

STUDY TITLE: Pilot Randomized Control Trial: Comparing the Effectiveness of Buzzy versus Intradermal Lidocaine for Peripheral Intravenous Cannulation in Adults

STUDY SPONSOR: NONE

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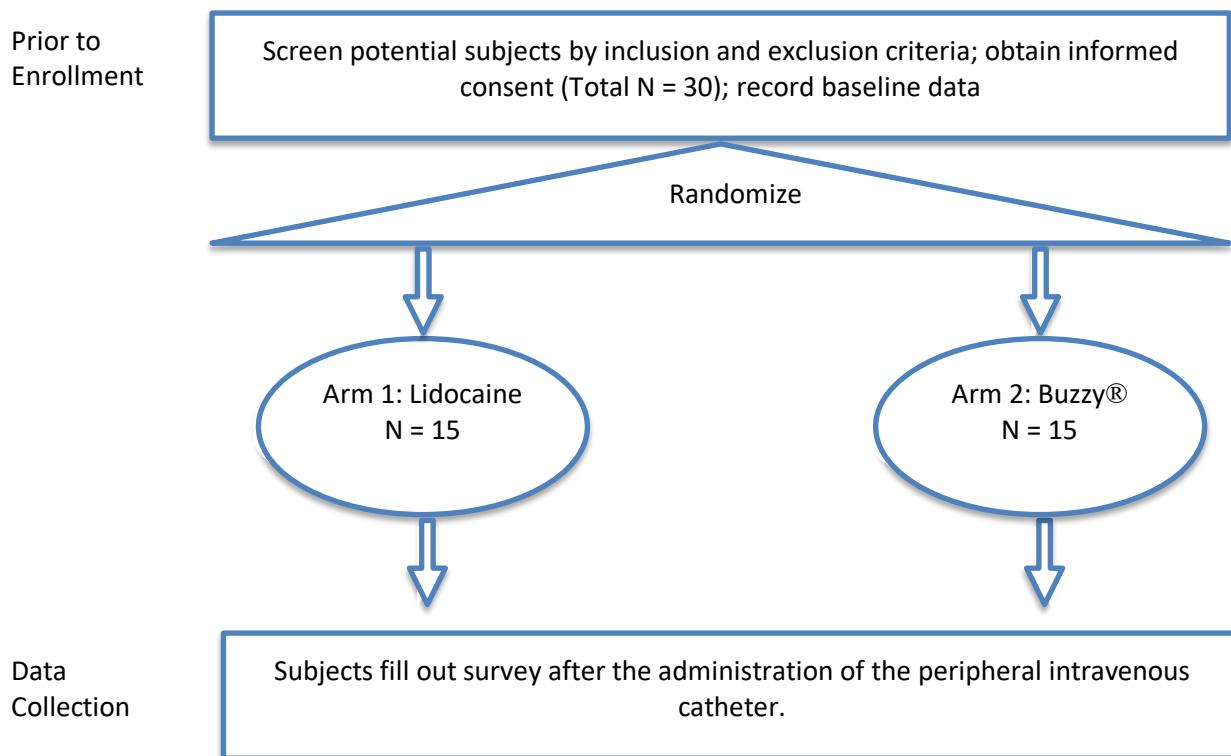
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A. Study Schema



B. Introduction

B.1 Background and Rationale

1. **Describe the relevant prior experience and gaps in current knowledge:** Intravenous peripheral catheter insertion is one of the most common procedures in all health care settings,^{1,2} but it often causes pain and anxiety for patients. A myriad of techniques have been explored to reduce patient discomfort, such as topical anesthesia,³⁻⁵ cooling of the skin,⁶ vibration,⁷ and even distraction with flash lights.⁸ Some literature is available on a reusable, thermomechanical device called Buzzy® (MMJ Labs, Atlanta, GA), which combines cold with vibration and has been reported to be very effective in reducing needle-related procedural pain in children.⁹ However, so far, there is limited data available in regards to whether this device can improve the patient experience with intravenous peripheral catheter insertion for adults.^{7,10}
2. **Describe any relevant preliminary data:** Baxter et al.¹⁰ conducted a preliminary study comparing pain reported in healthy adult volunteers undergoing venous access and found that those who received Buzzy® had significantly less pain than those with no prophylactic intervention. In comparison, Redfern et al.⁷ conducted a randomized clinical trial on adult patients undergoing intravenous catheter insertion prior to elective orthopedic surgical procedures and found no significant difference in mean pain score between the Buzzy group and the control group. However, as the authors of Redfern et al.⁷ suggest, Buzzy® might not have been effective in that particular adult population possibly because of the timing when Buzzy® was applied to the patients.
3. **Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how it will add to existing knowledge:** A systematic review and meta-analysis reviewed the effectiveness of current pharmacological methods for reducing the pain associated with intravenous catheter insertion in adults and found that intradermal lidocaine 2% is the most effective

pharmacological methodology.¹¹ Although intradermal lidocaine 2% injection is effective, it is important to note that it requires the use of an additional needle stick.

According to the Center for Disease Control and Prevention (CDC), approximately 385,000 needle stick injuries and other sharps-related injuries occur annually by hospital employees. In other words, about 1,000 sharps injuries occur per day in American hospitals. Each time someone uses a needle, the risk of getting a needle stick injury increases.

Currently, at our institution, most nurses perform intravenous catheter insertion in adult patients without any prophylactic pain-relieving techniques. Anesthesia providers, at our institution, perform intravenous catheter insertion with either no prophylactic pain-relieving technique or with intradermal lidocaine injection prior to the performance of intravenous catheter procedure.

Based on the Gate Theory of Pain, which was first published in 1965 by Ronald Melzack and Patrick Wall in *Science*, non-painful signals, such as cold and vibration, can block pain signals from being interpreted as pain by the forebrain.¹² This is the theory behind why the device Buzzy® is effective in making patients feel more comfortable during peripheral intravenous catheter insertion. The use of this device is in theory beneficial because it eliminates the use of an additional needle and could therefore decrease the risk of accidental needle stick injury. Furthermore, the use of Buzzy® could potentially be financially beneficial because Buzzy® costs \$0.20 per use, while intradermal lidocaine 2% costs more than \$2 per use (the smallest size that lidocaine 2% comes in is a 2ml vial, which costs \$2 for our hospital, and each use of lidocaine 2% requires the use of a 25G needle and 3mL syringe, which both further increase the cost). In addition, Buzzy® is a reusable device, while the lidocaine vial, needle, and syringe are all one time use objects that continuously add to the global pollution problem.

Considering the potential benefits of Buzzy® to the patients, healthcare workers, hospital, and environment, we would like to conduct a non-inferiority randomized control trial to compare the effectiveness of Buzzy® to intradermal lidocaine 2% injection for intravenous catheter insertion in adult patients. However, since there is no published data available comparing the effectiveness of intradermal lidocaine 2% injection with that of Buzzy® for peripheral intravenous catheter insertion in adult patients, we would like to begin by conducting a pilot randomized control trial to establish a baseline and then to potentially use the results of this pilot study to calculate the necessary sample size needed for the future non-inferiority trial.

4. *Describe the relevance and usefulness of the objectives:*

Undergoing surgery or any health care procedure is often anxiety provoking for patients. If intravenous peripheral catheter insertion could be made less painful, thousands of patients could benefit. Furthermore, if Buzzy® is found to be an effective methodology for relieving pain associated with peripheral intravenous catheter insertion in adult patients, then more health care providers may end up utilizing the device, resulting in a potential decrease in needle-stick injuries, smaller financial burden, and less environmental pollution.

5. *Specify whether or not this is the first time the study drug, device, or intervention/procedure will be used in humans. If there has been experience with the study drug, device, or intervention/procedure in humans, detail the experience to date: Yes No, this is not the first time the study drug, device, or intervention/procedure will be used in humans*

6. *Is there an active control group?*

Yes No

If Yes, respond to all of the following:

a. *Check to confirm that the active control is an established effective intervention. If it is not, clarify how it is ethically justified to use this control in the study:* The active control group will be the intradermal lidocaine 2% injection. The use of intradermal lidocaine 2% injection is part of the standard of care at our hospital. Furthermore, a systematic review and meta-analysis demonstrated that

intradermal lidocaine 2% is the most effective pharmacological method for reducing the pain associated with intravenous catheter injection in adults.¹¹

b. **Describe any potential bias in the selection of the active control such that there will be an unfair advantage for the investigational intervention. For example, is the active control treatment known to be significantly less effective in this study population than another treatment:** or N/A

c. **Check to confirm that the sample size and the randomization ratio for this active control study is ethically justified with regard to the number of participants who will be exposed to the risks of the study.**

B.2 Risks to Subjects

1. **List the reasonably foreseeable risks, discomforts, hazards, and/or inconveniences to the subjects related to their participation in the research, including risk of unintentional loss of confidentiality. Include a description of the probability, magnitude, duration, reversibility, and potential consequences of the risks. Consider physical, psychological, social, legal, and economic risks:** Subjects could in theory experience some discomfort from the cold pack/vibration in the Buzzy® device; however, based on data reported in previous literature, when Buzzy® has been used in pediatric patients, patients actually reported that the Buzzy® made them feel more comfortable.¹²⁻¹⁴ Also, there is always a risk of unintentional loss of confidentiality, but we will make every effort to prevent that from happening by keeping all data in a secure location.

2. **State which study interventions may have unknown risks:** or N/A

3. **State which study interventions may have risks to an embryo or fetus (if a subject is or becomes pregnant) or to a nursing infant of a study subject:** or N/A

4. **Describe risks to people other than the participating subject, e.g., risks to family members, friends, others or risks to the community:** or N/A

1. **Are there any risks to study investigators or staff performing the study procedures due to research with high risk populations (e.g. prisoners, intravenous drug users, patients with major psychiatric issues, etc.)?:**

Yes No

B.3 Potential Benefits to Subjects

1. **Describe the potential benefits that individual subjects may experience from taking part in the research. Include the probability, magnitude, and duration of the potential benefits:** The patients may have less discomfort and less anxiety during peripheral intravenous cannulation.

Check if there is no direct benefit.

2. **Describe any benefit to the population from which the subject is drawn:** Future patients may also have less discomfort and less anxiety during peripheral intravenous cannulation. Also, future health care providers may have less risk of accidental needle stick injury because of the finding of this study. or N/A

3. **Describe any benefit to science, society, and humanity in general:** Adult patients may be more comfortable during peripheral intravenous cannulation in the future. There may also be fewer accidental needle stick injuries in the future. Furthermore, the findings of this study could help save some healthcare money and decrease the environmental pollution problem. or N/A

B.4 Alternatives

1. **Describe alternatives to participating in this research study (e.g. to decide not participate in the study, alternative treatments, no treatment (palliative care), etc.):** Patients who choose not to participate in this study will receive peripheral intravenous cannulation without the Buzzy® device.
2. **Describe the standard clinical care that may be an alternative:** Adult patients receive peripheral intravenous cannulation without any prophylaxis to the possible procedural pain, or they receive intradermal lidocaine injection prior to peripheral intravenous cannulation. N/A
3. **Describe how the subject can receive the research procedures/drug/device used in this study in a non-research setting:** Currently, the Buzzy® device is typically used on the pediatric population. Adults are not often offered the Buzzy® device, but, in certain hospitals, the Buzzy® device is also offered to adult patients. N/A

C. Objectives

1. **Describe the purpose, specific aims, or objectives of the study (i.e. the reason for performing the study in terms of the scientific question to be answered):**

Primary Aim: How much pain do adult patients experience with peripheral IV cannulation when Buzzy® device is used versus when intradermal lidocaine 2% is used?

Secondary Aim (1): How much satisfaction do adult patients experience with peripheral IV cannulation when Buzzy® device is used versus when intradermal lidocaine 2% is used?

Secondary Aim (2): How does first attempt during peripheral intravenous cannulation in adult patients compare when Buzzy® device is used versus when intradermal lidocaine 2% is used?

Secondary Aim (3): Does size of the peripheral intravenous catheter affect the pain that adult patients experience with peripheral IV cannulation?

Secondary Aim (4): Does location of the peripheral intravenous catheter placement affect the pain that adult patients experience with peripheral IV cannulation?

D. Enrollment and Withdrawal

D.1 Inclusion Criteria

1. **Describe the criteria that define who will be included in the study as a numbered list:**

1. Adults ages 18 to 99
2. Non-pregnant women and men
3. Adults that are able to consent
4. Patients requiring intravenous catheter insertion for their operation/procedure

D.2 Exclusion Criteria

1. **Describe the criteria that define who will be excluded in the study as a numbered list:**

1. Patients with Raynaud's syndrome, sickle cell disease, and/or extreme sensitivity to cold
2. Patients with a break or an abrasion on the skin where the Buzzy device would be placed
3. Patients with nerve damage affecting the extremity where the peripheral intravenous catheter would be placed

2. **Describe in detail how the eligibility criteria will be assessed and satisfied (e.g., medical record review, physical examination):** Based on the pre-operative history and physical exam performed by the CA-1 (PGY-2) anesthesiology resident (co-investigator of study).
3. **State who will determine eligibility. Note that those who are designated to determine eligibility must have appropriate training, expertise, and oversight, for example a physician PI or Co-I on a biomedical**

study: PI (anesthesiology attending) and Co-I (CA-1 (PGY-2) anesthesiology resident). These will be the physicians who will be taking care of these subjects.

4. **Can study subjects participate in another research study while participating in this research study:**
 Yes No

D.3 Withdrawal of Subjects

1. **Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent:** None
2. **Describe procedures that will be followed when subjects withdraw or are withdrawn from the research, including the possibility of partial withdrawal from study intervention with continued data collection:**
There will be no partial withdrawal from the study. Either the patient will take part in the study, which is just for the duration of the peripheral intravenous catheter insertion and the questionnaire that will take place before and after the procedure, or the patient will not take part in the study.
3. **Describe any necessary safety precautions to be applied to subjects who withdraw or are withdrawn (tapering drug doses, evaluative x-ray, etc.):** or N/A

D.4 Recruitment and Retention

D.4.1 Local Recruitment Methods

Describe the following attributes of the recruitment plan for the local Tufts site:

1. **When, where, and how potential subjects will be recruited:** The patients will be recruited in the pre-operative area.
 - a. **If potential subjects will be recruited by telephone, describe how many times the research team will attempt to call / leave a voice message:** N/A
 - i. Check to confirm that a script for **both** the telephone conversation and the voice message is included with the submission.
 - b. **When subjects respond to recruitment material, describe the information that will be provided to them about the study and the information that will be collected from subjects (e.g. name, telephone number, etc.). Describe also, how many times you will attempt to respond to call the subject back / leave a voice message:** N/A
 - c. Check to confirm that a script for **both** the telephone conversation and the voice message is included with the submission.
2. **Source of subjects (for example, patient population, local community, etc.):** Patients that will be scheduled for an operation at St. Elizabeth's Medical Center.
3. **Methods that will be used to identify potential subjects:** St. Elizabeth's Medical Center's Operating Room Scheduler will be used to identify potential subjects.
4. **If print and media advertisements will be used, specify when, where, how long and frequency of the advertisements that will be published/aired:** or N/A
 - a. Check to confirm that any necessary permission will be obtained for posting/airing these (for example, permission to post a flyer on a bulletin board).
5. **If recruitment material is being mailed or otherwise distributed, submit the proposed material and describe where/how the distribution list will be obtained:** or N/A
6. **Describe how the recruitment methods described will be effective in attracting the targeted subject population:** N/A

D.4.2 Study-Wide Recruitment Methods

Is this a multicenter study where subjects will be recruited by methods not under the control of the local Tufts site (e.g., call centers, national advertisements)?

Yes No

D.4.3 Payment

Will subjects receive money, gifts, or any other incentive for participating in this study?

This does not include reimbursement for expenses, which is considered in the next section.

Yes No

D.4.4 Reimbursement

Will subjects be reimbursed for their expenses, such as travel, parking, meals, or any other study related costs?

Yes No

E. Costs to Subjects

Does the research involve any costs to subjects?

Yes No

F. Study Design

F.1 Study Timelines

1. ***Describe the duration of an individual subject's participation in the study:*** Subjects will participate in the study just for the duration of the peripheral intravenous catheter insertion and for the time it takes them to answer the short questionnaire before and after the peripheral intravenous catheter insertion.
2. ***Describe the duration anticipated to enroll all study subjects at the Tufts study site:*** Up to 1 year
3. ***Describe the estimated date for investigators to complete this study (complete primary analyses):*** 1.5 years from the onset of the study.

F.2 Procedure

Co-I's will be CA-1 (PGY2) anesthesiology physician residents at St. Elizabeth's Medical Center. They all will have approximately the same level of performing informed consent and of performing peripheral intravenous catheter insertion. The PI will be an anesthesiology attending physician who will ensure that all of the Co-I's are well versed on the study protocol, informed consent process, use of intradermal lidocaine, use of Buzzy® device, and the peripheral intravenous catheter insertion technique. The Co-I's will utilize the Operating Room Scheduling Board to learn about the scheduled patients for the day. All of these patients will require a peripheral intravenous catheter for the scheduled procedure. If the patient does not yet have a working peripheral intravenous catheter, the Co-I will approach his/her patient and as part of the anesthesia consent process will explain that the Co-I will need to place a peripheral intravenous catheter, so that the patient can receive anesthesia during the operation. While obtaining consent for anesthesia, the Co-I will identify if the patient fits the inclusion criteria for the study and does not meet any of the exclusion criteria. If the patient does satisfy the inclusion criteria, then the Co-I will explain that insertion of a peripheral intravenous catheter may cause some discomfort. The Co-I will explain that some providers at this institution choose to administer the peripheral intravenous catheter without any pain preventative techniques while some choose to inject a numbing medication under the skin prior to the placement of the peripheral intravenous catheter. Also, some providers at other institutions use the Buzzy® device, which is a combination of an ice pack and a vibrator in the shape of a bumble bee, to place a peripheral intravenous catheter on children. This device is FDA approved. There is significant literature documentation that this Buzzy® device helps children feel less pain with peripheral intravenous catheter placement; however, the Buzzy® device has not been utilized that much in adult patients. The Co-I will explain that we are conducting a study to compare the effectiveness of Buzzy® device to that of the injection of the numbing medication under the skin. The Co-I will then ask

whether the patient may be interested in learning more about the study and potentially partaking in the study. If the patient says yes, then the Co-I will go over the consent form with the patient and explain that if the patient chooses to partake in the study, then he/she will randomly receive either the Buzzy® device or the numbing injection. The Co-I will answer any questions that the patient may have. If the patient consents to partaking in the study, then the Co-I will follow the randomization sheet with which pain-relieving technique to be administered to the patient. The Co-I will administer the appropriate technique and place the peripheral intravenous catheter.

Specifics of how the two interventions will be performed:

Experimental group - *Buzzy® device*: Subjects in this group will have the Buzzy® device applied to them. The Buzzy® consists of two components: (1) body of the bee, which provides vibration, and (2) removable and reusable ice wings, which provide the cold sensation. The body of the bee is powered by two alkaline AAA batteries, which could last for approximately 20 hours. There is a manual switch on the top part of the body of the bee that is used to activate and deactivate the vibration. The removable set of ice wings contain a total of 18 grams of ice and can stay frozen for about 10 minutes when exposed to room temperature. The Co-I who will be applying the Buzzy® device will follow the manufacturer's (MMJ Labs, Atlanta, Georgia, USA) recommendations and will (1) retrieve the set of ice wings from the freezer in the Preop Unit immediately before the peripheral intravenous catheter procedure, (2) insert the ice wings through the elastic bands fixed on the back of the Buzzy® device, (3) secure the Buzzy® device on the subject's arm with a reusable tourniquet, about 3-5cm proximal to where the peripheral intravenous catheter will be inserted, (4) turn the manual switch of the device on, (5) clean and prepare the area where the peripheral intravenous catheter will be inserted, (6) insert the peripheral intravenous catheter approximately 60 seconds after the Buzzy® device was applied, (7) keep the device turned on throughout the procedure, until at least the needle is removed, (8) remove the Buzzy® device and clean both components of the device (body of bee and ice wings) with a disinfectant cleaner, (9) and place the ice wings back in the freezer of the unit for a subsequent procedure.

Control group - *Intradermal lidocaine 2%*: Subjects in this group will have the intradermal lidocaine 2% administered to them. An individual vial of Lidocaine 2% will be utilized per subject. The lidocaine will be drawn up into a 3cc syringe, using a 25G needle. The Co-I will apply a reusable tourniquet to the subject's arm about 3-5cm proximal to where the peripheral intravenous catheter will be inserted. The area where the peripheral intravenous catheter will be inserted will be cleaned with an alcohol wipe. Lidocaine will then be injected intradermally, forming a small wheel underneath the skin. Within about 60 seconds of the intradermal injection, the peripheral intravenous catheter will be inserted. The remains of the lidocaine, lidocaine vial, needle, and syringe will be properly disposed into the sharps container.

The Co-I will fill out the top part of the questionnaire that is found below and ask the subject to fill out the bottom half of the questionnaire. The subject will then place the questionnaire into an envelope, without revealing the answers to the Co-I. This way the subject may feel more comfortable answering the questionnaire truthfully.

Once all subjects are enrolled, the data from the questionnaires will be entered into an excel sheet by one of the Co-I's. Data entry will be re-checked by another research team member to assure accuracy of data entry. Once data entry is complete, one of the Co-I's will perform the statistical analysis and the statistical analysis will be re-checked by a second research team member.

[Please note that we are aware that because of the current COVID-19 pandemic, most non-COVID-19 related studies are being placed on hold to minimize unnecessary interactions with patients. However, we would appreciate consideration of this study being done now since all the people that will be obtaining consent and conducting the study will be the essential personnel that will either way (regardless of whether the study will be taking place) will be taking care of these patients and placing those peripheral intravenous catheters. We believe that in such difficult times, any possible pain relief would be a significant benefit for patients. Furthermore, partaking in this study could be a nice distraction for these patients during these difficult times in the world.]

Below is the questionnaire that will be filled out for every subject:

Buzzy vs Intradermal Lidocaine for Peripheral Intravenous Cannulation in Adults
QUESTIONNAIRE

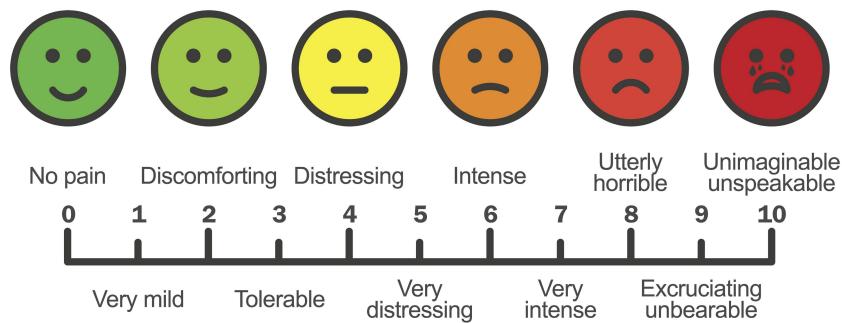
Questions to be answered by the Research Team:

Buzzy vs Intradermal Lidocaine for Peripheral Intravenous Cannulation in Adults

QUESTIONNAIRE

Questions to be answered by the Patient:

1) Please circle a number 0 to 10 in regard to how painful was the IV placement?



2) Please circle how satisfied you are with the IV placement?

Very Dissatisfied	Dissatisfied	Neither Satisfied nor Dissatisfied	Satisfied	Very Satisfied
(1)	(2)	(3)	(4)	(5)
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

2. *Is there a placebo control arm?*

Yes No

1. *Describe the following concerning pregnancy testing and birth control:*

- a. *What type of pregnancy testing and how frequently will be conducted on women of reproductive potential. If testing will not be conducted provide the reason:* N/A
- b. *What birth control methods women of reproductive potential will be instructed to use. If women will not be instructed about acceptable methods of birth control, clarify why:* N/A
- c. *What birth control methods men of reproductive potential will be instructed to use. If men will not be instructed about acceptable methods of birth control, clarify why:* N/A

2. *Describe the data that will be collected during the study and how the data will be obtained:*

- a. *If there are plans for long-term follow-up (once all research related procedures are complete), describe the data will be collected during this period:* or N/A

3. *Specify which procedures, tests, visits, etc. described above are part of usual standard of care at Tufts and which are performed solely for research purposes:* Insertion of intravenous catheter is part of the usual standard of care. The use of the Buzzy® device is not part of the current standard of care in adult patients at SEMC.

4. *Specify which tests are routinely performed for clinical care, but are providing data for the research, and which tests are only performed for research purposes:* No tests will be performed for the purposes of this study.

5. *For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.* or N/A

F.3 Evaluations

Will you perform any laboratory tests for this study?

Yes No

F.4 Collection and Storage of Human Biological Specimens (Tissue Banking)

Will biological specimens be stored for future, unspecified, research?

Yes No

G. Ethics and Protection of Human Subjects

G.1 Informed Consent Process

Will subjects be required to provide informed consent?

Yes No

If Yes, respond to all of the following:

1. *Where the consent process will take place (e.g. a private clinic room):* In the preoperative room.
2. *Anticipated amount of time a potential subject will have to make a decision about participation in the study:* About 5 minutes
3. *Processes to ensure ongoing consent throughout the study:* The PI will randomly observe the investigators obtaining consent to ensure that the consent continues to be done properly.

4. **Role of each research team member involved in the informed consent process (please note, for a biomedical study, a physician PI or Co-I should perform the informed consent process with subjects. A study coordinator may assist with this process; however, the PI or Co-I should be present to discuss the study with the subject and answer any questions, and the PI or Co-I should sign the ICF documenting that s/he has performed the informed consent process with the subject):** The PI (anesthesiology attending) and Co-I's (anesthesiology residents) of the study will be the ones that will be taking care of the subjects. They are the ones that will be consenting subjects for the study. They are all experienced in consenting patients because they do that on a daily basis, as part of their job, prior to administering anesthesia. The PI and Co-Is will not be at an increased risk to COVID-19 because of this study because the study members will be the ones who will be taking care of the subjects while the subjects are getting the peripheral intravenous catheter insertion and later on when the subjects will be receiving anesthesia for the scheduled surgeries, regardless whether the subjects choose to partake in this study.
5. *Check to confirm you will follow “[SOP: Informed Consent Process for Research \(HRP-090\)](#)”.*
If not, answer all of the following:
 - a. *Steps that will be taken to minimize the possibility of coercion or undue influence:*
 - b. *Steps that will be taken to ensure subjects' understanding:*
6. *Check to confirm that Non-English speakers will be enrolled using interpreters and IRB approved Short Forms per the [IRB's Short Form policy](#). If IRB approved Short Forms will not be used, describe which languages the consent will be fully translated into, who will conduct the consent interview, use of interpreters, use of IRB approved translated documents, etc.:*
7. *If non-English speakers are not eligible (excluded from enrollment) for this study, provide the ethical and scientific justification, including whether this would be equitable. For example, if non-English speakers are eligible for the study and could potentially benefit from participation, it would not be equitable to exclude them: N/A - non-English speakers are eligible for this study.*
8. *Check to confirm you will follow “[SOP: Written Documentation of Consent \(HRP-091\)](#)”.* *If not, describe how consent will be documented in writing:*
9. *Check to confirm you will follow “[SOP: Remote Consent Process \(HRP-092\)](#)” if there is ever a situation where consent will **not** be obtained in person. If you will follow a different process if there is ever a situation where consent will **not** be obtained in person, describe: N/A*

G.2 Waiver or Alteration of Consent Process

1. Is a waiver or alteration of the consent process being requested for this study?
 Yes **No**
2. Is a waiver of the consent process being requested for parents for research involving children?
 Yes **No**
3. Is a waiver of the consent process for planned emergency research being requested?
 Yes **No**

G.3 International Research

Refer to the IRB's [International Checklist](#) and [International Guidance](#) and include all relevant information described in those documents in this protocol: N/A

G.4 Confidentiality

1. *State where the study records, both electronic and/or paper documents including signed ICFs/assent forms, will be retained during the study (state the location for original document plus any copies that are*

made, e.g., if a copy of the ICF will be retained in the subject's medical record): The study records will be retained in a locked cabinet in Dr. Michael Schoor's office, in St. Elizabeth's Medical Center.

2. *State where study records will be retained when the study has been closed (long-term storage):* Study records will remain in a locked cabinet in Dr. Michael Schoor's office.

3. *State who, in addition to the research team, will have access to the study files, data, and/or specimens:* No one outside the research team will have access to the study files or data.

4. *Will data (or specimens) be sent outside of Tufts Medical Center or Tufts University and/or sent between Tufts Medical Center and Tufts University?*
 Yes No

5. *Explain how data and/or specimens will be transported (e.g. fax, mail, delivery, email, etc.):* Data will be transported for analysis purposes via the Tufts email, utilizing the word [SECURE] in the subject area to ensure confidentiality and security of the data.

6. *Explain how data and/or specimens will be coded. Specify if there is a key to the code that matches the subjects' study identification number with their name and who, in addition to the research team, will have access to it:* N/A

7. *Explain whether confidential genetic information will be collected from subjects:* or N/A

8. *Explain whether audio/videotapes and/or photographs of subjects could potentially identify the study subject. If so, indicate who will have access to (be able to view) these item, in addition to the research team, and how long the videotapes or photographs will be retained for the study and what the plan is for their destruction:* or N/A

9. *Check to confirm that study records will be retained for the timeframe described in the record retention policy of the "[SOP – Records Retention Timeframe – Investigators](#)". If they will not, describe the record retention plan for this study:*

10. *Check to confirm that you will follow the "[Confidentiality and Data Security Guidelines for Electronic Research Data](#)" for electronic data. If not, describe how your plan differs from these guidelines:*

11. *A Certificate of Confidentiality will be issued (for NIH studies) or obtained:* Yes N/A

G.5 Screening Data Collection Form/Screening Log

Will a screening data/screening log be used in this research study?

Yes No

G.6 Provisions to Protect the Privacy Interests of Subjects

1. *Describe the steps that will be taken to protect subjects' privacy interests (e.g. ensuring that discussion of the study will take place in a private area where subjects cannot be overheard):* N/A. This study involves the placement of a peripheral intravenous catheter, which is a procedure that is done on all patients that are about to undergo an operation/surgical procedure.

2. *Describe the steps that will be taken to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might or might not experience in response to questions, examinations, and procedures (e.g. ensuring that subjects are comfortable with the research team members performing the study procedures):* Patients will be explained that they can ask any

questions that they would like and if anything does not feel right to them at any moment, they are encouraged to speak up immediately. The study members that will be obtaining consent are experiencing in obtaining consent, since they are anesthesia providers.

G.7 Provisions to Monitor the Study to Ensure the Safety of Subjects

1. *Describe the plan to periodically evaluate the data regarding both harms and benefits to assess subject safety as follows:*
 - a. *The data that will be reviewed, including safety data, untoward events, and efficacy data:* This study involves no to very minimal risk to subjects. No interim data analysis is planned at this time.
 - b. *Who will review the data:* N/A
 - c. *How the safety information will be obtained and documented (e.g., case report forms, by telephone calls with participants, printouts of laboratory results, etc.):* No adverse reactions are expected from this study; however, if, in theory, one were to occur, it would be reported in the form of a case report format.
 - d. *The frequency of data collection, including when safety data collection starts:* As described above, data will be collected per subject. Subjects remain enrolled in the study only for the duration of the peripheral intravenous catheter insertion and for the quick survey that will take place immediately after the peripheral intravenous catheter insertion. Since this study involves no to very minimal risk to subjects, if an adverse reaction occurs at any point, then it will be reported.
 - e. *The frequency or periodicity of review of cumulative data:* Data will only be analyzed once the study is complete.
 - f. *The statistical tests for analyzing the safety data to determine whether harm is occurring:* N/A
 - g. *Any conditions that trigger an immediate suspension of the research or other action for the research:* N/A
2. *Describe the entity responsible for monitoring the data, and their respective roles (e.g., the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a Data and Safety Monitoring Board (DSMB) /Data Monitoring Committee (DMC), and/or some other entity, and the timeframe for reporting events to this entity:* N/A
3. *A copy of the DSMB/DMC Charter if the study is enclosed with the submission:* Yes N/A

G.8 Vulnerable Populations

1. *Can or will pregnant women be enrolled?*

Yes No

If Yes, respond to all of the following:

- a. *Describe any preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, that have been conducted that provide data for assessing potential risks to pregnant women and fetuses:* N/A
- b. *Are there any risk to the fetus from the study interventions or procedures. If yes, describe:* No, *there are no risks to the fetus from the study interventions or procedures*
- c. *Do the study interventions or procedures hold out the prospect of direct benefit for the woman or the fetus. If yes, describe:* No, *the study interventions or procedures do not hold out the prospect of direct benefit for the woman or the fetus.*

d. *If there is no prospect of benefit to the fetus, clarify whether the risk to the fetus is NOT greater than Minimal Risk, and whether the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means:* N/A

e. *The biomedical knowledge that is expected to result from this research for this population:*

f. *How any risk of this research is the least possible for achieving the objectives of the research:* N/A

g. *How mothers providing consent are informed of the reasonably foreseeable impact of the research on the fetus or neonate:* N/A

h. *Check to confirm that no inducements, monetary or otherwise, will be offered to terminate a pregnancy and that in the case of a fetus, the fetus is not the subject of a planned abortion.*

i. *Check to confirm that individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy or in determining the viability of a neonate.*

2. **Can or will the research involve neonates of uncertain viability or non-viable neonates?**

Yes No

3. **Can or will subjects who are not yet adults (neonates, children, teenagers) be enrolled?**

Yes No

4. **Can or will minors who are:**

- i) married, widowed, divorced; or
- ii) the parent of a child; or
- iii) a member of any of the armed forces; or
- iv) pregnant or believes herself to be pregnant; or
- v) living separate and apart from his/her parent or legal guardian, and is managing his/her own financial affairs

be approached for study participation for either themselves or their child?

Yes No

5. **Can or will wards of the state and/or children at risk of becoming wards of the state be enrolled (this includes foster children or any child that is in state custody)?**

Yes No

6. **Can or will cognitively impaired adults (adults with impaired-decision making capacity) or adults who may lose the capacity to consent be enrolled?**

Yes No

7. **Can or will prisoners be enrolled?**

Yes No

8. **Can or will students and/or employees be targeted for enrollment in this research?**

Yes No

9. **Transgender Subjects: Are you recording sex or gender for your study?**

Yes No

a. Is there a scientific and/or safety rationale for collecting information on whether a subject is transgender? Yes No

If **Yes**, respond to all of the following:

- i. **Provide the scientific/safety rationale for collecting information on whether a subject is transgender:** We do not want to exclude subjects from enrolling into the study based on sex or gender. We feel it is important to know whether the sex of the subject because that could be a confounding variable in terms of how one describes anxiety, pain, and satisfaction.
- ii. **Are transgender individuals eligible for participation in this study?** Yes No
If **No**, *Provide the scientific or safety rationale for excluding transgender or gender nonconforming individuals:*
- iii. **Check to confirm that relevant questions for transgender and gender nonconforming individuals have been incorporated into relevant study documents (i.e. protocol eligibility, screening forms, demographic questionnaires, surveys), per the [website guidance](#).**

H. Adverse Event Monitoring

H.1 Definitions

Define adverse events (AEs), serious adverse events (SAEs), and unanticipated problems for your study:
N/A

H.2 Reporting Procedures

1. *Describe the protocol-specific reporting procedures, including who will be responsible for each step (e.g., PI, Data Coordinating Center, Medical Monitor), which forms should be completed, timeframes for reporting, how reports will be distributed, and what follow-up is required:* N/A
2. *Include specific details of reporting procedures for:*
 - a. Deaths, life-threatening events, pregnancies: N/A
 - b. Other SAEs: N/A
 - c. Other AEs: N/A
 - d. Other UPS: N/A

H.3 Reportable New Information

Check to confirm that reportable new information will be reported to the IRB per the Tufts Health Sciences IRB's [Reportable New Information policy](#). If your reporting plan to the IRB differs from the IRB's policies, please describe it in detail or specify where this information is in the protocol:

I. Statistical Considerations

I.1 Study Endpoints

1. *Describe the primary and secondary study endpoints:* Primary study endpoint: Pain rating of the peripheral intravenous catheter insertion; Secondary study endpoint: Satisfaction rating of the peripheral intravenous catheter insertion
2. *Describe any primary or secondary safety endpoints:* N/A

I.2 Statistical Analysis

1. *Describe the statistical analyses that will be performed for this study:* Continuous variables will be analyzed via the Student's t-test and presented as mean +/- standard deviation. Categorical data will be analyzed via Chi-square test and presented as number and percentages. The intention-to-treat analysis will be used in this study. A P-value <0.05 will be considered statistically significant.
2. *Provide a power analysis:* Since there is currently no published study available comparing the two interventions that we plan on studying, we chose the study sample size based on the sample size rule of thumb for medical trials.¹³ The purpose of this study is to conduct a preliminary pilot trial for a potential future main trial designed with 90% power and two-sided 5% significance.

I.3 Number of Subjects

1. *Specify the number of subjects to be enrolled in total across all sites:* or N/A this is not a multicenter study.
2. *Specify the number of subjects to be enrolled at the Tufts site. Subjects who sign an ICF are considered “enrolled”. For studies that have a separate screening ICF, this number is the number of subjects who sign a screening ICF:* The goal will be to have a total of 30 subjects sign an ICF and complete the study based on the previously published sample size rule of thumb for medical trials.¹³
 - a. *Provide the rationale for enrolling this number of subjects at the Tufts site:* Although unlikely, subjects might sign ICF and then change their mind within a few minutes while the research team member is preparing to perform the peripheral intravenous catheter insertion. To ensure we have 30 subjects complete the study, we will enroll up to 40 subjects in this trial.
 - b. *Estimate the number of subjects expected to be enrolled at the Tufts site (i.e. sign the screening or study ICF) as well as the number needed to complete the study at the Tufts site:* Subjects will only be enrolled in the study for the duration of the peripheral intravenous catheter insertion procedure and the time it takes to answer the questionnaire; therefore, in theory, only one or two subjects will be enrolled at the same moment.
 - c. *If a large number of withdrawals and/or dropouts is expected, explain why:* N/A

I.4 Data Management

1. *Describe the data analysis plan, including descriptions of the data:* The only data that will be collected is what is described in the questionnaire above.
2. *Provide a power analysis:* As described above, since there is currently no published study available comparing the two interventions that we plan on studying, we chose the study sample size based on the sample size rule of thumb for medical trials.¹³ The purpose of this study is to conduct a preliminary pilot trial for a potential future main trial designed with 90% power and two-sided 5% significance.
3. *Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission:* Data will be collected in an envelope and stored in a locked cabinet in the PI's office. Only the research team members will have access to the data for analysis purposes. Data will not have subject identifying information on it.
4. *Describe any procedures that will be used for quality control of collected data:* Data entry will be confirmed by two research team members.
5. *Describe how data and specimens will be handled study-wide as follows:*
 - a. *What information will be included in that data or associated with the specimens:* Please see section “F.2 Procedures” for the data that will be collected. No specimens will be collected.
 - b. *Where and how data or specimens will be stored:* Data will be stored in a locked cabinet in the PI's office (as described above).
 - c. *How long the data or specimens will be stored:* Data will be stored at least until the results of the study will be published.
 - d. *Specify who will have access to the data or specimens:* The Research team will have access to the data.
 - e. *Specify who is responsible for receipt or transmission of the data or specimens:* The PI will be responsible for the receipt of the data.

- f. **Specify how data and specimens will be transported:** Data will be transported in a closed envelope from the preoperative area and to the PI's office, where it will be stored in a locked cabinet. If data will need to be transferred between research team members for statistical analysis purposes, the word [SECURE] will be included in the subject line of all emails.
- g. **Specify the plan for study data retention and storage (accounting for research team turnover):** Data will remain secure in the PI's office, in a locked cabinet.

I.5 Randomization

Will subjects be randomized?

Yes No

If Yes respond to all of the following:

1. **Describe the randomization procedures, including the ratio of subjects randomized to each study arm:** We will use <http://www.graphpad.com/quickcalcs/index.cfm> to generate a randomized sequence, with a ratio of subjects 1:1 in each arm. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3136079/>
2. **Describe the blinding procedures:** The Co-I's that will be conducting the statistical analysis will be blinded to which study arm the subjects were assigned to. N/A the study will not be blinded.

J. Drugs or Devices

1. Will the research involve drugs?

Yes No

If Yes, respond to all of the following:

- a. **If the drug is investigational (has an IND) identify the holder of the IND:** The drug, Lidocaine 2%, is not an investigational drug. It is a commonly used drug that is widely available.
- b. **Describe your plans to store, handle, and administer study drugs so that they will be used only on subjects and be used only by authorized investigators** N/A - this drug is used throughout the hospital for many procedures.
- c. **Who on the research team, in addition to the Principal Investigator, will be accountable for drug(s):** The PI and the Co-Is have access to Lidocaine 2% when they are interacting with patients.
- d. **Who will interface with the pharmacy:** The research team members will remove Lidocaine 2% from the Pyxis machine. The pharmacy fills the Pyxis machine.
- e. **If pre-printed orders will be created to obtain study drug(s) from the pharmacy, describe the procedures for reviewing and verifying the accuracy of the pre-printed orders prior to their being implemented:** N/A, there are no pre-printed orders
- f. **If computerized order sets are created and/or infusion devices need to be programmed to administer an investigational drug, indicate the mechanism to pre-review and verify their accuracy, including who will be involved in this process from the research team, pharmacy, and nursing:** or N/A, there are no computerized orders sets and/or infusion devices.
- g. **The study drug or procedure (including beneficial health care procedures) will be available to subjects after participation in the study:** Yes N/A
- h. **There are medications or other substances that should not be taken while participating in the study. A list of these are incorporated into the ICF or submitted to the IRB as a subject handout:** Yes N/A

i. *Handouts or instructions sheets that will be given to subjects on how to administer study drug(s) have been submitted to the IRB:* Yes N/A

2. Will the research involve devices?

Yes No

If Yes, respond to all of the following:

- a. *If the device has an IDE or a claim of abbreviated IDE (non-significant risk device) identify the holder of the IDE/Abbreviated IDE:* N/A
- b. *Describe your plans to store, handle, and administer study devices so that they will be used only on subjects and be used only by authorized investigators* The device does not have to be locked up and can be used by healthcare providers outside the study. This device is widely used throughout other hospitals.
- c. *Specify who will be responsible for the costs of implantation or placement of the device in subjects' bodies?*: or N/A, the device will not be implanted or placed inside the body.
- d. *Specify who will be responsible for the costs of removing the device from subjects' bodies?*: or N/A, the device will not be removed from the body.
- e. *Specify the cost of the device and who will be responsible for the cost:* The SEMC anesthesiology department will be responsible for the cost of the device. Buzzy® XL Healthcare price is \$99.95. It is designed for multi patient disinfection. or N/A, the device will be provided free of charge.
- f. *Who on the research team, in addition to the Principal Investigator, will be accountable for device(s):* The co-investigators.
- g. *Who will interface with the sponsor:* N/A
- h. *The study device or procedure (including beneficial health care procedures) will be available to subjects after participation in the study:* Yes N/A
- i. *Handouts or instructions sheets that will be given to subjects on how to use study device(s) have been submitted to the IRB:* Yes N/A

K. Study Administration

K.1 Setting

1. *Describe the sites / locations where your research team will conduct the research:* St. Elizabeth's Medical Center
2. *The research will take place at an international site, and the International Guidance and International Checklist were utilized:* Yes N/A

K.2 Registration

1. *Describe the steps the research team will take to ensure that a subject is appropriately enrolled or registered in the study prior to receiving any study intervention (e.g. describe and submit any protocol eligibility checklist that will be used, specify who on the research team will confirm eligibility and that consent was documented, etc.):* Enrollment into the study will be very shortly after the consent process, so the Co-I who will be obtaining consent will not start performing any procedure until he/she obtains the consent.

K.3 Resources Available

1. *Describe the roles/tasks of each research team member here (or alternatively, you may submit any current Delegation of Authority Log you may have which already has this information completed):* The Co-investigators will be enrolling subjects into the study and will be the ones who will be administering the treatment and collecting data. The PI and the Co-I's will be performing the statistical analysis and reviewing each others computations to ensure accuracy.
2. *Describe the qualifications (e.g., training, experience) of the PI and research team to perform their roles. Provide enough information for the IRB to determine the PI and research team are qualified to conduct the proposed research. Alternatively, you can submit the current CVs for the research team instead:* The PI is an anesthesiology attending at St. Elizabeth's Medical Center. The Co-I's are second year anesthesiology resident physicians (aka CA-1's). They have all at least completed medical school training and one year of residency. They are all qualified to obtain consent from patients and have significant experience doing so.
3. *Describe the coverage plan to address any issues (including subject safety issues) that occur while the PI is away and/or unavailable. The research team member designated to serve as the acting PI in the PI's absence should have similar training and expertise as the PI:* N/A
4. *Describe the process to ensure the research team members have adequate oversight and are adequately trained regarding the protocol, study procedures, and their roles and responsibilities:* Prior to enrollment of subjects, the PI will review the protocol, study procedures, and roles/responsibilities with each one of the Co-I's.
5. *Medical or psychological resources that subjects might need, such as for emergencies or medical issues, are available for the study:* Yes N/A

K.4 IRB Review

1. *Check to confirm that an appropriate IRB registered with the OHRP, will review and approve this study.*
2. *Check to confirm that any amendments to the protocol or informed consent documents will be reviewed and approved by the IRB prior to use, unless required to eliminate an apparent immediate hazard to subjects.*

K.5 Multi-Site Research

Is this a multi-site study where Tufts is the sponsor, primary grant recipient, or coordinating site?:

Yes No

K.6 Community-Based Participatory Research

Can or will this study involve community-based participatory research?

Yes No

K.7 Sharing Results with Subjects

Will results (overall study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) be shared with subjects or others (e.g., the subject's primary care physician or the subject's treating physician)?

Yes No

L. References

Provide a list of references for all citations included in the protocol

1. Hadaway L. Short peripheral intravenous catheters and infections. *Journal of infusion nursing : the official publication of the Infusion Nurses Society*. 2012;35(4):230-240.
2. Wallis MC, McGrail M, Webster J, et al. Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. *Infection control and hospital epidemiology*. 2014;35(1):63-68.
3. Chen BK, Cunningham BB. Topical anesthetics in children: agents and techniques that equally comfort patients, parents, and clinicians. *Current opinion in pediatrics*. 2001;13(4):324-330.
4. Hijazi R, Taylor D, Richardson J. Effect of topical alkane vapocoolant spray on pain with intravenous cannulation in patients in emergency departments: randomised double blind placebo controlled trial. *BMJ (Clinical research ed)*. 2009;338:b215.
5. Ehrenstrom-Reiz G, Reiz S, Stockman O. Topical anaesthesia with EMLA, a new lidocaine-prilocaine cream and the Cusum technique for detection of minimal application time. *Acta Anaesthesiol Scand*. 1983;27(6):510-512.
6. Richman PB, Singer AJ, Flanagan M, Thode HC, Jr. The effectiveness of ice as a topical anesthetic for the insertion of intravenous catheters. *Am J Emerg Med*. 1999;17(3):255-257.
7. Redfern RE, Micham J, Sievert D, Chen JT. Effects of Thermomechanical Stimulation During Intravenous Catheter Insertion in Adults: A Prospective Randomized Study. *Journal of infusion nursing : the official publication of the Infusion Nurses Society*. 2018;41(5):294-300.
8. Agarwal A, Yadav G, Gupta D, Tandon M, Singh PK, Singh U. The role of a flash of light for attenuation of venous cannulation pain: a prospective, randomized, placebo-controlled study. *Anesth Analg*. 2008;106(3):814-816, table of contents.
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10. Baxter AL, Leong T, Mathew B. External thermomechanical stimulation versus vapocoolant for adult venipuncture pain: pilot data on a novel device. *The Clinical journal of pain*. 2009;25(8):705-710.
11. Bond M, Crathorne L, Peters J, et al. First do no harm: pain relief for the peripheral venous cannulation of adults, a systematic review and network meta-analysis. *BMC anesthesiology*. 2016;16(1):81.
12. Mendell LM. Constructing and deconstructing the gate theory of pain. *Pain*. 2014;155(2):210-216.
13. Whitehead AL, Julious SA, Cooper CL, Campbell MJ. Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. *Statistical methods in medical research*. 2016;25(3):1057-1073.