What is PAIN?

The Prehospital Analgesia INtervention Trial, or simply PAIN, is a research study that is being done to compare two pain medications, fentanyl and ketamine, in patients with traumatic injuries who need treatment for pain before they get to the hospital.

The management of pain following a serious injury is an essential part of caring for an injured patient. Opioids, like fentanyl, are commonly used to treat pain. This study compares fentanyl to ketamine, which is not an opioid, to see if people have fewer or less severe side effects with one medication over the other. We will look at the results from this study to better understand the best way to treat pain in future trauma patients.

What makes this an Exception from Informed Consent (EFIC) study?

Visit the link or ask the study team (PAINStudy@uvmhealth.org) for details on why this study is being conducted with an exception from informed consent. › https://www.litesnetwork.org/projects/emergency-research

How is this study regulated?

Visit the link or ask the study team (PAINStudy@uvmhealth.org) for details on how this and all EFIC studies are regulated and monitored › https://www.litesnetwork.org/projects/emergency-research

Who will be included?

PAIN will include adults who are:

- Males 18 years and older and females 50 years and older
- Severely injured patients that require pain medication through an IV
- Patients being transported to a hospital participating in PAIN

Where is this study being done?

This study is being done at the following trauma centers across the country:

- UPMC Presbyterian Hospital and UPMC Mercy Hospital (Pittsburgh, PA)
- Allegheny General Hospital (Pittsburgh, PA)
- Cooper University Hospital (Camden, NJ)
- Froedtert Hospital (Milwaukee, WI)
- UC San Diego Medical Center (San Diego, CA)
- Zuckerberg San Francisco General Hospital (San Francisco, CA)
- University of Cincinnati Medical Center (Cincinnati, OH)
- University of Utah Hospital (Salt Lake City, UT)

- Carolinas Medical Center (Charlotte, NC)
- Robert Packer Hospital (Sayre, PA)
- University of Vermont Medical Center (Burlington, VT)
- University of Wisconsin University Hospital (Madison, WI)

How long will this study last?
This study will enroll up to 994 patients over several years. As with all LITES EFIC projects, updates to the study status will be posted to https://clinicaltrials.gov/study/NCT05437575

Who is funding this study?
This research is supported by Department of Defense (DoD) contract W81XWH-16-D-0024, Task Order W81XWH19F0539 with the goal of providing evidence-based, life-saving techniques and strategies for providing the best trauma care.

Why pain management in the prehospital setting?
Trauma patients with severe injuries need to receive pain medications quickly. Giving pain medication as soon as possible after severe injury has many benefits, including:

- Reduced suffering
- Allow EMS providers to give lifesaving treatments (ex. tourniquets, splinting) more easily
- May lessen health problems caused by the injury
- May decrease long term problems such as chronic pain and post-traumatic stress disorder (PTSD)

Why are these medications part of a research study if they are both used by paramedics?
The management of pain after a severe injury is an essential part of caring for an injured patient. Opioids, like fentanyl, are commonly used to treat pain. This study will compare fentanyl to ketamine, which is not an opioid, to see if people have fewer or less severe side effects with one medication over the other. Fentanyl and ketamine are both currently used to treat pain in patients before they get to the hospital, but it is not known if one is safer for patients with traumatic injuries. We are doing this study to find out if one medication is safer than the other.

What are the risks of these medications? Are there any benefits?
Patients in the study will receive either fentanyl or ketamine for pain management.

Any pain medicine has potential risks; however, these are rare, especially in the low doses that will be given in this study. Fentanyl can be associated with low blood pressure, low oxygen

levels, and the need for a breathing tube. In some cases, ketamine may cause hallucinations, agitation, anxiety, or feelings of disconnectedness.

We are unsure if there are benefits to receiving one medication over the other, but researchers think that a low dose of ketamine may be better at lowering the risk of death and serious health effects for seriously injured patients who are in pain.

How are people enrolled in the study?

People may be enrolled in the PAIN study if they have severe injuries, need pain medicine, and are being taken to a hospital participating in the PAIN study.

Normally, researchers must ask a person for their consent before they can be in a study – this means reading information, talking with doctors and nurses, and having time to think about whether to join. Severe traumatic injuries must be treated right away, so there may not be time for an injured person to give consent for the PAIN trial. Sometimes researchers can talk to the patient's family to ask for consent. However, in the emergency of traumatic injury, the family is often not around or can't be found before the injured person must be treated.

This study could not be done without special permission to include people before getting consent. This permission is called Exception From Informed Consent, or EFIC. Once the enrolled person is better and can consent or their family arrives at the hospital, the researchers will ask for consent to continue with the study. For more information regarding EFIC, please visit: https://www.litesnetwork.org/projects/emergency-research

How do I opt out of the study?

You can opt-out of the study by calling 1-800-664-0557, emailing PAINstudy@edc.pitt.edu, or by filling out the form at the bottom of www.LITESnetwork.org/PAIN so the LITES Network can provide you with a hypoallergenic silicone bracelet to wear that indicates that you should not be enrolled into the study.

If you wish to refuse participation in the study following an injury, you can refuse at the time of treatment by EMS. Please note that opting out of the study only means that you will not be part of the study. Opting out will not prevent you from getting pain medication as part of your normal care.

What happens if a person receives the opt out bracelet, but isn't wearing it at the time of being taken by EMS?

If you receive an opt out bracelet but are not wearing it at the time of your injury, it is possible you could be enrolled in the study, unless you or someone accompanying you are able to say that you do not want to be included in the research. If this happens, you may receive study medication, fentanyl citrate or ketamine hydrochloride, which are both commonly given to injured patients to treat pain.

Please note that opting out of the study only means that you will not be part of this study. Opting out will not prevent you from getting pain medication (potentially including one of these two medications) as part of your normal care.

If I decide to participate in the follow-up calls, what are my obligations during the 6 month follow up period? What tests and appointments should I expect?

The six-month follow-up is completely voluntary. If you do not want to participate, you won't be contacted by the study team.

If you wish to participate and consent, there are no additional medical tests or appointments. Instead, you will provide your contact information to the study team and fill out a survey about your experience with pain, anxiety and pain medications. The study team will contact you again at 3 months and 6 months to ask similar questions about ongoing pain, pain medications, anxiety and post-traumatic stress disorder. You can choose to stop participating in these surveys at any time.

What happens if someone chooses not to participate?

Participation in the study can stop at any time – the patient or appropriate family member just needs to tell the study team.

If at any point the patient, or their family member if they are incapacitated, states that they don't want to participate, that is their right. If this happens before study medication is given, the patient will be treated according to standard medical care for their condition including receiving pain medication which may include either fentanyl citrate or ketamine hydrochloride.

In the hospital, research staff will explain the study to the patient and their family members and ask for consent for the patient to continue in the study. If the patient, or their family member if they are incapacitated, does not consent or states that they don't want to participate during this conversation or any time after study medication is given, review of their medical records (for

safety and to see if one medication may be better than the other) will stop and they will not complete the study surveys.

If enrolled into the study, will I be able to find out which medication I received?
Patients enrolled in FDA-approved EFIC studies are generally not told which of the medications they received when the study is blinded. This means neither the patient nor their doctor is told which medication is given to prevent any bias against the drug. Both the patient and the doctor will be informed that the patient received the study drug, which is either fentanyl citrate or ketamine hydrochloride. Both medications are commonly used to treat pain. If something were to happen where the doctor caring for the patient needs to know which was given, a plan is in place to give that information quickly.

Is it possible that a future study may administer vaccinations to patients without consent?
The PAIN study is not a vaccine trial and vaccine research is out of the scope of practice for the LITES Network. Therefore, we cannot speculate about vaccines being assessed with an Exception From Informed Consent study.