce ‘fear, demoralization, anxiety, and depression’.<sup>3</sup> Pain accounts for up to 78% of ED visits,<sup>4,5</sup> where acute pain continues to be undermanaged and/or improperly managed.<sup>4,6</sup>

**Usual ED Care for Pain Management and the Opioid Epidemic:** In 2012, U.S. providers prescribed 50 times more opioids than the rest of the world combined,<sup>7</sup> reflecting a persistent national epidemic causing 130 deaths daily.<sup>8</sup> Unique to the current U.S. opioid epidemic is the role of medical prescribing.<sup>9</sup> While recent programs focused on the ED have resulted in a decrease of ED opioid prescriptions nationally,<sup>10</sup> opioids remain a primary method of acute pain treatment.<sup>11</sup> The probability of long-term opioid use increases after as few as five days of prescribed opioids as the initial treatment of pain.<sup>12</sup> In a large study, 17% of opioid-naïve ED patients prescribed opioids for acute pain were still receiving opioids 1 year later.<sup>13</sup> In addition to addictive potential, the immediate adverse effect profile of opioids can be underappreciated given their common use. Both major (respiratory distress) and minor adverse effects (constipation, nausea/vomiting, dizziness, sedation, pruritus and urinary retention) are burdensome for patients and negatively impact health and well-being. Options that demonstrate feasibility, efficacy, and effectiveness are needed to treat pain and mitigate reliance on opioids.

**Acupuncture therapy in the treatment of pain:** The Joint Commission has urged caution regarding opioid use in hospitals,<sup>14</sup> revising their pain management standard, effective Jan 1, 2018, requiring their accredited hospitals and facilities provide non-pharmacologic therapy options for pain, with acupuncture as one option.<sup>15</sup> Acupuncture therapy is defined as the insertion of needles or the application of heat, pressure or electrical stimulation at a point or points on the surface of the body, predetermined on the basis of the theory of the physiological interrelationship of body organs with an associated point or combination of points for diseases, disorders and dysfunctions of the body for the purpose of achieving a therapeutic or prophylactic effect.<sup>16</sup>

**Acupuncture therapy for chronic pain:** Poorly managed or acute exacerbation of chronic pain is not uncommon in the ED.<sup>17</sup> In an individual patient data meta-analysis (39 trials and 20,837 patients), acupuncture was found to be superior to placebo/sham controls and usual care in the treatment of chronic pain (low back, neck, shoulder, osteoarthritis of the knee and headache/migraine), where 85% of benefit persisted at one year following care.<sup>18</sup> Acupuncture is recommended by the NIH for low back pain and knee osteoarthritis.<sup>19</sup> It is a primary treatment option recommended for chronic low back and neck pain without serious pathology by the Global Spine Care Initiative.<sup>20</sup> For acute/subacute low back pain, a common presentation in the ED, a systematic review<sup>21</sup> supported the ACP recommendation of acupuncture as a first-line treatment.<sup>22</sup>

**Acupuncture therapy for anxiety:** Catastrophizing and anxiety are shown to increase patient self-reported pain levels in the ED.<sup>23</sup> Moreover, anxiety plays a role in post-operative and post-procedural complications.<sup>24</sup> Acupuncture’s effect on pain can also reduce anxiety, depression, nausea and vomiting and facilitate restful sleep and increase a patient’s well-being.<sup>9</sup> Acupuncture reduces anxiety in many clinical settings.<sup>25,26,27</sup>

**Acupuncture therapy safety:** Acupuncture has a low risk of adverse events. The NIH Consensus Statement on Acupuncture published in 1998 found that ‘the incidence of adverse effects is substantially lower than that of many drugs or other accepted procedures for the same conditions.<sup>28</sup> Systematic reviews and surveys have clarified that acupuncture is safe when performed by appropriately trained practitioners<sup>29-36</sup> with infrequent minor side effects such as feeling relaxed, elated, tired or having sensation or itching at point of insertion.<sup>33</sup> Rare serious complications such as infection or pneumothorax are directly related to insufficient training.<sup>34,35,37</sup>

**Need for *Pragmatic Trials and Implementation Evaluations with Acupuncture*:** Well-designed pragmatic trials are needed to clarify the feasibility and effectiveness of acupuncture for acute pain. Pragmatic clinical trials (PCTs) are performed in real-world clinical settings with highly generalizable populations to generate actionable clinical evidence at a fraction of the typical cost/time needed to conduct a traditional clinical trial.<sup>38,39</sup> PCTs are part of the NIH's vision for bridging the gap between research and care,<sup>39,40</sup> and are also supported through initiatives at the Center for Medicare & Medicaid, the Agency for Healthcare Research and Quality, the Patient Centered Outcomes Research Institute (PCORI), Practice-Based Research Networks (PBRNs) and community-based participatory research initiatives across the Federal government.<sup>41</sup> Designed to inform clinical decisions, to improve practice and policy, PCTs engage patients, practitioners, and health system communities. Classical efficacy RCTs such as 'traditional randomized controlled trials' (tRCTs) compare interventions against a control using rigid study protocols and minimal variation in a highly defined and carefully selected population. In 17 years, only 14% of tRCT research findings led to widespread changes in care.<sup>38,42</sup> The NIH Collaboratory on pragmatic trials recommends early/ongoing stakeholder engagement.<sup>39</sup> Accordingly, our study incorporates a mixed methods implementation evaluation which will 1) carefully assess process outcomes (acceptability, feasibility, and intervention fidelity); and 2) collect interview and observational data with the goal of understanding barriers and facilitators to implementation.

**Acupuncture for Acute Pain in ED:** Reviewing the scientific literature, we find five credible RCTs<sup>43-47</sup> and several observational studies<sup>48-51</sup> that explored the effect of acupuncture in the ED on pain intensity. There were only two strong RCTs. In the first, acupuncture was found to be superior to parenteral morphine for pain relief with fewer adverse effects.<sup>45</sup> In a second, a multicenter randomized non-inferiority trial, acupuncture was found comparable to pharmacotherapy for acute pain relief in ED patients.<sup>47</sup> **However, systematic reviews<sup>52-56</sup> from 2012-2018 conclude that although results of acupuncture in the ED are promising, there is insufficient evidence to recommend acupuncture in the ED and future multi-center RCTs are required.**

**Further, we find critical gaps in the current evidence<sup>43-47</sup> necessitating additional research.**

1. No RCT<sup>43-47</sup> has enrolled many minority patients, limiting the applicability of results.
2. Study sample sizes have been small<sup>43,44,46</sup> and only one study included multiple-sites.<sup>47</sup>
3. The multi-site study<sup>47</sup> restricted enrollment to migraine, ankle sprain or acute low back pain, thereby limiting the applicability and generalizability of results.
4. All but one study<sup>47</sup> left the selection of acupuncture points for the treated conditions to the acupuncturist's discretion, leaving room for wide variability of the acupuncture delivered.<sup>57</sup>
5. Only the multi-site study<sup>47</sup> reported blinding of data collectors, but since data were collected on paper, the risk of assessor un-blinding remained.
6. Only two studies assessed ED opioid utilization,<sup>46,47</sup> but neither assessed opioid use at follow-up.
7. While two studies utilized auricular acupuncture therapy<sup>43,46</sup> neither study examined pain relief beyond two days after discharge.
8. The multi-site study<sup>47</sup> surveyed patients' views of acupuncture at ED discharge and two days later; however ED providers' perceptions on acupuncture for pain relief are unknown.
9. No RCT<sup>43-47</sup> has included systematic implementation and/or process data.

**These gaps will be filled by this study.** Since acupuncture therapy may provide a means to safely reduce pain in the ED without reliance on opioids, and in light of the risks and challenges associated with opioids and the ongoing inadequate treatment of ED pain, **studying the impact of acupuncture therapy on pain and opioid-related outcomes in ED patients is both timely and important.** Implementation outcomes and process data collected in the study will inform future research.

## 2.2 Study Rationale

### **PRELIMINARY DATA**

#### **Observational Study 1: Abbott Northwestern Hospital Emergency Department (ANW ED)**

Using supplemental funding from his R01 NIH grant (1R01AT006518), Dr. Dusek conducted an observational study of acupuncture in the ED.<sup>51</sup> Acupuncture was available for about 15-20 hours per week from November 2013 to December 2014 in the 35-bed ANW ED. Acupuncture was provided by a licensed acupuncturist upon referral of ED physicians or mid-level providers. The primary outcome was change in pain intensity from before to after acupuncture using a 0-10 verbal NRS pain scale.<sup>58,59</sup> The 0-10 NRS is commonly used in the ED, and scores correlate with the visual analog scale.<sup>60</sup> It has also been used in clinical trials.<sup>61</sup> Anxiety was also measured on the NRS at the same time. The acupuncturist collected pain and anxiety scores before/after acupuncture via an EPIC-based flowsheet used in Dusek's R01 study of acute patients.<sup>62-64</sup>

**Results:** Acupuncture was well-accepted by providers: 73% referred at least one patient for acupuncture during the study period. Of 436 patients referred, 279 were approached by the acupuncturist during their ED visit. Informed consent was obtained from 89% (248/279) of patients. The final sample consisted of 182 patients presenting with acute pain who received acupuncture and had a post-treatment score. The sample was representative of the overall ANW ED population: average age was 45.3 (16.7 SD), 67.6% were female and 39.0% were non-white. In the final sample, 49% (88/182) of patients received pain medications prior to acupuncture and reported a mean of 6.88 on the pain pre-treatment score and a 30-min post-treatment change of -2.68 units (SD 2.23). In comparison, 51% (94/182) received no pain medications before acupuncture and reported 6.71 on the pain pre-treatment score and a 30-min post-treatment change of -2.37 units (SD 2.23). As a -2.0 unit decrease in pain on NRS is considered clinically significant,<sup>65</sup> patients in both groups exceeded this threshold. Finally, across both groups, the pre-treatment anxiety score was 4.73 (3.43 SD) and the 30-min post-treatment change was -2.27 units (SD 2.66). Pain and anxiety change scores were correlated ( $p=0.004$ ).

**“Lessons learned” from the observational study:** (1) majority (73%) of ED providers accepted acupuncture via referrals; (2) majority (90%) of patients accepted acupuncture; (3) clinically significant decreases were found in both “pain medication” and “no pain medication” groups; (4) only 25% of “no pain medication” patients required opioid medications after acupuncture and prior to ED discharge; and (5) both pain and anxiety levels were reduced via acupuncture. We acknowledge limitations to this study: there was no comparison group; patients were not randomized; the acupuncturist was involved in data collection; and patients were referred to acupuncture by their physicians. To overcome these limitations, we conducted the following pilot RCT.

#### **Pilot Randomized Control Trial (RCT): (ANW ED)**

Dr. Dusek conducted a pilot RCT (article in preparation) with a primary goal of developing the operational procedures necessary for implementing a large-scale RCT. Patients presenting to the ANW ED were screened to participate in the pilot RCT by a study coordinator (SC) stationed at the triage desk. Those determined to be eligible (Eligibility Criteria below in Section C) were equally randomized to either Acupuncture or Usual Care. Following randomization, the SC collected the “pre” time point data via electronic tablet using a specialized study database (StudyTrax). For all subjects and all time points, the SC was blind to patient responses as the

database obscured patient responses from the SC. For patients randomized to Acupuncture, the acupuncturist informed the SC when the intervention was complete (~45 minutes), which triggered the SC to collect “post” data. For patients randomized to Usual Care, at 60 min (+/- 15 min) the SC collected post-data. Then the SC followed patient track board, so patients marked for discharge could provide ED discharge scores.

**Results:** During the 7 month study period, the SC screened 418 patients for eligibility criteria, including but not limited to pain score  $\geq 4$ . Following screening, 59 were deemed eligible, and 46 consented and randomized to Acupuncture (n=23) or Usual Care (n=23) with 2 subjects in the Acupuncture group withdrawing after consent. The average age was 36.3 (15.5 SD), 78% were female and 55.0% were non-white. Those randomized to Acupuncture reported a pre-treatment pain score of 8.18 (SD 1.62), a 60-min post-treatment pain decrease of -3.0 units (SD 2.51), decrease at ED discharge of -2.71 units (SD 1.86) and reduction at 30-day follow-up of -5.28 (3.0) units. The Usual Care group had a pre-treatment pain score of 7.91 (SD 1.41), a 60-min post-treatment pain decrease of -1.56 units (SD 2.37), decrease at ED discharge of -2.53 units (SD 2.27) and reduction at 30-day follow-up of -3.41 (4.0) units. Since the aim of the pilot RCT was to determine feasibility, as a result no between-group analyses were conducted.

“Lessons learned” included that: (1) an RCT was feasible in a busy ED; (2) ~14% (59/418) of screened patients met eligibility criteria; (3) ~78% (46/59) of eligible patients consented to participate; (4) ~78% of both Acupuncture and Usual Care patients provided post-treatment and ED discharge scores; (5) electronic data collection was feasible for blinding the study team assessor to patient scores; but (6) only ~35% (16/46) of both groups completed the 30-day follow-up via phone call, so new methods for follow-up are needed.

### **Observational Study 2: University Hospitals (UH) Broadview Heights ED**

Upon joining University Hospitals & Case Western Reserve University in Oct 2018, Dr. Dusek launched a 4-week observational study to replicate/extend the procedures used in the ANW ED observational study (above). Changes included the use of auricular ear seeds to potentially extend pain relief, and reducing 30 day follow-up to a 1-week (+/- 2 days) phone call. Goals were to: (1) determine whether auricular ear seeds would be tolerated by patients; and (2) preliminarily explore if ear seeds provided extended pain relief at 1-week.

**Results:** During the study period, the acupuncturist was referred and then approached 24 patients. Informed consent was obtained from 79% (19/24) of patients. The average pain pre-treatment score was 4.68, and the post-treatment change was a decrease of -2.07 units and ED discharge change was a reduction of -1.68 units. Ear seeds were used in a majority (14/19) of patients. Phone calls were only successful in 8 patients due to the holidays. Seven of eight patients reported retaining the ear seeds in place until the 1-week follow-up. The 1-week pain reduction was of -3.68 units.

“Lessons learned”: (1) extended auricular therapy (ear seeds) was well tolerated by patients; and (2) ear seeds may provide pain relief at 1-week.

**Rationale for the Proposed Study:** Despite these positive findings in the pilot RCT and two observational studies, there are several issues that need to be addressed before proceeding to a future definitive study. First, a better understanding of process outcomes such as recruitment/reach, stakeholder acceptability, and intervention fidelity are needed to ensure optimal recruitment and minimal patient attrition. We will assess these outcomes carefully in this study. We are also introducing several improvements at the outset. For example, to improve retention, we will reduce the follow up period to 1-week and use text messaging features of REDCap. To improve fidelity, we will develop a ‘responsive’ manualized-based intervention (consensus protocol with options) and a corresponding fidelity assessment tool. Finally, intervention observations and interviews with stakeholders (ED providers and administrators, ED patients and study acupuncturists) will provide valuable explanatory data regarding barriers and

facilitators to implementation that will be useful for a future, multi-site, pragmatic, definitive RCT. **Taken together, our understanding of the current gaps in the literature, promising results from our observational studies, and our operational knowledge gained from the pilot RCT combine to provide the necessary evidence and expertise to support the conduct of the proposed, multi-site feasibility clinical trial.**

### **Aim 1: Develop a Manualized Acupuncture Intervention**

The responsive manualization will allow adequate standardization of the acupuncture approach to allow for reproducible treatment, but also include a possible set of additional options for the acupuncturist to choose from to suit the specific clinical presentation. We will convene a group with expertise in acupuncture for acute pain to participate in a modified Delphi process on consensus steps and staging of an acupuncture intervention. This process adapts the Medical Research Council's guidance of 2000<sup>67</sup> and 2008<sup>68</sup> in developing and evaluating complex interventions that have interacting components. Responsive manualization has been engaged as a means of promoting standardization as well as flexibility in acupuncture research<sup>69</sup> for trials on depression,<sup>70</sup> stroke,<sup>71</sup> and chronic pain.<sup>72,73</sup> The Delphi technique, developed by the Rand Corporation in the 1950s, is a widely used and accepted method for achieving convergence of opinion concerning real-world knowledge solicited from experts within certain topic areas<sup>74</sup> and has been used in the development of research protocols and manuals.<sup>75</sup> The technique typically involves a formal process of gathering information from experts via questionnaire and then in at least one or two subsequent rounds, evaluating contributions with experts and arriving at a consensus. Our first round will work with practitioners experienced in acute pain in ED/inpatient settings to create a list of questions the investigators and practitioners confirm are essential for consensus. The second round will submit those questions to the panel of experienced acupuncture consultants for their input and suggest changes; the final round will confirm consensus on findings. Our consensus acupuncture intervention may include an interview, palpation, common acupuncture points on the body and ears for pain, optional points, points for extended auricular therapy and any additional techniques that are amenable to the acute care setting. Dr. Arya Nielsen, who is experienced in manual development for acupuncture trials, will lead the responsive manualization process (as in a PCORI-funded study<sup>76</sup>) and serve as the study's acupuncture expert. In accord with the responsive manualization effort, Dr. Nielsen will lead the development and definition of the treatment fidelity assessment parameters with the acute care acupuncture experts.

## **3. STUDY DESIGN**

### *Type/design of trial*

This is a multi-site single visit, feasibility randomized control trial of acupuncture in the ED versus Usual Care.

### *Specific unit(s) of assignment and unit(s) of observation.*

The unit of assignment is at the patient level. Specifically, acute pain patients enrolled in the ED will be randomly assigned to either acupuncture or usual care. The unit of observation is the patient.

### *Primary and secondary outcomes*

The primary outcomes of the study will be the recruitment and retention patients into the study. The secondary outcomes will be the development of a responsive acupuncture intervention and assessment of implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. Secondary outcomes will be assessed via qualitative interviews and structured observation to assess feasibility of

implementation.

#### *Study population and groups/arms including sample size*

The study population are: (1) One hundred fifty (50/site) plus 15 pilot (5/site) adults presenting to the ED with acute non-emergent (musculoskeletal, back, pelvic, non-cardiac chest, abdominal, flank or head) pain  $\geq 4$  on a 0-10-point NRS due to non-penetrating injury. (2) Thirty ED stakeholders (10/site) including ED providers (physicians, nurse practitioners, physician assistants, and registered nurses) and ED staff employed at one of the three sites for at least one year including the study period as well as acupuncturists who are employed or credentialed by one of the participating institutions to perform acupuncture in the emergency department as part of the study. (3) Of the 150 subject noted above, patients who are randomized to the acupuncture group will be contacted to participate in a brief qualitative interview about 3 weeks after their ED visit. The expectation is that 15 patient participants per site will consent to the qualitative interviews about their experience of receiving acupuncture as part of the RCT.

#### *Study locations*

##### **Randomized Control Trial**

Subjects will be recruited as described above from: the UH Cleveland Medical Center ED (site 1), the VUMC ED (site 2) and the Hillcrest UCSD ED (site 3).

##### **Structured Field Observation**

Three, 6 hour shifts will be observed at each site during active patient recruitment and treatment.

##### **Qualitative Interviews**

Patient qualitative interviews will be conducted via the audio-only function of a HIPAA-compliant commercial tele-health platform: (e.g. Zoom Health Professional or Doxy.me) or over the phone and will be recorded and transcribed. Provider interviews will happen in person in a private room or via the audio-only function of a HIPAA-compliant commercial tele-health platform: (e.g. Zoom Health Professional or Doxy.me) or over the phone. Study staff at the Einstein Coordinating Center conducting the interviews via secure online platform will be in a private room when interviewing the participants.

#### *Approximate duration of enrollment period and follow-up*

Patients will be enrolled for approximately 4 weeks. Each site will enroll for 6-9 months, and enrollment at the last site will be completed approximately 12 months after enrollment at the first site begins.

#### *Description of intervention and administration*

##### **Intervention Arms**

Acupuncture therapy. At each ED recruiting site, acupuncture intervention will be provided by one of two licensed acupuncturists with the option of a third backup acupuncturist for flexibility in coverage. Since there will be various pain presentations (musculoskeletal: back, neck, limb pain, abdominal or flank pain, headache etc), the acupuncture intervention will adhere to the responsive manualized protocol (developed in Year 1 of the grant). The responsive manualized protocol promotes standardization as well as flexibility based on the acupuncturist's assessment of a patient's presentation within a predetermined framework and contextual considerations such as accessibility of various parts of a patient's body. Receiving acupuncture will not affect the patient's usual care in that any medications (including opioid medications) will be administered as usual,

as clinically needed, after collection of ‘post’ scores and under the direction of the patient’s emergency care provider team.

Consistent with pragmatic trials,<sup>39</sup> we have chosen to compare Acupuncture therapy to Usual Care rather than to a sham acupuncture treatment. At this stage of investigating acupuncture in the ED, we agree with the current consensus view in the acupuncture research community that research designs such as those used to study new pharmaceutical treatments are not adequate in the study of effectiveness for therapies like acupuncture.<sup>66</sup> Further rationale for this choice stems from the consensus of the DoD/NIH Acupuncture for the Treatment of Acute Pain Workshop.<sup>67</sup> After two days of meeting with experts in statistics, acute pain and acupuncture, there was agreement from DoD, VA and civilian experts that design of acupuncture studies should compare acupuncture plus usual care to usual care alone. Our proposal is also consistent with the NIH Collaboratory recommendation for pragmatic trials (PCTs, see section above).<sup>40</sup>

The study acupuncturists will adhere to the following approach:

- The responsive manualized acupuncture therapy intervention will be based on staging an interview/conversation, palpation, and selection of points or methods for treatment based on presenting factors. The acupuncturist will record the specific acupuncture points, the number of needles used, length of needle retention, length of session time, any limitations on session time, points used for extended auricular therapy, if applicable, and response from point stimulation based on parameters of the manualization protocol (Aim 1). A consensus of common points utilized for acute pain in the ED can be expected with additional points to be used at the discretion of the acupuncturist treating a patient. Hand rotation and perturbation of needles to de qi status is allowed; electrical stimulation or moxibustion are not included in this trial. Needle retention time can vary and may range from 5-40 minutes, but commonly will be 15-30 minutes. Total session time may vary due to the patients’ tolerance of the treatment, acupuncturists’ assessment of the patient or workflow consideration of the ED, such as a patient needing to leave the room for imaging to be performed.
- Sterile, single-use non-coated acupuncture needles will be used for this study. Needles in sizes .22x13mm, .25x25mm, .25x40mm, and .30x40mm, and will be available. The choice of needle size used will be left to the discretion of the acupuncturists treating the patient.
- Treatment regimen: Each patient randomized to the Acupuncture arm will be provided no more than one treatment per admission to the ED. Due to workflow considerations of the ED of this pragmatic RCT, it is possible that some patients randomized to the Acupuncture arm of the study will not receive acupuncture.
- Acupuncturists will attempt to provide the acupuncture intervention as close to the beginning of the patient’s ED visit as possible, after evaluation by the attending ED provider. The rationale for this decision is to help evaluate the use of acupuncture as a first line intervention for pain relief.
- Extended therapy pressure: Ear seeds will be retained on auricular acupuncture points in order to “extend the treatment benefit after ED care”. We will use vaccaria seed with latex adhesive, and have a non-latex alternative for patients with latex allergy. Use and location of the ear seeds will be at the discretion of the acupuncturist. Patients will keep them on the ears after discharge from the ED, and are directed to leave them on until they fall off or remove them if they become uncomfortable. The ear seeds can be peeled off and thrown into the trash.

- Acupuncturists will be nationally board certified and remain current with the National Commission for the Certification of Acupuncture and Oriental Medicine (NCCAOM) which includes passing of infection control standards exam; they will also have a valid and current state acupuncture license.

During active enrollment for each site, Dr. Nielsen will lead weekly team meetings with treating acupuncturists to discuss cases and use of the manual, exploring whether the manual may restrict an acupuncturist's ability to respond to unique patient presentations. These discussions will provide an ongoing assessment of usability based on these stakeholders' experience or insights in the ED.

**Usual Care:** Patients assigned to the Usual Care arm will receive care and treatment for pain and any other symptoms or conditions as would usually be provided in the ED, in accordance with the relevant pain management and care policy at each participating ED. Furthermore, we have designed our study so that the medications provided to Usual Care patients will have enough time to take effect serving as a more pragmatic control to the Acupuncture arm than sham acupuncture.

### **Randomization**

Random assignments will be made by the study statistician in permuted blocks of size 2 and 4. The block size will also be randomly generated to minimize correct prediction of assignments and preserve approximate balance between groups, using the rand function in SAS. Administrative personnel from the BraveNet Coordinating Center will prepare each randomization packet in a sealed envelope and send these to each site in batches. A date/signature label will be placed over the envelope seal. Randomization envelopes will be stored in locked cabinets and opened by study staff (SC or RA) after completion of the informed consent process and baseline data collection.

## **4. SELECTION AND ENROLLMENT OF PARTICIPANTS**

### **4.1 Inclusion Criteria**

Participants must meet all of the inclusion criteria to participate in this study.

#### Randomized Control Trial

	<b>Inclusion Criteria</b>
1.	≥18 years of age
2.	Ability to communicate in English
3.	Level 3, 4, 5 on triage rate scale
4.	Acute musculoskeletal, back, pelvic, non-cardiac chest, abdominal, and headache pain (≥4 on the NRS) due to non-penetrating injury.

#### Qualitative Interviews

	<b>Inclusion Criteria</b>
1.	ED providers (physicians, nurse practitioners, physician assistants, and registered nurses) and ED staff employed in the UH Cleveland Medical Center ED (site 1),

	the VUMC ED (site 2) and the Hillcrest UCSD (site 3) for at least one year including the study period.
2.	Acupuncturists who are employed or credentialed by one of the participating institutions to perform acupuncture in the emergency department as part of the study.
3.	Patients who received acupuncture as part of the RCT.
4.	Access to the internet and a smart phone, computer or tablet.

#### 4.2 Exclusion Criteria

All candidates meeting any of the exclusion criteria at baseline will be excluded from study participation

##### Randomized Control Trial

	<b>Exclusion Criteria</b>
1.	Fever exceeding 100° F
2.	Presenting with a chief complaint of a psychological / psychiatric concern
3.	Presenting with chief complaint of Migraine
4.	Current Pregnancy
5.	Self-reported or documented opioid medication taken orally within 4 hours
6.	Presenting with chief complaint of Joint Dislocation
7.	Presenting with chief complaint of Bone Fracture
8.	Confirmed or suspected COVID-19

##### Qualitative Interviews

N/A

#### 4.3 Study Enrollment Procedures

##### **Recruitment Methods**

Randomized Control Trial: When a patient arrives in the participating ED (UH Cleveland Medical Center ED (site 1), the Vanderbilt University Medical Center (VUMC) ED (site 2) and the Hillcrest University of California San Diego (UCSD) ED (site 3)), they will be triaged by the triage nurse per current ED procedures. Pending permission of site ED leadership, pre-treatment study flyers can be posted at triage, in waiting areas, or in treatment spaces to offer a passive introduction to the study. Within the triage unit, potential subjects will be identified flagged by nursing staff and/or a member of the research staff. Patients who rate pain four or greater on the 11-point NRS scale will be considered for the study. At that time, the Study Coordinator (SC) or the Research Assistant (RA) will verify the patient's initial eligibility (age, understanding of English language, presence of pain) using the EHR. If the patient is potentially eligible, the SC or RA, if able, will approach the patient while in the waiting room to be seen by their provider to hand them the patient recruitment flyer. The SC or RA will continue to monitor his or her status and location within the ED using the EHR. The patient will then be roomed and seen by the ED clinical provider. If the ED provider determines that patient does not have a clinical condition prohibiting study participation, s/he will sign a study approval form and give back to the SC or RA. Thereafter, the SC or RA will approach the potential subject to introduce the study. If the person is interested in study participation

after they have been assigned to a room, the SC or RA will assess patient's capacity to understand and sign documentation, if patient is capable then they will seek to obtain informed consent. The consent will inform the patient that if they are randomized to receive acupuncture a study team member may contact them to ask if they would like to participate in an additional interview, and that they may refuse to participate in the interview portion of the study without affecting their participation in the other portion of the research. They will be informed that the interview will be recorded and transcribed and that a study information sheet will be shared and reviewed with them prior to the start of the interview. If the patient is not interested in participating in the study or refuses to provide their phone number and email for follow up assessments, a reason for refusal will be documented by the SC or RA in our computerized study database.

Individuals who participate in the ED data collection procedures will be remunerated \$25 and those who complete the 1-week and 4-week follow-up assessments will be remunerated an additional \$25 per visit. Remuneration will happen within 45 days of the patients' ED stay. There is no current plan for recruitment or advertisement materials due to the nature of this study and immediate recruitment of subjects.

**Qualitative Interviews:** Patient recruitment methods: Patients who participate in the RCT will have been informed as part of the informed consent process that they may be contacted to participate in a qualitative interview if they are assigned to the acupuncture group, and they will have been given the option to opt out of being contacted for the interview. Study staff from the Einstein Coordinating Center, who will be research credentialed, will contact the patients in the acupuncture group via email and/or phone within a week of their ED visit to schedule the interview and to share the study information sheet for them to review. Participant contact with the research staff for qualitative interviews will be documented in REDCap with up to 5 attempts to schedule the qualitative interview.

Provider recruitment methods: We will use staff rosters to identify physicians, nurse practitioners, physician assistants, nurses and ED staff who have been employed by in the ED at one of the three sites during the data collection period, to ensure familiarity with the study. Site credentialed study staff from the Einstein Coordinating Center will contact these providers, whether in person during their site visit for the structured observation, or by email followed by phone, to invite them to participate and to share study information sheet for them to review.

All individuals who participate in the qualitative interviews will be remunerated \$25 within 30 days of the interview. The qualitative interview team from Einstein Coordinating Center will inform respective site study staff once a patient's qualitative interview is complete. Site study staff will contact the patient with the e-gift card code or mail a physical gift card and will mark in REDCap when this was completed.

#### **Documentation of reasons for ineligibility.**

We will maintain a screening and enrollment log to document ineligibility reasons and for non-participation of eligible candidates.

#### **Consent Process**

**Randomized Control Trial:** The consent process will occur after the patient has gone through the triage process and been assigned to a room within the ED. The consent process will be conducted by dedicated research staff (SC or RA) that have been trained

in obtaining informed consent. The status and location of the patient will be monitored by research staff using the EHR to ensure the patient is approached at an appropriate time.

All potential participants will be examined by an ED provider to ensure they do not need emergent care and have sufficient mental capacity to participate in the study. If the ED provider determines that patient does not have a clinical condition prohibiting study participation, s/he will sign a study approval form. Research staff will assess patient capacity to understand and sign study documentation prior to obtaining consent. If patient is capable to continue, research staff (SC or RA) will consent potential participants. In doing so, they will explain the study, including benefits, risks and interventions. The research staff will stress to the patient that participation is voluntary and they may withdraw from the study at any time. Consent decline or withdrawal from the study will not affect the patient's continued care in the ED. As per other studies conducted by the PI, the research staff will be trained to answer all questions that may arise. Privacy will be ensured by conducting all study related interactions, including the consent process, within the patient's private ED treatment room. Patients will be provided ample time to go through the consent process and ask any questions. Time for decision making will be minimized due to the fast-paced and urgent nature of the ED. After a member of the research staff explains the consent form, study requirements and answers all of the patient's questions about the study, patients will provide written consent. Only the participating patients themselves will be allowed to provide consent for inclusion into the study. No legally authorized representative (LAR) may enroll a patient into the study. Study activity may only continue after the patient has provided written consent. If a patient declines to participate or is unable to sign the consent document, a reason for refusal will be asked and documented in the study database. It will be considered a declination of participation if a patient refuses to provide study staff with their phone number and email address during the baseline assessment. Patients who decline participation will not be allowed to opt into the study for the remainder of that particular ED visit. However, they would be eligible to participate at a future ED visit if interested and if the study is still in the recruitment phase. If a patient enrolls in the study, he or she will no longer be eligible for study participation during future ED visits within the recruitment period. We will utilize the EHR, and the 21 CFR Part 11 compliant data collection tool (e.g., REDCap), to verify the patient has not previously participated in the study.

#### Qualitative Interviews:

*Patient consent process:* Patients who are consented to participate in the RCT will be informed as part of that consent process that if they are randomized to receive acupuncture as part of the study, we may approach them to invite them to participate in an interview. The consent form will include language informing the patient that the interview will take place via the audio-only function of a HIPAA-compliant commercial tele-health platform: (e.g. Zoom Health Professional or Doxy.me) and will be recorded and transcribed. There will also be an option for the participant to opt out of being contacted for the interview. Research credentialed study staff at the Einstein Coordinating Center will contact participants randomized to the acupuncture arm within a week after their ED visit to schedule the interview and to share the study information sheet to review. Participant contact with the research staff for qualitative interviews will be documented in REDCap with up to 5 attempts to schedule the qualitative interview. At the time of the interview, the interviewer will review the study information sheet with the patient. This document will explain that the interview will be recorded and transcribed,

and will reiterate the voluntariness of participation. The document will explain that if the participant continues with the interview, they are agreeing that they have read the information and that they voluntarily agree to participate and to be recorded for transcription purposes.

*Provider consent process:* Identified providers will be contacted by research credentialed study staff at The Einstein Coordinating Center, either in person during their site visit or via email followed by phone, and invited to participate in the interview. They will schedule the interview at the providers' convenience. A study information sheet will be shared via email with the provider ahead of the interview, and will be reviewed at the beginning of the scheduled interview. This document will explain that the interview will be recorded and transcribed, and will reiterate the voluntariness of participation. The document will explain that if the participant continues with the interview, they are agreeing that they have read the information and that they voluntarily agree to participate and to be recorded and transcribed.

The research staff conducting the informed consent process will introduce the study as an investigation to describe perspectives and experiences related to implementation of the acupuncture study in the ED. The study information sheet will be reviewed with each participant, and participants will be encouraged to ask questions throughout the process. Research staff will stress the points that this is a voluntary study, and that a participant is able to refuse to take part in any part of the study or to withdraw from the study at any time, without any impact on their care or on their employment/consulting privileges at the sites. Consent to be interviewed and for the interview to be recorded will be obtained verbally. Only individuals able to consent of their own volition will be enrolled.

Structured Observations: Observations of screening and recruitment will be conducted by UH Research Credentialed study staff. The study coordinator or research assistant who recruit patients in the ED will introduce the additional study staff and explain that they are observing the interactions and taking notes. They will be given the opportunity to verbally refuse to be observed during consent. The consent form will also have an option to opt out of further observation of study procedures. Study staff in the ED, including the acupuncturists, will provide written consent ahead of time to be observed during the observation site visit.

### **Randomization**

Random assignments will be made by the study statistician in permuted blocks of size 2 and 4. The block size will also be randomly generated to minimize correct prediction of assignments and preserve approximate balance between groups, using the rand function in SAS. The randomization module will be built into REDCap. Study staff (SC or RA) will enable randomization in REDCap for each participant after completion of the informed consent process and baseline data collection. If the REDCap randomization module is not available, envelopes will be used. Personnel from the Albert Einstein School of Medicine will prepare each randomization packet in a sealed envelope and send these to each site in batches. A date/signature label will be placed over the envelope seal. Randomization envelopes will be stored in locked cabinets and opened by study staff (SC or RA) after completion of the informed consent process and baseline data collection.

## 5. STUDY INTERVENTIONS

### 5.1 Interventions, Administration, and Duration

At each ED site, acupuncture intervention will be provided by one of two licensed acupuncturists with the option of a third backup acupuncturist for flexibility in coverage. Since there will be various pain presentations (musculoskeletal: back, neck, limb pain, abdominal or flank pain, headache etc.), the acupuncture intervention will adhere to the manualized protocol (developed in year 1 of the grant). The manualized protocol promotes standardization as well as flexibility based on the acupuncturist's assessment of the patient's presentation within a predetermined framework and contextual considerations such as accessibility of various parts of a patient's body. Receiving acupuncture will not affect the patient's usual care in that any medications (including opioid medications) will be administered as usual, as needed, after collection of 'post' scores and under the direction of the patient's emergency care provider team.

Consistent with pragmatic trials,<sup>39</sup> we have chosen to compare Acupuncture therapy to Usual Care rather than to a sham acupuncture treatment. At this stage of investigating acupuncture in the ED, we agree with the current consensus view in the acupuncture research community that research designs such as those used to study new pharmaceutical treatments are not adequate in the study of effectiveness for therapies like acupuncture.<sup>66</sup> Further rationale for this choice stems from the consensus of the DoD/NIH Acupuncture for the Treatment of Acute Pain Workshop.<sup>67</sup> After two days of meeting with experts in statistics, acute pain and acupuncture, there was agreement from DoD, VA and civilian experts that design of acupuncture studies should compare acupuncture plus usual care to usual care alone. Our proposal is also consistent with the NIH Collaboratory recommendation for pragmatic trials.<sup>40</sup>

The study acupuncturists will adhere to the following approach:

- The acupuncture therapy intervention will be based on staging an interview/conversation, palpation, and selection of points or methods for treatment based on presenting factors. The acupuncturist will record the specific acupuncture points, the number of needles used, length of needle retention if applicable, length of session time, any limitations on session time, points used for extended auricular therapy, if applicable, and response from point stimulation based on parameters of the responsive manualization protocol (Aim 1). A consensus of common points utilized for acute pain in the ED can be expected with additional points at the discretion of the acupuncturist treating the patient. Hand rotation and perturbation of needles to de qi status is allowed; electrical stimulation or moxibustion are not included in this trial. Needle retention time can vary and may range from 5-40 minutes, but commonly will be 15-30 minutes. Total session time may vary due to the patients' tolerance of the treatment, acupuncturists' assessment of the patient or workflow consideration of the ED, such as a patient needing to leave the room for imaging to be performed.
- Sterile, single-use non-coated acupuncture needles will be used for this study. Needles in sizes of .22x13mm, .25x25mm, .25x40mm, and .30x40mm, and will be available. The choice of needle size used will be left to the discretion of the acupuncturists treating the patient.
- Treatment regimen: Each patient randomized to the Acupuncture arm will be provided no more than one treatment per admission to the ED. Due to workflow considerations of the ED of this pragmatic RCT, it is possible that some patients randomized to the Acupuncture arm of the study will not receive acupuncture.
- Extended therapy pressure: Ear seeds will be retained on auricular acupuncture points in order to "extend the treatment benefit after ED care". We will use vaccaria seed with latex adhesive, and have a non-latex alternative for patients with latex allergy. Use and location of the ear seeds will be at the discretion of the acupuncturist. Patients will keep them on the ears after discharge from the ED, and are directed to leave them on until they fall off or

remove them if they become uncomfortable. The ear seeds can be peeled off and thrown into the trash

- Acupuncturists will attempt to provide the acupuncture intervention as close to the beginning of the patient's ED visit as possible, after evaluation by the attending ED provider. The rationale for this decision is to help evaluate the use of acupuncture as a first line intervention for pain relief.
- Acupuncturists will be nationally board certified and remain current with the National Commission for the Certification of Acupuncture and Oriental Medicine (NCCAOM) which includes passing of infection control standards exam; they will also have a valid and current state acupuncture license.
- Acupuncturists will provide the participant with the Acupuncture Post Care information sheet (attached to the IRB smart application) at the completion of the acupuncture treatment. This sheet has information about the ear seeds and general after care instructions.

During active enrollment for each site, Dr. Nielsen will lead weekly team meetings with treating acupuncturists to discuss cases and use of the manual, exploring whether the manual may restrict an acupuncturist's ability to respond to unique patient presentations. These discussions will provide an ongoing assessment of usability based on these stakeholders' experience or insights in the ED.

**Usual Care:** Patients assigned to the Usual Care arm will receive care and treatment for pain and any other symptoms or conditions as would usually be provided in the ED, in accordance with the relevant pain management and care policy at each participating ED. Furthermore, we have designed our study (see Figure 1) so that the medications provided to Usual Care patients will have enough time to take effect serving as a more pragmatic control to the Acupuncture arm than sham acupuncture.

Based on our successful prior experience with our observational study and RCT, the likelihood of adverse physical, psychological, social, and legal risks is expected to be very small.

Acupuncture carries very slight risks for

- Bleeding,
- Bruising,
- Fainting (acushock)
- Needling pain

In the event a patient experiences an adverse event (AE), they will be treated by providers in the site ED and will have access to emergency response equipment as necessary.

Acupuncture involves inserting thin, sterile needles in the skin. The needles are not inserted into the skin very far. Sometimes the needles cause slight discomfort or minor bleeding. Any acupuncturist who provides treatments in this study will be licensed by the state in which they practice.

Monitoring of the study for AEs will be continuous throughout the study. In the event of an AE or SAE, it will be reported to the UH IRB in compliance with UH IRB standards.

## 5.2 Handling of Study Interventions

Sterile, single-use non-coated acupuncture needles will be used for this study. Needle sizes of .22x13mm, .25x25mm, .25x40mm, and .30x40mm will be available. The choice of needle size used will be left to the discretion of the acupuncturists treating the patient. Ear seeds will be

retained on auricular acupuncture points in order to “extend the treatment benefit after ED care”. We will use vaccaria seed with latex adhesive, and have a non-latex alternative for patients with latex allergy. Use and location of the ear seeds will be at the discretion of the acupuncturist.

### **5.3 Concomitant Interventions**

#### **5.3.1 Allowed Interventions**

As the study is taking place in the active clinical ED, the responsible ED clinician will have the ability to prescribe any medications or interventions to maintain the health of a participant regardless of the treatment assignment of the participant.

#### **5.3.2 Required Interventions**

Acupuncture is required for those in the treatment group

#### **5.3.3 Prohibited Interventions**

For those in the treatment group, pain medications will be delayed until after completion of acupuncture intervention.

### **5.4 Adherence Assessment**

N/A

## **6. STUDY PROCEDURES**

### **6.1 Schedule of Evaluations**

#### **Randomized Control Trial**

**Treatment Variables.** Main patient reported treatment outcomes (PROs) include pain intensity and anxiety. The use of self-reported pain ratings to assess pain is standard clinical practice.<sup>68,69</sup> Although self-report of pain intensity is subjective, a reliable physiological measure to quantify pain has not been identified.<sup>70</sup> These measures will be collected via tablet computer in the PHI-approved data collection tool (REDCap). A similar process was used in Dusek's pilot RCT. The study staff will hand the patient a tablet for confidential self-administration. Once the patient completes the questionnaires, the answers will be masked so the research staff will not have access to the scores. To keep research staff blinded to scores, the data collection tool will be designed so that the study staff will only be able to determine that valid pain and anxiety scores were entered by the patient. In other words, staff will not have access to the actual pain or anxiety scores until the statistician conducts the final analysis. Data will be collected as shown in Table below.

Treatment Variables	Measure/Source	Data Collection Time point			
		Pre-Treatment	Post-Treatment	ED Discharge	1-week and 4 Follow-up
<b>Primary Assessment (* and bold)</b>					
Pain Intensity	<i>Numeric Rating Scale, 0-10<sup>58,59</sup></i>	X	X*	X*	X^
<b>Secondary Assessment (^ and italic)</b>					
All pain medications in the ED	EHR			X^	
Anxiety	<i>Numeric Rating Scale, 0-10<sup>58,59</sup></i>	X	X^	X^	X^
Pain medication/opioid use	<i>Self-report</i>				X^
<b>Baseline variables of interest</b>					
Demographics	<i>EHR data and self-report</i>	X			
Current Medications		X			
Opioid use – last 30 days		X			
Previous acupuncture use	<i>Self-report</i>	X			
ED visits in last year		X			
<b>Other variables of interest</b>					
Expectancy	<i>Self-report</i>	X			
Satisfaction questions			X	X	X
ED impact (ACUPUNCTURE ONLY)				X	

## Qualitative Interviews

U01 Acupuncture Study  
Patient Interview Topic Guide  
Preliminary Draft 10-23-20

1. Pain narrative—history, cause, impact, course, treatment experiences

Possible prompts:

- i. Tell me about your pain condition...
- ii. How long have you had it?
- iii. What causes it?
- iv. How does it impact you?
- v. Tell me about your pain condition over time—wax/wane? Always the same?
- vi. Tell me about your treatment and management experiences

2. Attitudes/perception of acupuncture—previous treatment history, beliefs

Possible prompts

- i. What was your experience of acupuncture before your (index) ED visit?
- ii. What were your views of acupuncture?
- iii. Did your views change after your ED acupuncture visit?

3. Index ER Visit—the decision to visit the ED, previous ED visits, description of the visit

Possible Prompts

- i. Why did you decide to go to the ER? Have you visited the ER before? For the same problem? Tell me about it.
- ii. Tell me about your visit? What was it like in the ER during that visit? Tell me about it.

4. Acupuncture Study in the ED—the decision to participate

Possible Prompts

- i. Why did you decide to participate in the Acupuncture study? Tell me about that.

5. Experience of acupuncture in the ED—index visit

Possible Prompts

- i. Describe your experience with acupuncture during that visit—timing, location, length of treatment, behavior of the acupuncturist, other ED staff
- ii. Did it impact your pain? Right away or after a while? Tell me about it?
- iii. What surprised you about this experience?
- iv. Are there ways it could have been improved?
- v. Did you receive other treatments? Tell me about that.

6. Post treatment experiences

Possible Prompts

- i. Tell me about what happened after your visit? Where did you go? What did you do?
- ii. Tell me about your pain. Was it better after your visit? Did it get better over time? Is it better now? Tell me about it
- iii. What do you attribute your improvement/lack of improvement to?
- iv. If the acupuncture helped, how or why did it help?
- v. Are you or would you seek further acupuncture treatments?
- vi. Did other treatments you received also help?
- vii. Were there treatments you did not receive that would have helped?

7. Pain in the future

- i. How do you see your pain in the future?

ii. Would you seek out ED treatment again if you experienced the same pain?

Why or why not?

- iii. Would you seek out acupuncture, in the ED or outside the ED? Why or why not?

1. Treating pain in the ER—experiences, perceptions, challenges

Possible prompts:

- i. Tell me about treating pain in the ER
- ii. What are some of the challenges?
- iii. What are typical cases?
- iv. How do you usually treat them?
- v. Is treating pain in the ER challenging?
- vi. What would make your job of treating pain in the ER easier?

2. Attitudes/perception of acupuncture—previous treatment history, beliefs

Possible prompts:

- i. Can you describe your personal experiences with acupuncture, if any?
- ii. Can you describe your professional experiences with acupuncture, if any?
- 1. Is it helpful for patients?
- a. All patients? Some patients? Why does it work better/worse for some?
- iii. Overall, what were your view of acupuncture? Does it work? How do you think it works?

3. Acupuncture in the ER—initial perceptions of the research project

Possible Prompts

- i. What was your initial reaction to the idea of introducing acupuncture into the ER setting? What were some of the benefits you perceived? Challenges?
- ii. Now that the project is underway, have there been any surprises? Did the acupuncture work as well/as poorly as you expected?
- iii. What were some of the hiccups/Issues that occurred with this research project?
- iv. What about the burden of the project?
- v. What is your view, now, of the value of inserting acupuncture in the ER?
- vi. After your experiences with our research project, what do you think about implementing acupuncture on an ongoing basis in the ER?
- vii. If yes:
  - 1. What would be some of the challenges? How would you overcome them?
  - 2. What would be the benefits?
- viii. If no:
  - 1. Why not? Tell me about that

## Structured Observations

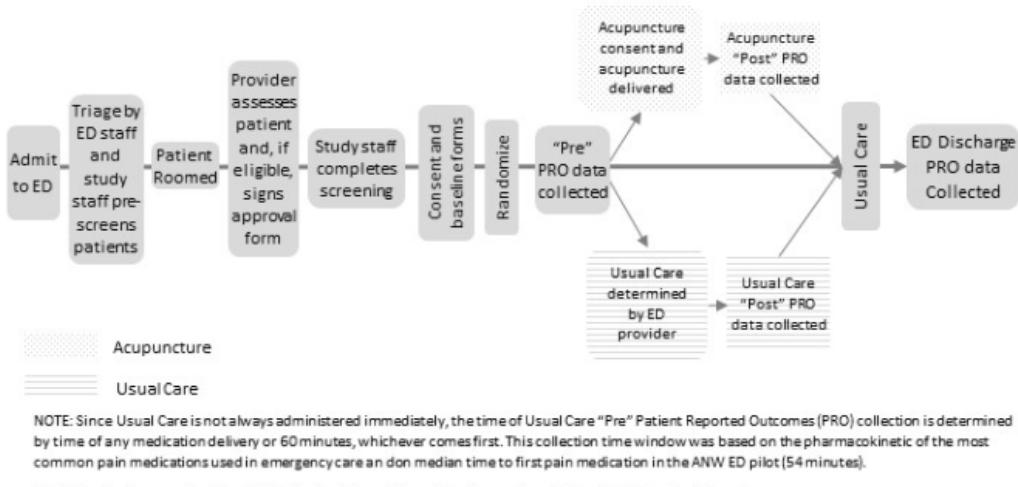
ACUITY
<p><b>FIELD NOTES TEMPLATE</b></p> <p><b>NOTE: ONLY CONSENTED PATIENTS WILL BE OBSERVED DURING STUDY PROCEDURES. OBSERVERS WILL WEAR APPROPRIATE PPE AND MAINTAIN A SIX FOOT DISTANCE FROM STAFF AND PATIENTS AT ALL TIME</b></p> <p><b>OBSERVER:</b> <b>DATE:</b> <b>SITE:</b> <b>TIME OF OBSERVATION:</b> <b>INITIAL DESCRIPTION</b>—level of activity, noise, temperature, mood, in the ER:</p> <p><b>Acupuncture Participants (Research staff, ED staff, and Participants)</b></p> <p><b>1. PRESENTATION IN THE ED:</b> <i>The patient's initial presentation and interactions between patients and ED staff. Note patient verbal and nonverbal behaviors, tone of interactions, pain behaviors,</i></p> <p>Persons involved: Notes:</p> <p><b>2. INITIAL INTERACTIONS BETWEEN RESEARCH AND ED STAFF</b>—<i>Study coordinator and ED staff interactions. Note staff response to request for participant enrollment.</i></p> <p>Persons involved: Notes:</p> <p><b>3. ENROLLMENT AND STUDY PROCEDURES</b>—<i>Initial approach, consent, randomization. Note patient verbal and nonverbal behaviors, pain behaviors, questions asked, tone of voice.</i></p> <p>Persons involved: Notes:</p>

<p><b>1. THE ACUPUNCTURE SESSION</b>—<i>Note patient verbal and nonverbal behaviors, interactions between acupuncture provider and patient</i></p> <p><b>Persons involved:</b> <b>Notes:</b></p> <p><b>1. POST ACUPUNCTURE INTERACTIONS</b>—<i>Note patient verbal and nonverbal behaviors and interactions with staff, location of observation, pain behaviors, etc.</i></p> <p><b>Persons involved:</b> <b>Notes:</b></p>
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## 6.2 Description of Evaluations

### 6.2.1 Screening Evaluation

At each ED, the Study Coordinator (SC) or Research Assistant (SC) and acupuncturist will work as a team, staffing an average 2.5, 4-6 hour recruitment/intervention sessions per week, varying the times and days across sites as this may influence adoption. As in Figure 1, after the ED RN conducts the initial triage activity, the SC or RA ("study staff") will identify and conduct initial eligibility pre-screening in the in the ED triage unit. The patient will then be roomed and seen by the ED clinical provider. If the ED provider determines that patient does not have a clinical condition prohibiting study participation, s/he will sign a study approval form (see below). The study staff will then approach the patient for study participation.



## Provider sign off

<p><b>Acupuncture in the Emergency Department for Pain Management (ACUITY)</b></p> <p>If the patient is randomized to the acupuncture arm, please withhold pain and anxiety medications until after the acupuncture session.</p> <p>The study coordinator will inform you what arm they are assigned to and when their session has ended.</p> <p>In order for this patient to be eligible to participate in the "Acupuncture in the ED" study, please verify you have examined the patient and believe to the best of your knowledge, at this time, that the patient does not have the following conditions:</p> <p><input type="checkbox"/> Critical status / Trauma <input type="checkbox"/> Bone fracture <input type="checkbox"/> Joint dislocation <input type="checkbox"/> Migraine <input type="checkbox"/> Psychological / psychiatric concern <input type="checkbox"/> Clinical judgement / Other:</p> <p>If you deem the patient eligible for the study, the patient will be randomized to acupuncture or usual care.</p> <p><input type="checkbox"/> Patient can continue in study      <input type="checkbox"/> Patient is excluded from study</p> <p>Sign: _____</p>
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### **Consenting Procedure**

We have requested a partial HIPAA waiver for prescreening. Therefore, patients will only be consented once the screening process is over and eligibility is confirmed.

The consent process will occur after the patient has gone through the triage process and been assigned to a room within the ED. The consent process will be conducted by dedicated research staff (SC or RA) that have been trained in obtaining informed consent and who have current Human Subjects Protection and Good Clinical Practice certifications. The status and location of the patient will be monitored by research staff using the EHR to ensure the patient is approached at an appropriate time.

All potential participants will be examined by an ED provider to ensure they do not need emergent care and have sufficient mental capacity to participate in the study. If the ED provider determines that patient does not have a clinical condition prohibiting study participation, s/he will sign a study approval form. Research staff will assess patient capacity to understand and sign study documentation prior to obtaining consent. If patient is capable to continue research staff (SC or RA) will consent potential participants. In doing so, they will explain the study, including benefits, risks and interventions. The research staff will stress to the patient that participation is voluntary and they may withdraw from the study at any time. Consent decline or withdrawal from the study will not affect the patient's continued care in the ED. As per other studies conducted by the PI, the research staff will be trained to answer all questions that may arise. Privacy will be ensured by conducting all study related interactions, including the consent process, within the patient's private ED treatment room. Patients will be provided ample time to go through the consent process and ask any questions. Time for decision making will be minimized due to the fast-paced and urgent nature of the ED. After a member of the research staff explains the consent form, study requirements and answers all of the patient's questions about the study, patients will provide written consent. Only the participating patients themselves will be allowed to provide consent for inclusion into the study. No legally authorized representative (LAR) may enroll a patient into the study. Study activity may only continue after the patient has provided

written consent. If a patient declines to participate or is unable to sign consent documents, a reason for refusal will be asked and documented in the study database. It will be considered a declination of participation if a patient refuses to provide study staff with their phone number and email address during the baseline assessment. Patients who decline participation will not be allowed to opt into the study for the remainder of that particular ED visit. However, they would be eligible to participate at a future ED visit if interested and if the study is still in the recruitment phase. If a patient enrolls in the study, he or she will no longer be eligible for study participation during future ED visits within the recruitment period. We will utilize the EHR, and the 21 CFR Part 11 compliant data collection tool (e.g., REDCap), to verify the patient has not previously participated in the study.

Documentation of Informed Consent will follow Connor Integrative Health Network's Standard Operation Procedures (SOP) for Obtaining Informed Consent and Re-Consent, which includes a Research Informed Consent Documentation template. The Documentation form captures the date and time of consent, the name of the study and IRB number, name of person consenting, individuals present during consent process, the names of anyone else involved in the decision making process, the name of the staff member obtaining informed consent, if the subject verbalized understanding of the study, if the consent process happened in a private setting, if the subject received a copy of the signed consent, etc. This form will be signed by the person obtaining consent and by the PI and retained with the original copy of the signed consent.

## **Screening**

All screening activities must be completed before consent and study enrollment. Consent and study enrollment will happen shortly after screening given the nature of the ED environment and emergent nature of the patients' acute pain. Study staff will use the EHR and information from the triage nurse to determine initial eligibility. All potential participants will be examined by an ED provider to ensure they do not need emergent care and have sufficient mental capacity to participate in the study. If the ED provider determines that patient does not have a clinical condition prohibiting study participation, s/he will sign a study approval form.

### **6.2.2 Enrollment, Baseline, and/or Randomization**

#### **Enrollment**

Subjects are considered enrolled once the informed consent document has been signed and randomization has occurred. Only one written informed consent document will be used, as we have requested a partial HIPAA waiver for screening.

#### **Baseline Assessments**

- Pre-Treatment Pain Intensity Assessment (Pre) using a 0-10 NRS<sup>58,59</sup> will be collected: a) for acupuncture patients, before administration of acupuncture; b) for usual care patients who receive a pain medication order within 60 minutes (+/- 15 minutes) of being roomed, just before or at administration of pain medication; or c) for usual care patients who have not received a medication order within 60 minutes (+/- 15 minutes) of being roomed, at 60 minutes (+/- 15 minutes). The collection time window of 60 minutes was based on median time from being roomed to first pain medication (54 minutes) using data obtained from the ANW ED pilot study (See Figure 1). Pre-treatment pain assessments will be timed to be completed immediately prior to the administration of either the acupuncture or usual care treatments.
- Anxiety scores using a 0-10 NRS<sup>58,59</sup>

- Expectancy will be measured with the following questions.
  - By the end of the treatment period in the ER, how much improvement in your pain symptoms do you think will occur?  
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Now, please close your eyes for a few moments and try to identify what you really feel about the treatment and its likely success. Then answer the following questions:

- At this point, how much do you really feel that the treatment will help you to reduce your pain symptoms?  
1 2 3 4 5 6 7 8 9  
Not at all Somewhat Very much
- By the end of your treatment period in the ER, how much improvement in your pain symptoms do you really feel will occur?  
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

## **Randomization**

Immediately after screening, obtaining informed consent from eligible patients, and collecting baseline data, the study staff will randomize patients to either Acupuncture or Usual Care.

### **6.2.3 Blinding**

Data collectors in the ED will be masked to study outcomes of a given patient by use of electronic data collection methods.

### **6.2.4 Follow-up Visits**

#### Post Treatment Assessment

- Post-Treatment Pain Assessment (Post) using a 0-10 NRS<sup>58,59</sup> will be collected within 60 minutes (+/- 15 minutes) of the Pre-Treatment score, thus including the acupuncture and usual care periods. Based on pharmacokinetics of the most common pain medications used in emergency care one hour is the maximum time to effectiveness for any pain medication currently administered in most EDs.
- Anxiety scores using a 0-10 NRS<sup>58,59</sup> will be collected at the same time as pain intensity.
- Satisfaction and will be measured through brief questions. All participants will be asked to answer;
  - “How satisfied are you with how your pain was managed during your ED visit” on the 5-point Likert scale.
  - “Overall how satisfied are you with your treatment during your ED visit?” on the same Likert Scale. CI across sites as well as across patient groups such as different presenting complaints and patient demographics.

#### ED Discharge Assessment

ED Discharge Assessment (ED Discharge) will be obtained within 15 minutes of patients' discharge from the ED, for both acupuncture and usual care patients. If the study staff's shift has ended and it has been longer than 15 minutes since collecting post-treatment scores, study staff will collect discharge scores from the participant and leave for the day. Discharge scores will not be attempted to be collected if the participant is discharged within 15 minutes of when post treatment scores were collected. This will not be considered missing data.

- Pain Assessment (Post) using a 0-10 NRS<sup>58,59</sup>

- Anxiety scores using a 0-10 NRS<sup>58,59</sup>
- Satisfaction and will be measured through brief questions. All participants will be asked to answer;
  - “How satisfied are you with how your pain was managed during your ED visit” on the 5-point Likert scale.
  - “Overall how satisfied are you with your treatment during your ED visit?” on the same Likert Scale. CI across sites as well as across patient groups such as different presenting complaints and patient demographics.
- ED Impact and will be measured through a brief question given to Acupuncture patients only at ED discharge, participants will be asked to answer;
  - “Please rate the impact of acupuncture on your ED visit today.” on the 5-point Likert scale.
- All pain medications utilized in the ED will be obtained from the EHR after patient discharge.

#### One Week Follow-Up Assessment Visit

1 week follow-up Assessment (Follow-up) will be obtained via REDCap based text message or email (or phone call from research staff) at 1 week (+/- 4 days) of patient’s ED discharge for both arms. To maintain assessor blinding, any 1-week phone calls (if needed) will be conducted by a research staff (SC or RA) who did not interact with the patient during their study participation in the ED.

- Pain Assessment (Post) using a 0-10 NRS<sup>58,59</sup>
- Anxiety scores using a 0-10 NRS<sup>58,59</sup>
- Satisfaction and will be measured through brief questions. All participants will be asked to answer;
  - “How satisfied are you with how your pain was managed during your ED visit” on the 5-point Likert scale.
  - “Overall how satisfied are you with your treatment during your ED visit?” on the same Likert Scale.
- Pain medications utilized from ED discharge to 1 week after discharge will be obtained from patients via phone call, email, or text messaging via the secure REDCap electronic data collection tool.

#### **6.2.5 Completion/Final Evaluation**

##### Four Week Follow-Up Assessment Visit

4 week follow-up Assessment (Follow-up) will be obtained via REDCap based text message or email (or phone call from research staff) at 4 week (+/- 4 days) of patient’s ED discharge for both arms. To maintain assessor blinding, any 4-week phone calls (if needed) will be conducted by a research staff (SC or RA) who did not interact with the patient during their study participation in the ED.

- Pain Assessment (Post) using a 0-10 NRS<sup>58,59</sup>
- Anxiety scores using a 0-10 NRS<sup>58,59</sup>
- Satisfaction and will be measured through brief questions. All participants will be asked to answer;
  - “How satisfied are you with how your pain was managed during your ED visit” on the 5-point Likert scale.
  - “Overall how satisfied are you with your treatment during your ED visit?” on the same Likert Scale.
- Pain medications utilized from ED Discharge to 4 weeks after discharge will be obtained

from patients via phone call, email, or text messaging via the secure REDCap electronic data collection tool.

### Early Termination

The study doctor or the sponsor can stop a subject's participation at any time without their consent for the following reasons:

- If it appears to be medically harmful to them;
- If they fail to follow directions for participating in the study;
- If it is discovered that they do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment (e.g. the target number of subjects has entered the study.)
- If the patient's clinical condition worsens emergently as determined by the ED physician/clinician.

## **7. SAFETY ASSESSMENTS**

Monitoring of the study for AEs will be continuous throughout the study. In the event of an AE or SAE, it will be reported to the UH IRB in compliance with UH IRB standards.

The investigative team will monitor the data security, data integrity, and patient safety. The study team will meet at least every 2-4 weeks to assess for adherence to protocol and review any safety events.

Based on our successful prior experience with our observational study and RCT), the likelihood of adverse physical, psychological, social, and legal risks is expected to be very small.

Acupuncture carries very slight risks for:

- Bleeding,
- Bruising,
- Fainting (acushock)
- Needling pain

In the event a patient experiences an adverse event (AE), they will be treated by providers in the site ED and will have access to emergency response equipment as necessary.

Acupuncture involves inserting thin, sterile needles in the skin. The needles are not inserted into the skin very far. Sometimes the needles cause slight discomfort or minor bleeding. Any acupuncturist who provides treatments in this study will be licensed by the state in which they practice.

### **7.1 Specification of Safety Parameters**

N/A

### **7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters**

N/A

### **7.3 Adverse Events and Serious Adverse Events**

An adverse event (AE) is any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events are

to be recording regardless of their relationship to the study intervention and through follow-up. A serious adverse event (SAE) is any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly.

## **7.4 Reporting Procedures**

### **RESPONSIBLE INDIVIDUALS**

The Principal Investigator (PI) is responsible for assessing all AE and SAEs reported by research staff. Research staff are responsible for documenting and reporting to the PI and IRB if necessary any events reported by patient or their respective doctor.

### **PROCEDURES**

Reporting Adverse Events: Research staff will document AE on Connor Integrative Health Network's (CIHN) AE log after becoming aware of the event. The PI or their delegated research staff will review and sign off on AE and assign causality and severity/intensity.

Reporting Serious Adverse Events: Research staff will document SAE on CIHN AE log after becoming aware of the event. The PI or their delegated research staff will review, sign off on SAE and assign causality and severity/intensity. If the event satisfies all three of the FDA requirements for reporting SAEs it will be reported to the IRB;

- a. Serious
- b. Unanticipated, and
- c. Related to study product or study procedures

If the event is clarified as an SAE and deemed reportable to the IRB, delegated research staff will report event to the IRB within 5 days of being notified of event via the University Hospital's Cleveland Medical Center's (UHCMC) IRB's "Reportable New information Smart Form" (RNI). If more information becomes available to CIHN regarding SAE, delegated research staff will inform and follow-up with IRB.

## **7.5 Follow-up for Adverse Events**

Delegated research staff is responsible for all follow-up associated with AEs and SAEs and reporting this information to the IRB until the AE occurs.

## **7.6 Safety Monitoring**

The NCCIH requires that all Human Subjects research studies undergo independent monitoring, and NCCIH Program Officials will provide specific guidelines to the PI for the study. According an Independent Monitoring Committee will be assembled by the PI with approval required by the NCCIH.

# **8. INTERVENTION DISCONTINUATION**

### Early Termination

The study doctor or the sponsor can stop a subject's participation at any time without their consent for the following reasons:

- If it appears to be medically harmful to them;
- If they fail to follow directions for participating in the study;
- If it is discovered that they do not meet the study requirements;

- If the study is canceled; or
- For administrative reasons, including competitive enrollment (e.g. the target number of subjects has entered the study.)
- If the patient's clinical condition worsens emergently as determined by physician.

## 9. STATISTICAL CONSIDERATIONS

### 9.1 General Design Issues

#### Primary Objective

The primary objective is to refine procedures for conducting a future fully powered multi-site RCT in 3 EDs.

#### Secondary Objectives

The secondary objectives of this study are to: examine the feasibility of data collection in the RCT, develop a responsive acupuncture intervention and assess implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. This study will include qualitative interviews and structured observation to assess feasibility of implementation.

### 9.2 Sample Size and Randomization

#### Sample size justification for feasibility study

We justify the sample size of the proposed feasibility study by first considering the sample size that would be required for the future UG3/UH3 multi-site non-inferiority RCT. Per NCCIH guidance<sup>89</sup> and the literature,<sup>90-92</sup> we recognize that results from pilot/feasibility studies are not suitable for determining power. Rather clinically significant differences are required for the power calculation.<sup>90-92</sup> The verbally administered NRS has been validated and a minimum clinically significant change for acute pain intensity has been shown range from 1.3 (95% CI 1.0, 1.5)<sup>65,93</sup> to 2.0.

For non-inferiority trials it more conservative to use the lower estimate of clinical significance. Following convention we divide the minimally reported clinically significant change by two<sup>94</sup> to obtain a non-inferiority margin of 0.65 (=1.3/2). That is, to test whether Acupuncture group is at most 0.65 units inferior to the Usual Care group, a sample sizes of 510 (255 Acupuncture vs 255 Usual Care) will achieve 80% power to detect non-inferiority. We will use a one-sided Mann-Whitney test with type 1 error 0.05.

The power calculation is based on the assumption that pain improvement between the Acupuncture therapy and Usual Care groups is equivalent and that the actual score distributions are normal. We assumed a standard deviation of 2.52 for the Acupuncture group based on our previous collection of pain scores related to acupuncture in the ED (see Preliminary Data: ANW Pilot RCT), and 3.2 for the Usual Care group, an estimate drawn from a study measuring effects of IV morphine at 60 minutes in the ED.<sup>95</sup> Using the same retention rate for the post-treatment PRO data collection of the pilot RCT (~78%), the target sample increases to a total sample size of 654 (327 Acupuncture vs 327 Usual Care) for a future UG3/UH3 efficacy RCT.

Since the goal of the current U01 proposal is to test feasibility of the study procedures used in the single-site pilot RCT, we plan to enroll 150 participants (50 per site). Additionally, a pilot 5 subjects per site will be consented and brought through the study protocol, but will not be counted toward the n=150 enrollment. The 150 enrollment number is both pragmatic for

achieving our goals related to assessing feasibility, acceptability and fidelity and is about 25% of the eventual sample size required for a future definitive non-inferiority study. We contend that our ability to recruit about 25% of the anticipated sample size for a future definitive RCT would demonstrate our collective capabilities.

### **Treatment Assignment Procedures**

Random assignments will be made by the study statistician in permuted blocks of size 2 and 4. The block size will also be randomly generated to minimize correct prediction of assignments and preserve approximate balance between groups, using the rand function in SAS.

Administrative personnel from the BraveNet Coordinating Center will prepare each randomization packet in a sealed envelope and send these to each site in batches. A date/signature label will be placed over the envelope seal. Randomization envelopes will be stored in locked cabinets and opened by study staff (SC or RA) after completion of the informed consent process and baseline data collection.

### **9.3 Definition of Populations**

N/A

### **9.4 Interim Analyses and Stopping Rules**

N/A

### **9.5 Outcomes**

#### Implementation and Treatment Outcomes

All data analyses will be preceded by extensive data checking and verification to identify and resolve the reasons for missing values, inconsistencies, and out-of-range values. Although we anticipate little missing data based on our experience, we will carefully examine whether missingness is completely at random, at random or informative. Models proposed for analysis can handle incomplete data but do require at least that missingness be at random. Descriptive statistics of primary outcomes: pain intensity change scores for Pre-Treatment to Post-Treatment and Pre-treatment to ED Discharge as well as secondary outcomes will be conducted to assess their distribution overall and by sites as well as demographic characteristics (e.g. sex, age group, race, household income, pain location among others). The variables will be summarized using descriptive statistics (sample size, mean, standard deviation, median, minimum, and maximum) for continuous variables and by the number and percentage of patients for categorical variables. We will report 95% exact confidence interval of median<sup>84</sup> for the key continuous variables and 95% exact binomial confidence interval<sup>85</sup> for categorical variables. All assessments will include sex as a biological variable as described below.

#### Feasibility of Recruitment and Retention

We will assess recruitment rates (# enrolled / # eligible), pace of accrual, data completeness, and retention at each data collection point, overall and across sites. We will assess variables across different patient groups (including age, race, sex), and across the study arms. Provider adoption will be assessed by the proportion of their eligible patients that clinicians approve for study participation. We will assess variables across different provider characteristics (including age, race, sex), and across the study sites. Completeness of data collection and retention at each time point: we will also track completeness of data collection, and patterns and proportions of missing data at each time point. We will compare these proportions overall and across sites and by demographics as described above.

#### Acceptability

At ED discharge, 1-week and 4-week follow-up, all participants will be asked to answer; “How satisfied are you with how your pain was managed during your ED visit” on the 5-point Likert scale. A second question is “Overall how satisfied are you with your treatment during your ED visit?” on the same Likert Scale. At the end of enrollment, the SC or RA at each site will contact ED staff to complete a brief survey (via REDCap) to assess their general satisfaction with the acupuncture intervention by answering “How satisfied are you with the way that the acupuncture intervention was implemented in your setting” and “To what degree do you view the acupuncture intervention as effective in managing patient pain?” on 5-point Likert scales. We will compare across sites and across patient groups (e.g. pain location, patient demographics etc). We will calculate the proportion of subjects answering each question and 95% exact CI across sites as well as across patient groups such as different presenting complaints and patient demographics. We will assess variables across different provider characteristics (including age, race, sex), and across the study sites.

#### Fidelity

Assessing fidelity will reveal proportion of patients who are treated in a manner consistent with the manualized intervention and treatment fidelity parameters determined by consensus of acupuncture experts in accord with Aim 1. We expect that the treatment fidelity measures will include: the dose (minimum number of needles, minimum points treated, minimum duration of needle retention time), and the delivery (was the intervention delivered as planned or cut short due to ED flow).<sup>86</sup> Dr. Nielsen will review the documentation of all acupuncture interventions and assess manual fidelity. She will assess the proportion of cases where acupuncturists treated the patient ‘off manual’ (and why), as well as assessing whether minimum standards for number of needles used, points treated and needle retention time were met. Assessment will be across different practitioners, times of day, sites, and by participant demographics (e.g. sex and pain complaints).

#### Qualitative Analysis

Drs. McKee and Karasz have collaborated frequently, using large, mixed methods data sets to bring together implementation data and conduct detailed analyses. To analyze interview and observational data, we will use QSR’s NVivo, a computer program that facilitates 1) the rapid organization and retrieval of thematically linked data; and 2) the use of quantitative grouping variables to classify cases and generate complex comparisons. In a first step of thematic analysis, a preliminary coding scheme will be developed and applied to a subset of the data and then revised as needed. This process will be repeated on subsets of data until it is judged sufficiently accurate and comprehensive. Data will be uploaded into NVivo and coded. Memos will be created for each interview describing the major themes emerging in the transcript. Next, coded data will be retrieved and used to create case summaries of key themes related to implementation processes at each site. Quantitative implementation outcome data collected in Aim 2 will be used where relevant to create groups for the purpose of comparison. Within site analyses will include comparisons of relevant groups (e.g. comparing perceptions of the intervention across different genders and ethnic groups; patients who achieve satisfactory pain relief vs those who do not; providers who are more vs less satisfied with the protocol, among others). In the cross site analyses, we will examine differences in barriers, facilitators and implementation processes across sites with the goal of generating inferences regarding the important factors shaping differences in implementation outcomes (e.g. presuming that sites differ on rates of recruitment, examining our qualitative data to generate hypotheses regarding the causes of this documented difference).

#### Potential Challenges and Alternate Strategies

As noted above, we expect to recruit 50 subjects (+ 5 pilot subjects) in 9 months of active

enrollment at each site. Results from our pilot RCT indicate a 78% enrollment rate. Using more conservative estimates of eligible patients consenting to participate (e.g. 50%), we would still have ample opportunity to recruit enough patients in 9 months/site. However, if recruitment lags, we can extend the duration of recruitment by 3 months or increase the number of enrollment hours per week at each site.

### **9.5.1 Primary Outcome**

The primary objective is to refine procedures for conducting a future fully powered multi-site RCT in 3 EDs.

1. Successful recruitment of eligible participants into the study. [ Time Frame: At Enrollment ]

The recruitment rate (# enrolled / # eligible) will be assessed for the overall study. Separate recruitment rates will be calculated by site

### **9.5.2 Secondary Outcomes**

The secondary objectives of this study are to: examine the feasibility of data collection in the RCT, develop a responsive acupuncture intervention and assess implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. This study will include qualitative interviews and structured observation to assess feasibility of implementation.

1. Number of participants retained in the study [ Time Frame: Immediately after the acupuncture intervention or usual care (an average of 60 minutes), at the end of individual patient's discharge from the ED (expected average of 2 hours), 1-week and 4-week follow-up assessments ]

Retained patients will be defined as those providing patient reported outcomes scores (e.g., pain, anxiety) at ED discharge, 1 week and 4-week follow-up assessments. Separate retention rates (# retained / # enrolled) will be assessed overall and by site. Separate retention rates will also be calculated for each of the three timeframes.

2. Proportion of Emergency Department clinical provider's eligible participants that are clinically approved for study participation. [ Time Frame: At Enrollment ]

Patient adoption rates will be defined as the number of approved individuals for inclusion in the study by ED clinical providers (MD, DO, NP, PA) divided by number of individuals who were prescreened for study participation by the research team for enrollment. Rates will be calculated the overall study and by site.

3. Patient acceptability of pain management and treatment within the Emergency Department [ Time Frame: Immediately after the acupuncture intervention or usual care (an average of 60 minutes), at the end of individual patient's discharge from the ED (expected average of 2 hours), 1-week and 4-week follow-up assessments ]

Participants will be asked to rate their satisfaction with how their pain was managed and their satisfaction with assigned treatment at ED discharge. Separate scores will be

calculated for the 1 and 4-week follow-up assessments. All enrolled participants will be asked to answer one question: "How satisfied are you with how your pain was managed during your ED visit" on the 5-point Likert scale (1-Very Satisfied--5-Strongly Dissatisfied). A second question will be asked only of acupuncture-assigned patients: "Overall how satisfied are you with the acupuncture treatment you received your ED visit?" on the same 5-point Likert Scale.

4. Provider satisfaction with acupuncture treatment within the Emergency Department  
[ Time Frame: At end of enrollment period for ED provider's site ]

ED clinical providers (MD, DO, NP, PA) who had patients enrolled in the study will be asked to rate their general satisfaction with how their patients' pain was managed by acupuncture as part of the study. Providers will answer two questions: "How satisfied were you with the acupuncture intervention as delivered in your setting?" and "To what degree was the acupuncture satisfied/helpful-5-Very dissatisfied/Not at all helpful).

## 9.6 Data Analyses

**Aim 2: Conduct a feasibility RCT to examine the feasibility of data collection, intervention implementation and treatment outcomes overall and across sites.**

**Aim 2a. Evaluate the feasibility of research procedures, including data quality completeness, and participant recruitment and retention, using study records**

**Overall Approach.** Using study records and administrative data we will track recruitment (proportion of eligible patients recruited), document recruitment rates (time to recruit intended sample), and rates of loss to follow up. Data collection forms collected at each time point will be evaluated for quality and completeness. In addition, all quantitative data analyses will be preceded by extensive data checking and verification to identify and resolve the reasons for missing values, inconsistencies, and out-of-range values. Although we anticipate some missing data based on our experience, we will carefully examine whether missingness is completely at random (MCAR), at random (MAR) or informative (MNAR). Models proposed for analysis can handle incomplete data but do require at least that missingness be at random. Modelling will consider using multiple imputation techniques of covariates to reduce potential biases. To assess recruitment, we will track the number of eligible patients presenting to the ED and the proportion who agree to participate. Basic demographics and presenting complaint will be collected for all eligible patients, allowing us to identify subgroups who are more or less likely to participate. Similarly approaches will be used to assess rates of loss to follow up at all data collection points. We will assess variables across different patient groups (including age, race, sex), and across the study arms as well as overall and by sites.

**Aim 2b. Evaluate the implementation of the acupuncture intervention, using both quantitative data (study records, stakeholder surveys) and qualitative data (interviews and observations).**

**Overall approach.** We base our selection of implementation outcomes on the synthesis and recommendations outlined by Proctor et al in their authoritative 2011 paper<sup>99</sup>. We include all of

the early phase outcomes, excluding cost, proposed in this widely cited framework, including: Feasibility (“practicability”), provider adoption, perceptions of appropriateness, acceptability, and treatment fidelity. These will be assessed both quantitatively and qualitatively. In addition to implementation outcomes, we will also examine implementation processes, strategies, stakeholder experiences, and barriers and facilitators to implementation using both qualitative interviews and real-time observations. For a list of implementation constructs, variables, and data sources, see Table 1.

**Table 1: Implementation Variables and Sources**

Construct	Variable	Data Collection/Source
<i>Outcomes</i>		
<b>Feasibility</b>	# recruited patients / # eligible # completed sessions /# recruited	Study records Provider assessment, real-time observations, qualitative interviews
<b>Adoption</b>	# approved / # recruited	Study records
<b>Appropriateness</b>	Suitability for ED setting	1 item survey, qualitative interviews
<b>Acceptability</b>	Satisfaction/helpfulness	1 item survey, qualitative interviews
<b>Fidelity</b>	Adherence to Responsive Manualization	Dr. Nielson reviews study records and discusses with study acupuncturists
<b>Stakeholder strategies</b>	<i>Processes and steps taken</i>	Qualitative Interviews
<b>Barriers and facilitators</b>	<i>Strengths/weaknesses of the program</i> <i>Contextual influences at patient, provider, local, and institutional level</i>	Qualitative interviews/structured observation

*Aim 2b1. Assess Implementation outcomes: feasibility, adoption, appropriateness, and acceptability.*

Feasibility is defined as the degree to which AC can be successfully implemented in the ED setting. This is operationalized as **recruitment** (see Aim 2a); and **uptake** (the proportion of recruited patients who receive a complete AC session, measured by a single question assessment: “*Did patient xx receive a completed treatment session at this visit?*”). Feasibility of the study will also be assessed qualitatively, through stakeholder interviews focusing on barriers and facilitators to implementation, and real-time observations of the uptake of the intervention in the ED setting. For a description of qualitative data collection and analysis, see section 2b2 below.

Provider adoption is defined as the intention to engage with the innovation/intervention. This is operationalized as the proportion of an ED physician’s recruited patients who are approved for study participation. As elsewhere, we will assess variables across different provider characteristics (including age, race, sex), overall and across the study sites to assess group differences in this outcome and those below.

Perception of appropriateness is defined as the perceived **suitability** of the intervention to the ED setting. ED providers will be asked: “*To what degree do you view the acupuncture*

*intervention as useful or suitable for this ED setting?” (1-very appropriate—5-Very inappropriate); Perceptions of appropriateness will also be explored through qualitative interviews.*

**‘Acceptability’** is defined as perceptions of the palatability of an innovation, or satisfaction by stakeholders with aspects of an innovation. It is more specific than overall satisfaction with a service.<sup>99</sup> For this study, acceptability among ED staff is operationalized in our quantitative assessment as satisfaction with the acupuncture intervention as delivered in the ED setting. **Providers** will answer two questions: “How satisfied were you with the acupuncture intervention as delivered in your setting?” and “*To what degree was the acupuncture intervention helpful in managing patient pain in your ED setting?*” (1-Very satisfied/helpful—5-Very dissatisfied/Not at all helpful). Enrolled **participants** will be asked to answer two questions at treatment completion and at 1 week follow up: “*How satisfied are you with how your pain was managed during your ED visit?*” on the 5-point Likert scale (1-Very Satisfied--5-Strongly Dissatisfied). A second question is “*Overall how satisfied are you with the acupuncture treatment you received your ED visit?*” on the same 5-point Likert Scale. Acceptability of the intervention will also be explored in depth in semi structured stakeholder interviews.

**‘Fidelity’** in this study is defined as the proportion of patients who are treated in a manner consistent with the manualized intervention. The exact treatment fidelity parameters will be determined by consensus of acupuncture experts in accord with Aim 1. We expect that the treatment fidelity measures will include: the dose (minimum number of needles, minimum number of points treated, minimum duration of needle retention time), and the session delivery (was the intervention delivered as planned or cut short due to ED flow). Dr. Nielsen will review the chart documentation of all acupuncture interventions and assess manual fidelity. She will assess the proportion of cases where acupuncturists treated the patient ‘off manual’ (and why), as well as assessing whether minimum standards for number of needles used, points treated and needle retention time were met. Assessment will be across different practitioners, times of day, sites, and by participant demographics (e.g. sex) and presenting complaints.

*Aim 2b2. Assess implementation processes, strategies, and barriers/facilitators to implementation using semi structured stakeholder interviews and structured observations*

*Overall approach for qualitative data collection in Aim 2b1 and 2b2.*

We will conduct **qualitative interviews** with a broad range of relevant staff stakeholders (n~10/site), including ED providers, ED staff, and acupuncturists. A second component is **field observation** in participating EDs.

Dr. Karasz will conduct structured observations at each of the three sites during one 2-day field visit to each site, observing the implementation of acupuncture in the ED in real time. The observations will be recorded in detailed field notes and transcribed into a full description when the observation is complete.

Lessons learned from field observation and preliminary analysis of process implementation at each site may inform implementation at subsequent sites.

The success of program implementation depends on many factors, as described in Damschroder, et al’s influential CFIR framework.<sup>100</sup> The CFIR includes 5 ‘domains’ influencing implementation: the intervention, inner and outer setting, individuals, and processes. We will use the CFIR domains to structure our inquiry and to make sure that our qualitative data collection instruments, coding system, and interim reports reflect the complex multiple levels of influence

that will shape the conduct and outcomes of the acupuncture intervention. We provide some examples of how CFIR domains will be operationalized as interview topics in the Table 2.

Table 2: CFIR Domains of Influence/Topics/Sample Questions

CFIR Domain Guide Topics	Sample Interview	Sample question
<b>Intervention</b>	Complexity Burden Need/utility	How useful was this intervention? How difficult was it to get it going in the ED? What was the burden and who bore the burden?
<b>Individuals</b>	Stakeholder Characteristics, attitudes, perceptions/The Pain Episode	How receptive were patients/nurses/front desk staff, etc. to the intervention?
<b>Outer Setting</b>	The larger political/historical context Socio-economic factors	How has the opioid epidemic influenced your views of the Acupuncture intervention? How do socioeconomic factors influence your patients' pain and other treatment needs?
<b>Inner Setting</b>	Characteristics of the ER such as norms, values, readiness for change Crowding/staffing/s pace/other resources	How receptive were ED staff to this intervention? Why? What time of day/day of week was it easiest to implement the Acupuncture intervention? Most difficult? How did communication among staff influence the implementation
<b>Processes</b>	<i>Stakeholder strategies and processes</i>	What was your process in planning for this intervention? Whose help was needed in moving this intervention forward and how did you engage them?--What efforts did the Champion make to move this forward?

#### *Qualitative Interview Methods.*

**Stakeholder sample.** We will recruit a sample at each site that reflects key stakeholders, including both staff and patients, at that site. The **staff stakeholder** list will be prepared in consultation between project leadership and local collaborators. It will include the physician/providers whose patients were included in the trial, nurses and other medical providers, and the acupuncturist. A purposive sample of patient stakeholders will be recruited to reflect the diversity of patients assigned to the intervention. Patients who received acupuncture (n~15 per site) will be purposefully sampled to include multiple presenting complaints and both sexes, as well as older and younger patients. In keeping with good practices in qualitative research, sample sizes are not determined in advance. Sample sizes are determined by the emergence of data saturation, when no new themes arise in the analysis.

**Interview guide.** We will develop a semi-structured interview guide that focuses on likely implementation barriers and facilitators, including: interactions and communications with the research team, patient flow, burden of the intervention, perceived need and benefits of the intervention, etc. As described above, we will use the domains of the CFIR to organize the topic guides that will be developed for the qualitative interviews. Interview recordings will be moved

from the handheld digital recording device to a secure server immediately after each interview. Interviews will be professionally transcribed.

#### *Structured Observation Methods.*

Observational data provides an important perspective that differs from that of individual interviews. While interviews permit an in-depth exploration of reasoning, motives, and perspectives, they are also highly vulnerable to various types of bias. Observational data, by contrast, provides powerful, real time evidence regarding stakeholder behaviors and interactions within the local environment. During a 2-3-day site visit to each site, the Implementation Team leader, Dr. Karasz, will conduct structured observations of protocol implementation. The length and timing of each observation will be determined through consultation with project leadership and local staff. If possible, observations will be conducted at different times reflecting the normal ebb and flow of patient care at the local site. Daytime, night, weekend, and week day observational periods will be included as feasible in the sample. Observations will be focused largely on the influences of actors and contextual factors on implementation uptake/feasibility. Examples could include: **disruptive behavior** or manifestations of severe illness/pain; **staff strategies** to mitigate or address these in order to facilitate treatment uptake; provider statements or **interactions** that interfere with uptake; **environmental variables** (a 'slow night' in the ED that results in extra rooms to be used for the intervention, or the difference between a weekend and weekday night); etc. Following the observation, the report form will form the basis of a complete detailed field observation will be analyzed along with interview data using the strategies described below.

**Analysis of Aim 2b.** To analyze qualitative interview and observational data, we will use QSR's NVivo, a computer program that facilitates 1) the rapid organization and retrieval of thematically linked data; and 2) the use of quantitative grouping variables to classify cases and generate complex comparisons. Interview and observational data will be transcribed and uploaded into a case library organized by site. In a first step, we will conduct a thematic qualitative analysis. First, a preliminary coding scheme will be developed, based on the framework. The scheme will then be applied to a subset of the data by members of the Implementation Team. Any differences in coding decisions will be discussed, and the coding scheme will be revised as needed. This process will be repeated on a second subset of the data, and the coding scheme subsequently revised in an iterative process until it is judged sufficiently accurate and comprehensive. At this point, the data will be uploaded into NVivo and coded by members of the team. Memos will be created for each interview describing the major themes emerging in the transcript. Memos will be used to determine the emergence of data saturation, described above.

Next, the coded data will be retrieved and used to create case summaries of key themes related to implementation processes at each site. The matrix functionality in NVivo will be used to conduct comparative analyses both within and across sites. *Within site analyses* will include comparisons of relevant groups. For example, we will compare different sexes and ethnic groups of patients in terms of their perceptions of the intervention. Examples of comparisons include: younger vs. elderly patients; night observations compared to day observations; weekday observations vs weekend observations. In the *cross site analyses*, we will examine differences in barriers, facilitators and implementation processes across the three sites with the goal of generating inferences regarding the important factors shaping differences in implementation outcomes. For example, presuming that the sites differ on rates of recruitment, we will examine our qualitative data to generate hypotheses regarding the causes of this documented difference. Similarly, sites that succeed better with recruitment, retention, or fidelity to the intervention will be compared to sites that are less successful.

**Mixed methods analysis.** Quantitative and qualitative data collected in Aim 2 will be integrated in a mixed methods analysis. We will use findings from the quantitative survey questions to create comparison groups for qualitative analysis. For example, providers who judge the protocol as 'acceptable' will be compared to those who do not. We will conduct comparative analyses to understand how qualitative themes are associated with these implementation outcomes.

## 10. DATA COLLECTION AND QUALITY ASSURANCE

### 10.1 Data Collection Forms

See attached draft of data collection form, which will be developed in REDCap.

### 10.2 Data Management

In our pilot RCT, we developed and successfully used a basic electronic data collection tool (StudyTRAX). In Year 1, we will build a comprehensive study management database and data collection platform using REDCap and confirm the ability to blind assessors to patient scores and text message subjects for the 1-week follow-up assessment. Our team has successfully used REDCap for multisite data collection in the BraveNet PBRN as well as across Dr. McKee's multi-clinic studies.

Informed consents and HIPAA authorizations will be collected as hard copy paper documents; these will be kept by the study team in individual patient binders in locked filing cabinets of a secure, badge-access location at each site.

Demographic and baseline data will be collected both by the SC and through EHR data extraction at baseline. The data collected by research staff will be entered directly into an electronic data collection tool. There will be no hard copies of this data.

Patient Reported Outcomes (PROs) (pain intensity and anxiety) will be collected by study staff (SC or RA), rather than by the acupuncturists delivering treatments. All PROs will be entered directly by the study participant on a tablet via REDCap and will disappear from view once entered so neither the participant nor research staff will have access to the scores. The scores will then be exported to a password protected database. There will be no hard copies of this data.

Satisfaction data will be collected as part of ED-discharge and at 1-week and 4-week follow up for patients. ED staff will complete a one-time brief survey at the end of the enrollment period.

EHR data will be electronically extracted by each site with HIPAA protected identifiers as limited datasets. The data extracted from EHR will be verified by MRN and date with our electronic platforms. EHR extracted data will include demographic data, pain medication use in the ED, and opioid prescriptions at discharge. Both Dusek and McKee have extensive experience in use of EHR data. There will be no hard copies of this data.

1-week and 4-week follow-up data (PROs, pain medication/opioid use) will be collected either directly from the participant through the electronic data collection tool (via text message prompt) or collected on paper survey and entered by a member of the research team if the follow-up is completed over the phone. As above, all 1-week and 4-week contacts will be conducted by a research staff (SC or RA) who did not interact with the patient during their study participation in the ED.

All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password

protected PCs by a designated data manager. Data in hard copy form will be stored in locked file cabinets within a secure, badge-access location at each site. Upon completion of study enrollment, members of the study team will verify the information contained within the database. After answering all queries in the database, the information contained will be locked and exported for analysis. Both the source (electronic data collection) data and exported databases will be stored as required by the respective rules and regulations (e.g., HIPAA authorizations will be maintained for at least six years).

## **10.3 Quality Assurance**

### **10.3.1 Training**

The site Study Coordinator (SC) will ensure that all study personnel have completed all required institution-specific and protocol-specific trainings and that these trainings are documented appropriately on the Training Log. The SC will also ensure that new personnel are appropriately documented on the Delegation of Responsibilities Log (DOR). While training should be completed and documented in real time, the Multi-Site Study Coordinator (MSC) will verify that all training is current and appropriately documented on a quarterly basis, as noted in section 10.3.2 below.

#### Institution-specific Training

All study staff will complete CITI or NIH Human Subjects training prior to commencement of study activities. The site staff is also required to receive Good Clinical Practice (GCP) training through CITI or the Society for Behavioral Health. Staff training certificates will be stored in the Regulatory Binder and documented on the Training Log.

#### Protocol-specific Training

Below is a summary of required initial training by role for new study personnel.

#### ***PI, Study Coordinators, Research Assistants and anyone recruiting patients:***

- ✓ Review and express understanding of the Site Initiation Visit (SIV) training slides
- ✓ Review and express understanding of the IRB protocol
- ✓ Review and express understanding of the NCCIH protocol
- ✓ Review and express understanding of the Informed Consents and Study Information Sheets
- ✓ Review and express understanding of the MOP

#### ***ED Physician and Students who are not recruiting patients:***

- ✓ Review and express understanding of the IRB protocol
- ✓ Review and express understanding of the Informed Consents and Study Information Sheets

#### **Statistician**

- ✓ Review and express understanding of the IRB protocol

### **10.3.2 Metrics**

Quality Assurance (QA) activities will be conducted at each subject study visit, as well as on a monthly, quarterly and annual schedule. Additional QA activities and reviews will be conducted on an as-needed basis in response to staff or process changes.

The following tools will be used to document QA activities for this study:

- ACUITY QA Essential Documents Review Tool
- ACUITY QA Monthly Consent and Eligibility Data Review Tool
- ACUITY QA Participant Data Review Tool
- ACUITY QA Quarterly Review Tool
- ACUITY QA Annual Review Tool

In addition the following checklists and reminders have been developed for this study's QA process:

- ACUITY Eligibility Checklist
- ACUITY Informed Consent Documentation
- ACUITY ED Visit checklist
- ACUITY Interview Visit Checklist
- ACUITY Protocol Deviation Log

#### ED Visit QA Activities:

The following is a detailed description of ED Visit QA activities

##### ED Visit:

- Prior to the ED shifts, the SC or Research Assistant (RA) will verify that the most current IRB-approved study consent documents are available for use. If re-consenting is required throughout the subject's participation in the study, the SC/RA will verify that the most current IRB approved consent is available prior to the study visit.
- The SC/RA will review and complete the REDCap **Eligibility Criteria form** before study activities begin.
- The SC/RA will review and complete the Eligibility Checklist.
- The SC/RA will document the consent process using the **ACUITY Research IC Documentation Form**. Before the subject leaves the clinic, the SC/RA will review the consent documentation and confirm adherence to the consent processes described in the MOP.
- At visit completion, the SC/RA will complete the **ED Visit Checklist** that captures the required elements of the visit.
- Queries and alerts, generated by the electronic data capture (EDC) system, occurring during the clinical visit will be corrected as soon as notified during data entry or as soon as time allows following the visit.

#### Qualitative Interviews Visit QA Activities:

- Prior to confirming subject study visits, the site interviewer will verify that the subject is scheduled for the appropriate appointment.
- During the visit, the interviewer will ensure that the subject still meets the eligibility requirements.
- At visit completion, the interviewer will complete the **Interview Visit Checklist** that captures the required elements of the visit.

#### Monthly QA Activities

The following is a detailed description of the Monthly QA review activities, which will be documented on the QA Monthly Consent and Eligibility Data Review Tool

- Consent Process Completion and Documentation: The site PI will review 100% of the site's executed consents using the QA Participant Data Review Tool.
- Eligibility Criteria and Documentation: the site PI will review 100% of the Eligibility checklists and source documentation.

### Quarterly QA Activities

The following is a detailed description of the Quarterly QA review activities, which will be documented on the **QA Quarterly Review Tool**.

- Consent Process Completion and Documentation: The SC or designee will review 100% of the site's executed consents using the **QA Participant Data Review Tool**.
- The SC will use the **QA Participant Data Review Tool** to review completion and accuracy of the source documents and the eCRFs for 100% of subjects at the site every 3 months.
- The SC will cross-check eCRF data for accuracy and completeness every 3 months. The SC will also review query reports to confirm that all manual and automatic queries have been resolved.
- Training Logs will be reviewed by the SC every 3 months to verify training is current and properly documented. This will include a review for institution-specific and protocol-specific trainings.
- The Site Regulatory Binders are updated by the SC when changes to licenses, certifications, credentials, IRB documents or CVs are made during the study. The SC will review the Site Regulatory Binder every 3 months to verify that all documents (paper and electronic) are maintained. This review will be documented and summarized in the **ACUITY Essential Documents Review Tool**. At least annually, the MSC will conduct a complete review of the each Site Regulatory Binder.

### Annual QA Activities

The following is a detailed description of the Annual QA review activities, which will be documented on the **ACUITY QA Annual Review Tool**.

The procedures and processes to ensure protocol adherence among the study personnel are set forth in the Manual of Procedures (MOP). The MOP is reviewed by the MSC every 12 months for applicability and accuracy.

This QA Plan will be reviewed for applicability and accuracy and updated as necessary every 12 months by the MSC. Additional QA needs identified at a study site will be communicated to the MSC. The MSC and MPI's will evaluate the need to update the QA plan, tools, and logs.

#### **10.3.3 Protocol Deviations**

A protocol deviation is any alteration/modification to the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation. Protocol deviations may result in

determinations of non-compliance, serious or continuing.

1. Minor Protocol Deviation: An incident involving noncompliance with the protocol but one that typically does not have a significant effect on the subject's rights, safety, welfare, or on the integrity of the resultant data
2. Major Protocol Deviation: A more serious incident involving noncompliance with the protocol usually involving critical study parameters. Major protocol deviations generally affect the subject's rights, safety, or welfare, or the integrity of the study data. A major protocol deviation can also be called a protocol violation.

Per UH IRB, protocol deviations must be reported by the PI or their designated research staff to the IRB within 5 days for major deviations, and at continuing review for minor deviations.

Deviations are reported electronically by the MSC or designee using the appropriate category on the UHCMC IRB's RNI form.

Research staff will document the protocol deviation on the **ACUITY Protocol Deviation Log** after becoming aware of the event. The site PI or their delegated research staff will review and sign off on the deviation and designate it as major or minor. The site PI or delegated staff is responsible for reporting the deviation to the MSC within 3 days for major deviations and quarterly for minor deviations. The MSC is responsible for all follow-up associated with protocol deviations and reporting this information to the UH IRB.

#### **10.3.4 Monitoring**

Each site will maintain the QA tools/logs either in a QA binder (for paper documents) or electronic folder. SCs will be responsible for site-specific QA activities. The MSC will be responsible for QA activities at the lead study site and will provide oversight for QA activities for the entire study.

Each SC will provide a **Quality Assurance Summary Report** to the MSC one month before the Data Safety and Monitoring Committee (DSMC) Report is due. The MSC will compile the site reports into a comprehensive, study-wide report that will be provided to NCCIH. The MSC will also summarize the information for inclusion in the DSMC Report. This summary will document the following:

- QA activities completed since the prior report submittal, including:
  - Frequency of reviews
  - Number of charts reviewed
  - Items covered by the review
- Identification of problem areas
- Corrective Action Plan(s)

In addition, the PI will propose an independent monitoring committee (requires NCCIH approval) to overview the study from a data and safety perspective.

## **11. PARTICIPANT RIGHTS AND CONFIDENTIALITY**

### **11.1 Institutional Review Board (IRB) Review**

This protocol and the informed consent document (Appendix A) and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for oversight of the study.

### **11.2 Informed Consent Forms**

A signed consent form will be obtained from each participant. Only the participating patients themselves will be allowed to provide consent for inclusion into the study. No legally authorized representative (LAR) may enroll a patient into the study. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be given to each participant or legal guardian and this fact will be documented in the participant's record.

### **11.3 Participant Confidentiality**

Any data, specimens, forms, reports, video recordings, and other records that leave the site will be identified only by a participant identification number (Participant ID, PID) to maintain confidentiality.

All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. The Einstein Coordinating Center will securely share data collected at their site and those received from the other two sites with Case Western Reserve University (CWRU)/University Hospitals (UH), the lead site and IRB of record. Data shared with CWRU/UH will be stored in a password protected database behind an electronic firewall on a secure UH server. Data in hard copy form will be stored in locked file cabinets within a secure, badge-access location at each site. Upon completion of study enrollment, members of the study team will verify the information contained within the database. After answering all queries in the database, the information contained will be locked and exported for analysis. Both the source (electronic data collection) data and exported databases will be stored as required by the respective rules and regulations (e.g., HIPAA authorizations will be maintained for at least six years).

Information will not be released without written permission of the participant, except as necessary for monitoring by IRB, the FDA, the NCCIH, and the OHRP.

### **11.4 Study Discontinuation**

The study may be discontinued at any time by the IRB, the NCCIH, the OHRP, the FDA, or other government agencies as part of their duties to ensure that research participants are protected.

## **12. COMMITTEES**

The 3-year project is designed to conduct and evaluate a feasibility study in 3 clinical sites, in preparation for a definitive, pragmatic, non-inferiority study of acupuncture vs usual care for pain in the emergency department (ED) setting.

To pursue these aims, we have assembled an experienced multidisciplinary team. In order to effectively manage these activities, we will organize the following groups. As this

is a U01 Cooperative Agreement, the NCCIH Representative would sit on the Steering Committee as available.

**The Executive Committee** will include Drs. Dusek and McKee as multi-PIs. They will meet weekly to ensure that the overall aims of the project are met in accordance with the projected timeline.

**The Steering Committee** will consist of Drs. McKee and Dusek as multi-PIs, Dr. Nielsen, Jessica Surdam (Overall Study Coordinator) and the site PIs (Dr. Vago [Vanderbilt University Medical Center], Dr. Kallenberg [University of California- San Diego], Dr. Dave Clark [NCCIH] and Drs. Kim and Karasz [Einstein Data Coordinating Center]. This team will meet monthly to oversee implementation of the study.

**The ED Physician and Site PI Committee** will consist of Drs. McKee and Dusek as multi-PIs, Dr. Hughes (UH/CWRU), Drs. Vago and Storrow (VUMC), Drs. Kallenberg and Coyne (UCSD) and Jessica Surdam (Overall Study Coordinator). This team will meet monthly to oversee the clinical implementation of the study protocol in preparation for the UG3/UH3 proposal.

**The Independent Monitoring Committee** will consist of several experts in the field of Complementary and Integrative Health. These include Dr. Natalia Morone MD, Dr. Scott Mist PhD, LAc, PhD, Dr. Maria Chao PhD and Dr. Roger Davis ScD. The IMC will meet quarterly with responsibility to oversee study accrual, as well as data and safety. The UH IRB is serving as the sIRB.

**The Data Coordinating Center** includes Drs. McKee, Karasz, Kim, Qi and Ms. Lechuga will meet monthly and as needed to ensure development of the REDCap data collection system and data analytics. The UH/Case Site will function as a **Clinical Coordinating Center** with Dr. Dusek MPI and Jessica Surdam MPH (Overall Study Coordinator) serving in that capacity. Dr. McKee MPI will periodically attend meetings (as needed).

**The Qualitative Interview team** includes Dr. Karasz, and Ms. Khurshid will be responsible conducting the structured qualitative interviews and structured observations.

**Site Research Teams** will consist of the site PI, ED physician champion, Study Coordinator, Research Assistant, and study acupuncturists. Dr. Nielsen (the study acupuncture expert will attend as needed. These teams will meet regularly leading up to and during the implementation of the feasibility study at their site, under the direction of the site PI.

**Acupuncture Protocol team** will be led by Drs. Nielsen and Dusek. Together they will convene a modified Delphi process with 5-8 experienced acupuncture experts. The results of the Delphi process will be a responsive acupuncture protocol for use in the U01. This team will also convene the study acupuncturists during the course of the active recruitment phase of the trial to ensure collaborative communication.

## 13. PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by the policies and procedures developed by the ACUITY Executive and Steering Committees. Any presentation, abstract, or manuscript will be made available for review by the sponsor and the NCCIH prior to submission.

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## 15. SUPPLEMENTS/APPENDICES

### Appendix A: Informed Consent Documents

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## A.1 Patient Written Informed Consent

### A.1.1 UH Patient Written Informed Consent

**Key Information:** The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

#### Why am I being invited to take part in a research study?

You are being asked to take part in this study because you came to the emergency room ER and are experiencing pain.

#### Things I should know about a research study

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

#### Introduction/Purpose

The purpose of this research is to determine if we are able to deliver acupuncture for pain relief in the ER, and to study see if acupuncture for pain relief in the ER is effective. This research will be carried out at three sites: UH Cleveland Medical Center and Ahuja Medical Ceneter ERs, the Vanderbilt University Medical Center ER and the Hillcrest University of California San Diego (UCSD) ER.

There will be a total of 165 patient participants across three research sites, with 55 enrolling from each site. Additionally, around 30 ER providers and staff will be interviewed to gain their perspective and experience related to how the study was carried out

#### Key Study Procedures

If you agree to participate, you will be randomly assigned to one of two groups. The treatment group will receive acupuncture and usual care during this ER visit, and the control group will receive usual care. Whichever group you are assigned to, we will also ask you a series of short questions about your symptoms before treatment, immediately after treatment, again before you are discharged from the ER, and then twice more via email, text or over the phone one week and one month after discharge. For the one week and one month follow up questionnaires, we'll also ask about your pain medication usage during the time since you were discharged.

If you are assigned to the acupuncture group, we may contact you to participate in an additional interview about your perspectives and experiences as a participant in the study who received acupuncture. The interview will be conducted via telephone or an approved telehealth application, and will be recorded and transcribed. Participation in the interview is completely voluntary and refusing to participate will not affect your participation in the rest of the study. If you agree to the interview, a study information sheet about the interview will be shared and reviewed with you before the interview begins and you will have an opportunity to ask questions or to refuse to participate.

There is a chance that additional study staff may also observe study procedures during your visit to the ER. Researchers will seek to observe the actions and interactions of relevant persons, including ER providers, other ER staff, patients, and the Site Study Coordinator or Site Research Assistant over the course of the your entire ER visit.

More detailed information about the study procedures can be found under “Detailed Study Procedures”.

### **Key Risks**

There are few potential risks of taking part in this study. Acupuncture carries very slight risks for bleeding, bruising, fainting, and needling pain. If you experience any of these, you will be treated by providers here in the ER.

Some of the questions that we will ask you might make you feel uncomfortable. You can skip any question you do not wish to answer.

As with any research study, there is a slight risk of losing privacy and confidentiality. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

More detailed information about the risks of this study can be found under “Detailed Risks”

### **Benefits**

You may not benefit from participation. Those randomized to acupuncture may have improved pain control but this cannot be guaranteed. You may experience better pain management, and reduced usage of opioid analgesics through the use of acupuncture if you are in the acupuncture group. This research may benefit future patients by improving the use of acupuncture along with usual care for pain management in the ER.

### **Alternatives to Study Participation**

The only alternative to participating in this study is to not participate.

### **Detailed Information: The following is more detailed information about this study in addition to the information listed above.**

#### **Detailed Study Procedures**

**If you are assigned to the treatment group**, after answering a few questions about your symptoms on a tablet you will receive acupuncture from a nationally board certified acupuncturist. The acupuncturist will describe details of the treatment, risks, cost and benefits in your private room. After that, you will receive the acupuncture treatment in your private room. Treatment will last between 30-45 minutes. Please note that if assigned to the acupuncture group, any pain medications that your provider may prescribe will be delayed while you receive treatment with acupuncture. Your individual acupuncture treatment will be based on your particular situation and will be determined by the treating acupuncturist. Sterile, single-use non-coated acupuncture needles will be used for this study. After the treatment, and again within 15 minutes of discharge, you will be asked the same series of questions on the tablet. One week and again one month after discharge you will be asked the same series of questions, and a few more about your pain relief medication usage since discharge, and your satisfaction with your treatment.

You may choose to receive a link to the questionnaires via text message or email, or you can choose to have a study team member call you to complete the questionnaire. The study team will also view your medical record to collect information about any pain medications used during your ER visit, and your demographics.

**Qualitative Interviews:** Additionally, 15 participants assigned to the treatment group from each research site will participate in an interview with study staff. Study staff will contact some participants who received acupuncture as part of the study by phone or by email to invite them to participate in the interview. The purpose of the interview is to describe perspectives and experiences related to the how the study of acupuncture in emergency room (ER) was carried out. We may or may not contact you to participate in the interview portion of the research. If we contact you, you may refuse to participate. Before the start of the interview, a study information sheet will be shared and reviewed with you and you will be given an opportunity to ask questions and/or to refuse participation in the interview. Refusing to participate in the interview will not affect your care or your participation in the rest of the study.

The interview will last approximately 45 minutes and will be conducted via telephone or an approved telehealth application. The interview will take place between 2-4 weeks after your visit to the ER. The interview will be securely recorded and transcribed. Both the transcription and the recording will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information.

If you are assigned to the acupuncture group, do you consent to being contacted for the interview portion of this research?

Yes

- I prefer an audio-only interview (by telephone)
- I prefer an audio and video interview (by telehealth)

No

**If you are assigned to the control group,** after answering a few questions about your symptoms on a tablet, you will receive usual ER care. Within 60 minutes, and again within 15 minutes before you are discharged, you will be asked the same series of questions on the tablet. One week and again one month after discharge you will be asked the same series of questions, and a few more about your pain relief medication usage since discharge, and your satisfaction with your treatment. You may choose to receive a link to the questionnaires via text message or email, or you can choose to have a study team member call you to complete the questionnaire. If you choose to receive a link to the questionnaire, a member of the study team may call you for follow up if we notice that the questionnaires have not been completed. The study team will also view your medical record to collect information about any pain medications used during your ER visit, and your demographics.

**Structured observation:** For those assigned to either the treatment or control groups, there is a chance that additional research study staff may also observe study procedures during your visit to the ER. These researchers will seek to observe the actions and interactions of relevant persons, including ER providers, other ER staff, patients, and the research study staff over the course of the your entire ER visit. You may

refuse to be observed by study staff and still participate in the research study. If applicable, do you consent to have your participation in this research study while in the ER observed by study staff today?

- Yes
- No
- NA

**Courtesy calls:** A member of the research study staff will call you 2-3 days after your ER visit to ensure that you have received the e-gift card for your time and to remind you that we will be sending a link or calling you in a few days to complete the one week follow up survey. Study staff will also call to remind you a few days before the four week follow up survey.

### **Detailed Risks**

The potential risks associated with participation in this study are minimal. Acupuncture carries very slight risks for bleeding, bruising, fainting (acushock), and needling pain. In the event you experience an adverse event (AE), you will be treated by providers in the site ER and will have access to emergency response equipment as necessary.

Acupuncture involves inserting thin, sterile needles in the skin. The needles are not inserted into the skin very far. Sometimes the needles cause slight discomfort or minor bleeding. The acupuncturist will explain the risks of acupuncture in detail and ask you to sign a separate acupuncture consent form. The acupuncturist will review this consent form with you. Any acupuncturist who provides treatments in this study will be licensed by the state in which they practice.

Some of the questions in the questionnaire might make you feel uncomfortable. You can skip any question they do not wish to answer.

As with any research study, there is a slight risk of losing privacy and confidentiality. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

### **Financial Information**

There will be no cost to you and your insurance will not be billed to take part in this study. For your participation during your ER visit, you will receive a \$25 e-gift card which will be emailed to you after your ER visit. For answering the follow up questions on the phone one week after discharge, you will receive an additional \$25 e-gift card, and for answering the follow up questions on the phone 4 weeks after discharge, you will receive a final \$25 e-gift card. If assigned to the acupuncture group and selected to participate in the interview, you will receive an additional \$25 e-gift card within 30 days of the completion of the interview.

### **Research-Related Injury**

In the event you suffer a research related injury as a result of being in this study, University Hospitals is available to provide medical treatment for such injury. Provision of such medical treatment does not imply any negligence or other wrongdoing on the part of University Hospitals, the Sponsor or any of the physicians or other study personnel. If you believe that you have been injured as a result of participating in the study, please immediately contact the Principal Investigator or your study doctor at University Hospitals. If you cannot reach the Principal Investigator or your study doctor, do not delay treatment.

You may seek treatment by another doctor. If you are seen or treated by a doctor other than the Principal Investigator or your study doctor, you should inform such doctor that you are in this study and, if possible, take this document with you to assist with your treatment. Always contact the Principal Investigator or your study doctor to alert them of any treatment you receive for an injury or illness you experience during this Study.

The costs for medical treatment as a result of a research related injury may be billed to you or your medical insurance plan, if applicable. Medical insurance plans may or may not cover costs for medical treatment of research related injuries. If you have insurance, you should check with your medical insurance plan before deciding to participate in this research study. In the event your medical insurance plan covers some or all of the treatment costs, you may still be responsible for co-pays or deductibles as required by your medical insurance plan.

Neither Sponsor nor University Hospitals has set aside any money to pay you or to pay for your treatment if you suffer a research related injury as a result of being in the study. There are no plans for University Hospitals or Sponsor to provide other forms of compensation (such as lost wages or other indirect losses) to you for research related injuries. You are not waiving any legal rights by signing this form, including the right to seek compensation for an injury. To help avoid injury, it is very important to follow all study directions.

### **Clinical Trial Information**

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE: A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

### **Termination of Participation**

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment (e.g. the target number of subjects has entered the study.)

### **Confidentiality**

All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Data in hard copy form will be stored in locked file cabinets within a secure, badge-access location at each site. Recordings of the interview with the acupuncture group participants

will be transcribed, and then the recording will be destroyed. The transcription will contain no identifying information.

#### Future use of De-Identified Data

Identifiers might be removed from your identifiable private information and after such removal the information could be used for future research studies or distributed to another investigator for future research studies without additional informed or consent.

It is possible, that in the future, additional research sites may be added. In this event, de-identified and or aggregate data collected during this research project may be shared with research personnel at these additional sites.

Your identifiable data will not be used for any future projects.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by The National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of your name, address, phone number, email address, medical record number and date of birth

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document (your name, address, phone number, email address, medical record number and date of birth).

#### **Privacy of Protected Health Information (HIPAA)**

The Health Insurance Portability & Accountability Act (HIPAA) is a Federal law that helps to protect the privacy of your health information and to whom this information may be shared within and outside of University Hospitals. This Authorization form is specifically for a research study entitled “Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study” (ACUITY) and will tell you what health information (called Protected Health Information or PHI) will

be collected for this research study, who will see your PHI and in what ways they can use the information. In order for the Principal Investigator, Jeffery Dusek, and the research study staff to collect and use your PHI, you must sign this authorization form. You will receive a copy of this signed Authorization for your records. If you do not sign this form, you may not join this study. Your decision to allow the use and disclosure of your PHI is voluntary and will have no impact on your treatment at University Hospitals. By signing this form, you are allowing the researchers for this study to use and disclose your PHI in the manner described below.

Generally the Principal Investigator and study staff at University Hospitals and Case Western Reserve University who are working on this research project will know that you are in a research study and will see and use your PHI. The researchers working on this study will collect the following PHI about you: your name, address, phone number, email address, medical record number and date of birth. This PHI will be used to contact you later for follow up, to extract information about your emergency department treatment, and for data analysis purposes. Your access to your PHI may be limited during the study to protect the study results.

Your PHI may also be shared with the following groups/persons associated with this research study or involved in the review of research: the study's Clinical Coordinating Center at Albert Einstein College of Medicine, the National Institutes of Health (study sponsor), other staff from the Principal Investigator's medical practice group; University Hospitals, including the Center for Clinical Research and the Law Department; Government representatives or Federal agencies, when required by law.

It is possible, that in the future, additional research sites may be added. In this event, your PHI that was collected during this research project may be shared with research personnel at these additional sites.

Your permission to use and disclose your PHI does not expire. However, you have the right to change your mind at any time and revoke your authorization. If you revoke your authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. Also, if you revoke your authorization you may no longer be able to participate in the research study. To revoke your permission, you must do so in writing by sending a letter to Jeffery Dusek, Director of Research, Connor Integrative Health Network, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Wearn 548, Cleveland, Ohio 44106; If you have a complaint or concerns about the privacy of your health information, you may also write to the UH Privacy Officer, Management Service Center, 3605 Warrensville Center, MSC 9105, Shaker Heights, OH 44122 or to the Federal Department of Health and Human Services (DHHS) at DHHS Regional Manager, Office of Civil Rights, US Department of Health and Human Services Government Center, JF Kennedy Federal Building, Room 1875, Boston, MA 02203. Complaints should be sent within 180 days of finding out about the problem.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and Federal law. University Hospitals is committed to protecting your confidentiality. Please understand that once your PHI has been disclosed to anyone outside of University Hospitals, there is a risk that your PHI may no longer be protected; however other Federal and State laws may provide continued protection of your information.

### **Summary of Your Rights as a Participant in a Research Study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating. If you experience physical injury or illness as a result of participating in this research study, medical care is available at University Hospitals Cleveland Medical Center (UHCMC), University Hospitals Ahuja Medical Center (UHAMC) or elsewhere; however, UH has no plans to provide free care or compensation for lost wages.

### **Disclosure of Your Study Records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

### **Contact Information**

\_\_\_\_\_ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator Jeffery Dusek, PhD can also be contacted at 617-519-8082. If you have any questions, concerns or complaints about the study in the future, you may also contact them later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research- related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

### **Signature**

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

X		
Signature of Participant	Date	Time

X	
Printed Name of Participant	

X	
Signature of person obtaining informed consent	
X	
Printed name of person obtaining informed consent	

## **A.1.2 UCSD Patient Written Informed Consent**

**Key Information:** The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

### **Why am I being invited to take part in a research study?**

You are being asked to take part in this study because you came to the emergency room (ER) and are experiencing pain.

### **Things I should know about a research study**

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

### **Introduction/Purpose**

The purpose of this research is to determine if we are able to deliver acupuncture for pain relief in the ER, and to study see if acupuncture for pain relief in the ER is effective. This research will be carried out at three sites: UH Cleveland Medical Center ER, the Vanderbilt University Medical Center ER and the UC San Diego (UCSD) Health ER, Hillcrest location. There will be a total of 165 patient participants across three research sites, with 55 enrolling from each site. Additionally, around 30 ER providers and staff will be interviewed to gain their perspective and experience related to how the study was carried out

### **Key Study Procedures**

If you agree to participate, you will be randomly assigned to one of two groups. The treatment group will receive acupuncture and usual care during this ER visit, and the control group will receive usual care. Whichever group you are assigned to, we will also ask you a series of short questions about your symptoms before treatment, immediately after treatment, again before you are discharged from the ER, and then twice more via email, text or over the phone one week and one month after discharge. For the one week and one month follow up questionnaires, we'll also ask about your pain medication usage during the time since you were discharged.

If you are assigned to the acupuncture group, we may contact you to participate in an additional interview about your perspectives and experiences as a participant in the study who received acupuncture. The interview will be conducted via telephone or an approved telehealth application, and will be recorded and transcribed. Participation in the interview is completely

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**Principal Investigator:** Gene A. Kallenberg, MD

voluntary and refusing to participate will not affect your participation in the rest of the study. If you agree to the interview, a study information sheet about the interview will be shared and reviewed with you before the interview begins and you will have an opportunity to ask questions or to refuse to participate.

There is a chance that additional study staff may also observe study procedures during your visit to the ER. Researchers will seek to observe the actions and interactions of relevant persons, including ER providers, other ER staff, patients, and the Site Study Coordinator or Site Research Assistant over the course of the your entire ER visit.

More detailed information about the study procedures can be found under “Detailed Study Procedures”.

**Key Risks**

There are few potential risks of taking part in this study. Acupuncture carries very slight risks for bleeding, bruising, fainting, and needling pain. If you experience any of these, you will be treated by providers here in the ER.

Some of the questions that we will ask you might make you feel uncomfortable. You can skip any question you do not wish to answer.

As with any research study, there is a slight risk of losing privacy and confidentiality. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

More detailed information about the risks of this study can be found under “Detailed Risks”

**Benefits**

You may not benefit from participation. Those randomized to acupuncture may have improved pain control but this cannot be guaranteed. You may experience better pain management, and reduced usage of opioid analgesics through the use of acupuncture if you are in the acupuncture group. This research may benefit future patients by improving the use of acupuncture along with usual care for pain management in the ER.

**Alternatives to Study Participation**

The only alternative to participating in this study is to not participate.

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**Detailed Information: The following is more detailed information about this study in addition to the information listed above.**

**Detailed Study Procedures**

If you are assigned to the treatment group, after answering a few questions about your symptoms on a tablet you will receive acupuncture from a nationally board certified acupuncturist. The acupuncturist will describe details of the treatment, risks, cost and benefits in your private room. After that, you will receive the acupuncture treatment in your private room. Treatment will last between 30-45 minutes. Please note that if assigned to the acupuncture group, any pain medications that your provider may prescribe will be delayed while you receive treatment with acupuncture. Your individual acupuncture treatment will be based on your particular situation and will be determined by the treating acupuncturist. Sterile, single-use non-coated acupuncture needles will be used for this study. After the treatment, and again within 15 minutes of discharge, you will be asked the same series of questions on the tablet. One week and again one month after discharge you will be asked the same series of questions, and a few more about your pain relief medication usage since discharge, and your satisfaction with your treatment. You may choose to receive a link to the questionnaires via text message or email, or you can choose to have a study team member call you to complete the questionnaire. The study team will also view your medical record to collect information about any pain medications used during your ER visit, and your demographics.

**Qualitative Interviews:** Additionally, 15 participants assigned to the treatment group from each research site will participate in an interview with study staff. Study staff will contact some participants who received acupuncture as part of the study by phone or by email to invite them to participate in the interview. The purpose of the interview is to describe perspectives and experiences related to the how the study of acupuncture in emergency room (ER) was carried out. We may or may not contact you to participate in the interview portion of the research. If we contact you, you may refuse to participate. Before the start of the interview, a study information sheet will be shared and reviewed with you and you will be given an opportunity to ask questions and/or to refuse participation in the interview. Refusing to participate in the interview will not affect your care or your participation in the rest of the study.

The interview will last approximately 45 minutes and will be conducted via telephone or an approved telehealth application. The interview will take place between 2-4 weeks after your visit to the ER. The interview will be securely recorded and transcribed. Both the transcription and the recording will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected

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PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information.

If you are assigned to the acupuncture group, do you consent to being contacted for the interview portion of this research?

- Yes
  - I prefer an audio-only interview (by telephone)
  - I prefer an audio and video interview (by telehealth)
- No

**If you are assigned to the control group,** after answering a few questions about your symptoms on a tablet, you will receive usual ER care. Within 60 minutes, and again within 15 minutes before you are discharged, you will be asked the same series of questions on the tablet. One week and again one month after discharge you will be asked the same series of questions, and a few more about your pain relief medication usage since discharge, and your satisfaction with your treatment. You may choose to receive a link to the questionnaires via text message or email, or you can choose to have a study team member call you to complete the questionnaire. If you choose to receive a link to the questionnaire, a member of the study team may call you for followup if we notice that the questionnaires have not been completed. The study team will also view your medical record to collect information about any pain medications used during your ER visit, and your demographics.

**Structured observation:** For those assigned to either the treatment or control groups, there is a chance that additional research study staff may also observe study procedures during your visit to the ER. These researchers will seek to observe the actions and interactions of relevant persons, including ER providers, other ER staff, patients, and the research study staff over the course of the your entire ER visit. You may refuse to be observed by study staff and still participate in the research study. If applicable, do you consent to have your participation in this research study while in the ER observed by study staff today?

- Yes
- No
- NA

**Courtesy calls:** A member of the research study staff will call you 2-3 days after your ER visit to ensure that you have received the e-gift card for your time and to remind you that we will be

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**Detailed Risks**

The potential risks associated with participation in this study are minimal. Acupuncture carries very slight risks for bleeding, bruising, fainting (acushock), and needling pain. In the event you experience an adverse event (AE), you will be treated by providers in the site ER and will have access to emergency response equipment as necessary.

Acupuncture involves inserting thin, sterile needles in the skin. The needles are not inserted into the skin very far. Sometimes the needles cause slight discomfort or minor bleeding. The acupuncturist will explain the risks of acupuncture in detail and ask you to sign a separate acupuncture consent form. The acupuncturist will review this consent form with you. Any acupuncturist who provides treatments in this study will be licensed by the state in which they practice.

Some of the questions in the questionnaire might make you feel uncomfortable. You can skip any question they do not wish to answer.

As with any research study, there is a slight risk of losing privacy and confidentiality. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

**Financial Information**

There will be no cost to you and your insurance will not be billed to take part in this study. For your participation during your ER visit, you will receive a \$25 e-gift card which will be emailed to you after your ER visit. For answering the follow up questions on the phone one week after discharge, you will receive an additional \$25 e-gift card, and for answering the follow up questions on the phone 4 weeks after discharge, you will receive a final \$25 e-gift card. If assigned to the acupuncture group and selected to participate in the interview, you will receive an additional \$25 e-gift card within 30 days of the completion of the interview.

**Research-Related Injury**

In the event you suffer a research related injury as a result of being in this study, UCSD Health is available to provide medical treatment for such injury. Provision of such medical treatment does not imply any negligence or other wrongdoing on the part of UCSD Health, the Sponsor or any of the physicians or other study personnel. If you believe that you have been injured as a result of participating in the study, please immediately contact the

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Principal Investigator or your study doctor at UCSD Health. If you cannot reach the Principal Investigator or your study doctor, do not delay treatment. You may seek treatment by another doctor. If you are seen or treated by a doctor other than the Principal Investigator or your study doctor, you should inform such doctor that you are in this study and, if possible, take this document with you to assist with your treatment. Always contact the Principal Investigator or your study doctor to alert them of any treatment you receive for an injury or illness you experience during this Study.

The costs for medical treatment as a result of a research related injury may be billed to you or your medical insurance plan, if applicable. Medical insurance plans may or may not cover costs for medical treatment of research related injuries. If you have insurance, you should check with your medical insurance plan before deciding to participate in this research study. In the event your medical insurance plan covers some or all of the treatment costs, you may still be responsible for co-pays or deductibles as required by your medical insurance plan.

Neither Sponsor nor UCSD Health has set aside any money to pay you or to pay for your treatment if you suffer a research related injury as a result of being in the study. There are no plans for UCSD Health or Sponsor to provide other forms of compensation (such as lost wages or other indirect losses) to you for research related injuries. You are not waiving any legal rights by signing this form, including the right to seek compensation for an injury. To help avoid injury, it is very important to follow all study directions.

**Clinical Trial Information**

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE: A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

**Termination of Participation**

Your decision to participate in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;

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- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons, including competitive enrollment (e.g. the target number of subjects has entered the study.)

**Confidentiality**

All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Data in hard copy form will be stored in locked filecabinets within a secure, badge-access location at each site. Recordings of the interview with theacupuncture group participants will be transcribed, and then the recording will be destroyed. Thetranscription will contain no identifying information.

**Future use of De-Identified Data**

Identifiers might be removed from your identifiable private information and after such removal the information could be used for future research studies or distributed to another investigator forfuture research studies without additional informed or consent.

It is possible, that in the future, additional research sites may be added. In this event, de-identified and or aggregate data collected during this research project may be shared with research personnel at these additional sites.

Your identifiable data will not be used for any future projects.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

**UNIVERSITY OF CALIFORNIA,  
SAN DIEGO  
CONSENT FOR INVESTIGATIONAL STUDIES**  
(v. 10.2019)

**Project Title:** Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study (ACUITY)

**Principal Investigator:** Gene A. Kallenberg, MD

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by The National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of your name, address, phone number, email address, medical record number and date of birth

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document (your name, address, phone number, email address, medical record number and date of birth).

**Privacy of Protected Health Information (HIPAA)**

The Health Insurance Portability & Accountability Act (HIPAA) is a Federal law that helps to protect the privacy of your health information and to whom this information may be shared within and outside of University Hospitals. This Authorization form is specifically for a research study entitled "Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study" (ACUITY) and will tell you what health information (called Protected Health Information or PHI) will be collected for this research study, who will see your PHI and in what ways they can use the information. In order for the Principal Investigator, Gene A. Kallenberg, MD, and the research study staff to collect and use your PHI, you must sign this authorization form. You will receive a copy of this signed Authorization for your records. If you do not sign this form, you may not join this study. Your decision to allow the use and disclosure of your PHI is voluntary and will have no impact on your treatment at UCSD Health. By signing this form, you are allowing the researchers for this study to use and disclose your PHI in the manner described below.

Generally the Principal Investigator and study staff at UCSD Health who are working on this research project will know that you are in a research study and will see and use your PHI. The researchers working on this study will collect the following PHI about you: your name, address, phone number, email address, medical record number and date of birth. This PHI will be used to contact you later for follow up, to extract

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SAN DIEGO  
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(v. 10.2019)

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**Principal Investigator:** Gene A. Kallenberg, MD

information about your emergency department treatment, and for data analysis purposes. Your access to your PHI may be limited during the study to protect the study results.

Your PHI may also be shared with the following groups/persons associated with this research study or involved in the review of research: the study's Clinical Coordinating Center at Albert Einstein College of Medicine, the National Institutes of Health (study sponsor), other staff from the Principal Investigator's medical practice group; UCSD Health; University Hospitals, including the Center for Clinical Research and the Law Department; Government representatives or Federal agencies, when required by law.

It is possible, that in the future, additional research sites may be added. In this event, your PHI that was collected during this research project may be shared with research personnel at these additional sites.

- Your permission to use and disclose your PHI does not expire. However, you have the right to change your mind at any time and revoke your authorization. If you revoke your authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. Also, if you revoke your authorization you may no longer be able to participate in the research study. To revoke your permission, you must do so in writing by sending a letter to Gene A. Kallenberg, MD, Director, UCSD Centers for Integrative Health, University of California, San Diego, 9500 Gilman Dr. La Jolla, CA 92093; If you have a complaint or concerns about the privacy of your health information, you may also write to the UCSD Campus Privacy Officer, Pegah K. Parsi, JD, MBA - CIPP/EU/US, CIPM at [pparsi@ucsd.edu](mailto:pparsi@ucsd.edu) or 858-822-4439, or to the Federal Department of Health and Human Services (DHHS) at DHHS Regional Manager, Office of Civil Rights, US Department of Health and Human Services Government Center, JF Kennedy Federal Building, Room 1875, Boston, MA 02203. Complaints should be sent within 180 days of finding out about the problem.

The researchers and staff agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and Federal law. University Hospitals is committed to protecting your confidentiality. Please understand that once your PHI has been disclosed to anyone outside of UCSD Health, there is a risk that your PHI may no longer be protected; however other Federal and State laws may provide continued protection of your information.

**UNIVERSITY OF CALIFORNIA,  
SAN DIEGO  
CONSENT FOR INVESTIGATIONAL STUDIES  
(v. 10.2019)**

**Project Title:** Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study (ACUITY)

**Principal Investigator:** Gene A. Kallenberg, MD

**Summary of Your Rights as a Participant in a Research Study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled.

If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating. If you experience physical injury or illness as a result of participating in this research study, medical care is available at University of California, San Diego (UCSD) Health or elsewhere; however, UCSD Health has no plans to provide free care or compensation for lost wages.

**Disclosure of Your Study Records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board and the UCSD Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

**Contact Information**

\_\_\_\_\_ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator, Gene A. Kallenberg, and/or his research associates have described to you what is going to be done, and the risks, hazards, and benefits involved. He can be contacted at [gkallenberg@health.ucsd.edu](mailto:gkallenberg@health.ucsd.edu) or at 619-543-5490. If you have any questions, concerns or complaints about the study in the future, you may also contact him later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the UCSD Human Research

Protections Program Office at 858-246-HRPP (858-246-4777). The Principal Investigator, Gene A. Kallenberg, and/or his research associates have described to you what is going to be done, and the risks, hazards, and benefits involved. He can be contacted at gkallenberg@health.ucsd.edu or at 619-543-5490. If you have any questions, concerns or complaints about the study in the future, you may also contact him later.

**Signature**

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

X	
Signature of Participant	
X	
Printed Name of Participant	

X	
Signature of person obtaining informed consent	
X	
Printed name of person obtaining informed consent	

## A.2 Study Staff Written Consent

### A.2.1 UH Study Staff Written Consent

**Key Information:** The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

#### **Why am I being invited to take part in a research study?**

You are being asked to participate because you are ACUITY study staff (UH IRB STUDY20200618).

#### **Things I should know about a research study**

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

#### **Introduction/Purpose**

The purpose of this research is conduct a feasibility randomized control trial (RCT) to examine the feasibility of data collection, acupuncture intervention implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. (UH Cleveland Medical Center and Ahuja Medical Center EDs (site 1), the Vanderbilt University Medical Center (VUMC) ED (site 2) and the Hillcrest University of California San Diego (UCSD) ED (site 3)). This study includes structured observation to help assess feasibility. Successful conduct of the proposed multi-site study will inform implementation of a future, definitive, pragmatic, multi-site, non-inferiority RCT of Acupuncture compared with Usual Care.

#### **Key Study Procedures**

Participation in this study will consist of being observed during the following applicable activities: screening, recruitment, consent and RCT study procedures in the ED. More detailed information about the study procedures can be found under “Detailed Study Procedures”.

#### **Key Risks**

There are no physical risks to participating in this study. More detailed information about the risks of this study can be found under “Detailed Risks”

#### **Benefits**

There is no direct benefit to participating in this study. This research may benefit future patients by improving the use of acupuncture along with usual care for pain management in the ED.

#### **Alternatives to Study Participation**

The only alternative is not to participate in the study.

**Detailed Information: The following is more detailed information about this study in addition to the information listed above.**

**Detailed Study Procedures**

Two to three 4-6 hour shifts (for a total of approximately 12 hours) will be observed at each site during active patient recruitment and treatment by the Einstein Coordinating Center PI and/or the Einstein Coordinating Center Research Coordinator. These study staff are UH Research Credentialed.

During the observation days, the study staff from Einstein will shadow local study staff as they screen, recruit, and consent patients and during study procedures including the receipt of acupuncture and data collection. No PHI or PII will be collected during this observation.

Through field notes, Einstein study staff will document behaviors and interactions during ED visits with the goal of developing hypotheses regarding factors influencing key study outcomes. Einstein study staff will remain in the ED and seek to record all key interactions between patients, research and ED staff.

**Detailed Risks**

There are no physical risks to participating in this study. As with any research study, there is a slight risk of losing privacy and confidentiality. We will not collect any identifying information in our observation notes. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

**Financial Information**

There will be no cost to you to participate in this research and there will be no compensation.

**Clinical Trial Information**

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE: A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

**Student/Employee Rights**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisor.

**Confidentiality**

No identifying information will be collected during observation. All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Data in hard copy form will be stored in locked file cabinets within a secure, badge-access location at each site. Recordings of the interview with the acupuncture group

participants will be transcribed, and then the recording will be destroyed. The transcription will contain no identifying information.

It is possible, that in the future, additional research sites may be added. In this event, the data collected during this research project may be shared with research personnel at these additional sites.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Center for Complementary and Integrative Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of any anonymous observation data collected.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

### **Summary of Your Rights as a Participant in a Research Study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating. If you experience physical injury or illness as a result of participating in this research study, medical care is available at University Hospitals Cleveland Medical Center (UHCMC), Ahuja Medical Center

(UHAMC) or elsewhere; however, UHCMC has no plans to provide free care or compensation for lost wages.

### **Disclosure of Your Study Records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

### **Contact Information**

\_\_\_\_\_ has described to you what is going to be done, the risks, hazards, and benefits involved. The Principal Investigator Jeffery Dusek can also be contacted at [Jeffery.Dusek@UHhospitals.org](mailto:Jeffery.Dusek@UHhospitals.org) or 216-519-8082. If you have any questions, concerns or complaints about the study in the future, you may also contact them later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

### **Signature**

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

<b>X</b>		
Signature of Participant	Date	Time
<b>X</b>		
Printed Name of Participant		

<b>X</b>		
Signature of person obtaining informed consent	Date	Time

**X**

Printed name of person obtaining informed consent

## **A.2.2 UCSD Study Staff Written Consent**

**Key Information:** The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

### **Why am I being invited to take part in a research study?**

You are being asked to participate because you are ACUITY study staff (UH IRB STUDY20200618).

### **Things I should know about a research study**

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

### **Introduction/Purpose**

The purpose of this research is conduct a feasibility randomized control trial (RCT) to examine the feasibility of data collection, acupuncture intervention implementation and treatment outcomes in emergency departments associated with 3 BraveNet research sites. (UH Cleveland Medical Center ED (site 1), the Vanderbilt University Medical Center (VUMC) ED (site 2) and the Hillcrest University of California San Diego (UCSD) ED (site 3)). This study includes structured observation to help assess feasibility. Successful conduct of the proposed multi-site study will inform implementation of a future, definitive, pragmatic, multi-site, non-inferiority RCT of Acupuncture compared with Usual Care.

### **Key Study Procedures**

Participation in this study will consist of being observed during the following applicable activities: screening, recruitment, consent and RCT study procedures in the ED. More detailed information about the study procedures can be found under “Detailed Study Procedures”.

### **Key Risks**

There are no physical risks to participating in this study. More detailed information about the risks of this study can be found under “Detailed Risks”

### **Benefits**

There is no direct benefit to participating in this study. This research may benefit future patients by improving the use of acupuncture along with usual care for pain management in the ED.

### **Alternatives to Study Participation**

The only alternative is not to participate in the study.

### **Detailed Information: The following is more detailed information about this study in addition to the information listed above.**

### **Detailed Study Procedures**

Two to three 4-6 hour shifts (for a total of approximately 12 hours) will be observed at each site during active patient recruitment and treatment by the Einstein Coordinating Center PI and/or the Einstein Coordinating Center Research Coordinator. These study staff are UH Research Credentialed.

During the observation days, the study staff from Einstein will shadow local study staff as they screen, recruit, and consent patients and during study procedures including the receipt of acupuncture and data collection. No PHI or PII will be collected during this observation.

Through field notes, Einstein study staff will document behaviors and interactions during ED visits with the goal of developing hypotheses regarding factors influencing key study outcomes. Einstein study staff will remain in the ED and seek to record all key interactions between patients, research and ED staff.

### **Detailed Risks**

There are no physical risks to participating in this study. As with any research study, there is a slight risk of losing privacy and confidentiality. We will not collect any identifying information in our observation notes. We will keep all paper records secure in locked file cabinets. All electronic records are kept on a password-protected database to which only research staff has access.

### **Financial Information/Costs for Participating**

There will be no cost to you to participate in this research and there will be no compensation.

### **Clinical Trial Information**

U.S. NATIONAL INSTITUTES OF HEALTH (NIH) CLINICAL TRIAL DATABASE: A description of this clinical trial will be available on <http://www.clinicaltrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time to find out information about the trial and basic results.

### **Student/Employee Rights**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisor.

### **Confidentiality**

No identifying information will be collected during observation. All electronic data will be kept in password protected databases behind an electronic firewall at sites and then securely sent to the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Data in hard copy form will be stored in locked file cabinets within a secure, badge-access location at each site. Recordings of the interview with the acupuncture group participants will be transcribed, and then the recording will be destroyed. The transcription will contain no identifying information.

It is possible, that in the future, additional research sites may be added. In this event, the data collected during this research project may be shared with research personnel at these additional sites.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Center for Complementary and Integrative Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of any anonymous observation data collected.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

### **Summary of Your Rights as a Participant in a Research Study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed. In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

### **Disclosure of Your Study Records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board (reviewing IRB), and the UCSD Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records.

In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

### **Contact Information**

\_\_\_\_\_ has described to you what is going to be done, and the risks, hazards, and benefits involved. He can be contacted at [gkallenberg@health.ucsd.edu](mailto:gkallenberg@health.ucsd.edu) or at 619-543-5490. If you have any questions, concerns or complaints about the study in the future, you may also contact him later.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, you may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) to inquire about your rights as a research subject or to report research-related problems.

### **Signature**

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

<b>X</b>		
Signature of Participant	Date	Time
<b>X</b>		
Printed Name of Participant		

<b>X</b>		
Signature of person obtaining informed consent	Date	Time
<b>X</b>		
Printed name of person obtaining informed consent		

## A.3 Patient Qualitative Interview Study Information Sheet

### A.3.1 UH Patient Qualitative Interview Study Information Sheet

#### **Introduction/Purpose**

You are invited to participate in an interview as part of **“Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study.”**

**(ACUITY)** The purpose of the interview is to describe perspectives and experiences related to the how this study in emergency room (ER) was carried out. You are being asked to participate because you received acupuncture for pain management at a recent ER visit as part of the above mentioned study in the University Hospitals (UH) Cleveland Medical Center/Ahuja Medical Center EDs, the Vanderbilt University Medical Center (VUMC) ED, or the Hillcrest University of California San Diego (UCSD). This research project is being conducted by **Jeffery Dusek, PhD, Director of Research at UH Connor Integrative Health Network** and should take 45 minutes to complete.

#### **Participation**

Your participation in the interview is voluntary. You may refuse to take part in the interview or exit the study at any time without penalty. Your participation will involve a 45 minute interview where we will ask you questions about your perceptions and experiences related to how the acupuncture study in the ER was carried out. The interview will take place either over telephone or via an approved telehealth application and will be recorded and transcribed. The recording will be destroyed once transcription is verified.

#### **Risks**

There is no physical risk to being in this study.

There is always a small risk that your information may be seen or accessed by someone who shouldn't have access

We will work to prevent this by

- Not including any identifying questions in the interview.
- Storing the recording and the transcription in a password protected database behind an electronic firewall at the Einstein Coordinating Center
- Destroying the recording once transcription is verified.
- Ensuring that the transcription contains no identifying information.
- Ensuring that only IRB approved study personnel have access to your data.

The survey questions ask about your ER visit and may be distressing to you as you think about your experiences. You may skip any questions you don't want to answer and you may end the interview at any time for any reason.

## **Benefits**

This research study is not intended to benefit you directly. We hope that the knowledge gained will help us to design and carry out a larger future study of acupuncture compared with usual care in additional ERs.

## **Alternatives to Study Participation**

The alternative to participation in this study is to NOT participate. This will not affect your care in any way.

## **Financial Information**

Your participation in this study will not involve cost to you.

For your participation in this interview, you will receive a \$25 gift card within 30 days of the interview.

## **Confidentiality**

We will work to protect your confidentiality by not including any identifying questions. Both the transcription and the recording of the interview will be stored in a password protected database behind an electronic firewall at the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information. No names or identifying information will be included in any publications or presentations based on these data, and your responses to this survey will remain confidential.

Your de-identified information may be used or shared with other researchers without your additional informed consent.

## **Students or Employees**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisors or professors.

## **Summary of your rights as a participant in a research study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

## **Disclosure of your study records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the

FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

## **Contact Information**

If you have questions at any time about the study or the procedures, you may contact **Afrida Khurshid** via email at [Afrida.Khurshid@UHhospitals.org](mailto:Afrida.Khurshid@UHhospitals.org) or via phone at **917-288-0334**

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

**By answering the interview questions, you are indicating that you agree to the following:**

- You have read the above information
- You voluntarily agree to participate and to be recorded for transcription purposes
- You are 18 years of age or older

You may keep a copy of this form for your records.

## **A.3.2 UCSD Patient Qualitative Interview Study Information Sheet**

### **Introduction/Purpose**

You are invited to participate in an interview as part of **“Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study.”**

**(ACUITY)** The purpose of the interview is to describe perspectives and experiences related to the how this study in emergency room (ER) was carried out. You are being asked to participate because you received acupuncture for pain management at a recent ER visit as part of the above mentioned study in the University Hospitals (UH) Cleveland Medical Center ED, the Vanderbilt University Medical Center (VUMC) ED, or the Hillcrest University of California San Diego (UCSD). This research project is being conducted by **Gene A. Kallenberg, MD, Director, UCSD Centers for Integrative Health at University of California, San Diego** and should take 45 minutes to complete.

### **Participation**

Your participation in the interview is voluntary. You may refuse to take part in the interview or exit the study at any time without penalty. Your participation will involve a 45 minute interview where we will ask you questions about your perceptions and experiences related to how the acupuncture study in the ER was carried out. The interview will take place either over telephone or via an approved telehealth application and will be recorded and transcribed. The recording will be destroyed once transcription is verified.

### **Risks**

There is no physical risk to being in this study.

There is always a small risk that your information may be seen or accessed by someone who shouldn't have access

We will work to prevent this by

- Not including any identifying questions in the interview.
- Storing the recording and the transcription in a password protected database behind an electronic firewall at the Einstein Coordinating Center
- Destroying the recording once transcription is verified.
- Ensuring that the transcription contains no identifying information.
- Ensuring that only IRB approved study personnel have access to your data.

The survey questions ask about your ER visit and may be distressing to you as you think about your experiences. You may skip any questions you don't want to answer and you may end the interview at any time for any reason.

### **Benefits**

This research study is not intended to benefit you directly. We hope that the knowledge gained will help us to design and carry out a larger future study of acupuncture compared with usual care in additional ERs.

## **Alternatives to Study Participation**

The alternative to participation in this study is to NOT participate. This will not affect your care in any way.

## **Financial Information**

Your participation in this study will not involve cost to you.

For your participation in this interview, you will receive a \$25 gift card within 30 days of the interview.

## **Confidentiality**

We will work to protect your confidentiality by not including any identifying questions. Both the transcription and the recording of the interview will be stored in a password protected database behind an electronic firewall at the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information. No names or identifying information will be included in any publications or presentations based on these data, and your responses to this survey will remain confidential.

Your de-identified information may be used or shared with other researchers without your additional informed consent.

## **Students or Employees**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisors or professors.

## **Summary of your rights as a participant in a research study**

Your participation in this research study is voluntary. Refusing to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

## **Disclosure of your study records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

## Contact Information

If you have questions at any time about the study or the procedures, you may contact **Afrida Khurshid** via email at [Afrida.Khurshid@UHhospitals.org](mailto:Afrida.Khurshid@UHhospitals.org) or via phone at **917-288-0334**.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the UCSD Human Research Protections Program Office at 858-246-HRPP (858-246-4777) or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

**By answering the interview questions, you are indicating that you agree to the following:**

- You have read the above information
- You voluntarily agree to participate and to be recorded for transcription purposes
- You are 18 years of age or older

You may keep a copy of this form for your records.

## A.4 ED Provider Qualitative Interview Study Information Sheet

### A.4.1 UH ED Provider Qualitative Interview Study Information Sheet

#### **Introduction/Purpose**

You are invited to participate in an interview as part of **“Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study.”**

**(ACUITY)** The purpose of the interview is to describe perspectives and experiences related to implementation of the acupuncture study in the emergency department (ED). You are being asked to participate because you are an ED provider (physician, nurse practitioner, physician assistant, or registered nurse), ED staff, or acupuncturists employed or credentialed in the University Hospitals (UH) Cleveland Medical Center/Ahuja Medical Center ED, the Vanderbilt University Medical Center (VUMC) ED, or the Hillcrest University of California San Diego (UCSD) for at least one year during the study period. This research project is being conducted by **Jeffery Dusek, PhD, Director of Research at UH Connor Integrative Health Network** and should take 45 minutes to complete.

#### **Participation**

Your participation in this research study is voluntary. You may refuse to take part in the study or exit the study at any time without penalty. Your participation in this study will involve participating in a 45 minute interview where we will ask you questions about your perceptions and experiences related to the implantation of the acupuncture study in the ED. The interview will take place either in a private room in person or remotely over the telephone or via a HIPAA-compliant commercial tele-health platform (e.g. Zoom Health Professional or Doxy.me) and will be recorded and transcribed. The recording will be destroyed once transcription is verified.

#### **Risks**

There is no physical risk to being in this study. There is always a small risk that your information may be seen or accessed by someone who shouldn't have access.

We will work to prevent this by

- Not including any identifying questions in the interview.
- Storing the recording and the transcription in a password protected database behind an electronic firewall at the Einstein Coordinating Center
- Destroying the recording once transcription is verified.
- Ensuring that the transcription contains no identifying information.
- Ensuring that only IRB approved study personnel have access to your data

#### **Benefits**

This research study is not intended to benefit you directly. We hope that the knowledge gained will help inform design and implementation of a future, pragmatic, multi-site, non-inferiority

randomized control trial of Acupuncture compared with Usual Care in additional BraveNet clinic-affiliated EDs.

## **Alternatives to Study Participation**

The alternative to participation in this study is to NOT participate. This will not affect your employment in any way.

## **Financial Information**

There is no cost to participate in this research. For your participation in this interview, you can choose between a \$50 Amazon gift card or a free Connor Integrative Health Network service for your time.

## **Confidentiality**

We will work to protect your confidentiality by not including any identifying questions. Both the transcription and the recording of the interview will be stored in a password protected database behind an electronic firewall at the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information. No names or identifying information will be included in any publications or presentations based on these data, and your responses to this survey will remain confidential.

Your de-identified information may be used or shared with other researchers without your additional informed consent.

## **Students or Employees**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisors or professors.

## **Summary of your rights as a participant in a research study**

Your participation in this research study is voluntary. Refusing to participate will not involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

## **Disclosure of your study records**

Efforts will be made to keep the personal information in your research record private and confidential, but absolute confidentiality cannot be guaranteed. The University Hospitals Cleveland Medical Center Institutional Review Board may review your study records. If this study is regulated by the Food and Drug Administration (FDA), there is a possibility that the FDA might inspect your records. In addition, for treatment studies, the study sponsor and possibly foreign regulatory agencies may also review your records. If your records are reviewed your identity could become known.

## Contact Information

If you have questions at any time about the study or the procedures, you may contact **Afrida Khurshid** via email at [Afrida.Khurshid@UHhospitals.org](mailto:Afrida.Khurshid@UHhospitals.org) or via phone at **917-288-0334**.

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979 or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

**By continuing with the interview, you are indicating that you agree to the following:**

- You have read the above information
- You voluntarily agree to participate and to be recorded for transcription purposes
- You are 18 years of age or older

You may keep a copy of this form for your records.

## **A.4.2 UCSD ED Provider Qualitative Interview Study Information Sheet**

### **Introduction/Purpose**

You are invited to participate in an interview as part of **“Acupuncture in the Emergency Department for Pain Management: A BraveNet Multi-Center Feasibility Study.”**

**(ACUITY)** The purpose of the interview is to describe perspectives and experiences related to implementation of the acupuncture study in the emergency department (ED). You are being asked to participate because you are an ED provider (physician, nurse practitioner, physician assistant, or registered nurse), ED staff, or acupuncturists employed or credentialed in the University Hospitals (UH) Cleveland Medical Center ED, the Vanderbilt University Medical Center (VUMC) ED, or the Hillcrest University of California San Diego (UCSD) for at least one year during the study period. This research project is being conducted by **Gene A. Kallenberg, MD, Director, UCSD Centers for Integrative Health at University of California, San Diego** and should take 45 minutes to complete.

### **Participation**

Your participation in this research study is voluntary. You may refuse to take part in the study or exit the study at any time without penalty. Your participation in this study will involve participating in a 45 minute interview where we will ask you questions about your perceptions and experiences related to the implantation of the acupuncture study in the ED. The interview will take place either in a private room in person or remotely over the telephone or via a HIPAA-compliant commercial tele-health platform (e.g. Zoom Health Professional or Doxy.me) and will be recorded and transcribed. The recording will be destroyed once transcription is verified.

### **Risks**

There is no physical risk to being in this study. There is always a small risk that your information may be seen or accessed by someone who shouldn't have access.

We will work to prevent this by

- Not including any identifying questions in the interview.
- Storing the recording and the transcription in a password protected database behind an electronic firewall at the Einstein Coordinating Center
- Destroying the recording once transcription is verified.
- Ensuring that the transcription contains no identifying information.
- Ensuring that only IRB approved study personnel have access to your data

### **Benefits**

This research study is not intended to benefit you directly. We hope that the knowledge gained will help inform design and implementation of a future, pragmatic, multi-site, non-inferiority randomized control trial of Acupuncture compared with Usual Care in additional BraveNet clinic-affiliated EDs.

## **Alternatives to Study Participation**

The alternative to participation in this study is to NOT participate. This will not affect your employment in any way.

## **Financial Information**

There is no cost to participate in this research. For your participation in this interview, you will receive a \$25 e-gift card within 30 days of the interview.

## **Confidentiality**

We will work to protect your confidentiality by not including any identifying questions. Both the transcription and the recording of the interview will be stored in a password protected database behind an electronic firewall at the Einstein Coordinating Center and maintained on password protected PCs by a designated data manager. Once transcription is verified, we will destroy the recording of the interview. The transcription will contain no identifying information. No names or identifying information will be included in any publications or presentations based on these data, and your responses to this survey will remain confidential.

Your de-identified information may be used or shared with other researchers without your additional informed consent.

## **Students or Employees**

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisors or professors.

## **Summary of your rights as a participant in a research study**

Your participation in this research study is voluntary. Refusing to participate will not involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

## **Disclosure of your study records**

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## **Contact Information**

If you have questions at any time about the study or the procedures, you may contact Afrida Khurshid via email at [Afrida.Khurshid@UHhospitals.org](mailto:Afrida.Khurshid@UHhospitals.org) or via phone at 917-288-0334

If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about; concerns regarding the study; research participant's rights; research-related injury; or other human subject issues, please call please call the UCSD Human Research Protections Program Office at 858-246-HRPP (858-246-4777) or write to: The Associate Chief Scientific Officer, The Center for Clinical Research, University Hospitals Cleveland Medical Center, 11100 Euclid Avenue, Lakeside 1400, Cleveland, Ohio, 44106-7061.

**By continuing with the interview, you are indicating that you agree to the following:**

- You have read the above information
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You may keep a copy of this form for your records.