Office of Clinical Research CRP First Friday

EFIC (Exception From Informed Consent): Trauma Research

Friday, November 3rd, 2023

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Learning Objectives:

1) Explain when EFIC studies are necessary..

2) Identify concerns a community may have with EFIC.

3) Name multiple ongoing EFIC trials in Trauma, active in our community

Target Audience:

Clinical Research Professionals (CRPs) at UC/H and Cincinnati Children's Hospital Medical Center (CCHMC): including Principal Investigators (PIs), Research Nurses (RNs), Critical Care Unit Nurses (RNs), Pharmacy Technicians and Regulatory Specialists.

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The University of Cincinnati is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The University of Cincinnati designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Participants should claim only the credit commensurate with the extent of their participation in the activity.

CRPs, NPs, PAs, and RNs can count activities certified for *AMA PRA Category 1 credit*™ for professional credit reporting purposes. Other healthcare professionals should inquire with their certifying or licensing boards.

Disclaimer Statement

The opinions expressed during the live activity are those of the faculty and do not necessarily represent the views of the University of Cincinnati. The information is presented for the purpose of advancing the attendees' professional development.

Off-Label Disclosure Statement:

Faculty members are required to inform the audience when they are discussing off-label, unapproved uses of devices and drugs. Physicians should consult full prescribing information before using any product mentioned during this educational activity.

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In accordance with the ACCME Standards for Integrity and Independence in Accredited Continuing Education and the University of Cincinnati policy, all faculty, planning committee members, and other individuals, who are in a position to control content, are required to disclose all relationships with ineligible companies* (commercial interests) within the last 24 months. All educational materials are reviewed for fair balance, scientific objectivity, and levels of evidence. The ACCME requires us to disqualify from involvement in the planning and implementation of accredited continuing education any individuals (1) who refuse to provide this information or (2) whose conflicts of interests cannot be mitigated.

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All relevant relationships have been mitigated. The following disclosures were made:

Planning Committee Members:

- Maria Stivers, MS; Course Director – *No Relevant Relationships*
- Nathaniel L. Harris, BS, Course Coordinator – *No Relevant Relationships*
- Heather Muskopf, CME Program Manager – *No Relevant Relationships*

Speaker:

Devin M Wakefield
Clinical Research Professional
University of Cincinnati
Department of Surgery
MSB 2106

No Relevant Relationships

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Compliance Corner

Flu Vaccination Reminder:

Proof of Flu vaccination is due by NOVEMBER 10th, 2023.

This requirement helps us protect our patients and each other during respiratory illness season.

You can receive your shot at any of our Employee Health and Well-being Blitz Days, and proof of your flu shot will be automatically uploaded for you. Blitz Days Information has been sent to your email.

If you receive your flu shot elsewhere:

- **UC Health employees and contractors**: In ReadySet, take the health survey and then upload your vaccine proof. Visit go.uchealth.com/readyset.
- **UCP employees**: Look for directions in your email.

Recently updated OCR Standard Operating Procedures:

- **UCH-OCR-FIN-SOP-002-06: UC Health Research Billing**
- **UCH-OCR-OPS-SOP-014-06: Prompt MIDAS Reporting of Serious Adverse Events that are both Unexpected and Related to the Research**
- **UCH-OCR-REV-SOP-009-06: Ancillary Research Services Review for UC Health Research approval**

All OCR SOPs are accessible from the UC Health intranet home page utilizing the Compliance 360 policy search function or reach out to the Office of Clinical Research with any questions or concerns.

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Thursday, November 16th, 2023, 12:00noon - 1:00pm
IN PERSON Presentation MSB E351 (with the option to join virtually)

Clinical Trial Agreement (CTA/Contract) and Informed Consent Form (ICF) Reviews: When and When Not to Edit

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Nate Harris
Bridget Kellner
Kareemah Mills

University of CINCINNATI

UC / UC Health
Clinical Research Orientation and Training (CRO&T)

Thursday, December 14th, 2023

9:00 am - 3:00 pm

Virtual presentation

The last day of registration is Friday, December 8th, 2023

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Register Here

Please reach out to Nate Harris, harrisnl@ucmail.uc.edu for any questions

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Today's Presentation:

Exception From Informed Consent (EFIC): Trauma Research

Join us for a discussion on Exception from Informed Consent (EFIC) trials for emergency research, specific to Trauma Surgery at UC. There are many EFIC trials that are actively enrolling in our community, and it is important to not only talk about the trials themselves, but explain what scenarios allow them to be conducted. We must also consider what steps have been taken to inform a massive community, who may take part.

Devin M Wakefield
Clinical Research Professional
University of Cincinnati
Department of Surgery

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Exception From Informed Consent (EFIC) – Trauma Research

Devin Wakefield, BSc

- Clinical Research Professional
- UC College of Medicine – Department of Surgery – Trauma Research
- wakefidm@ucmail.uc.edu

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Primary Objectives

After viewing this presentation, listeners will be able to…

- Explain when EFIC studies are allowed
- Identify important steps taken to inform a community
- Name multiple ongoing EFIC trials in Trauma, active in our community

What is EFIC?

Exception From Informed Consent

FDA GUIDANCE DOC 21 CFR 50.24

- Involves participants who are suffering from *life-threatening conditions* in emergent situations
- Urgent Intervention is required where available treatment is unknown/not proven
- No realistic way to prospectively screen patients
- Informed Consent can not be feasibly obtained due to nature of injury or circumstance
- The research must have some evidence of benefit to the subject, and risks considered reasonable given the situation
- Research could not practically be carried out without waiver

Consent Process

True Informed Consent Requires...

1. The capacity to make decisions
2. Disclosure of enough information to make an informed decision
3. The patient's ability to demonstrate understanding of that information
4. The ability to freely authorize treatment

***Does not mean 'Absence' of Informed Consent!**

Consent Process (cont.)

-Consent from participant or LAR should be sought as soon as possible following enrollment in the trial.

-Information of the trial and subjects' involvement must be disclosed

-”What has occurred thus far?”

-Risks and Benefits

-Consent for Continued Participation, and what that entails

-Informing in the event of subject death after enrollment

-Notification Letter sent to LAR

What other steps can be taken so that participants are informed?

Public Disclosure/ Community Consultation

Public Disclosure

Dissemination of information about the emergency research sufficient to allow a reasonable assumption that the communities are aware of the plans for the investigation, its risks and expected benefits.

Community Consultation

A reciprocal process and a genuine partnership between the community and a service provider that embodies human rights principles in a tangible way.

Public Disclosure – Example Recs.

Public Disclosure Menu - Pre-Trial

A (Optional)	B (Required)
Paid online advertisements (banner, block, or video ads purchased from Google, Facebook, YouTube, etc.)	National or local study website (provided by the coordinating center)
Social media/internet postings (YouTube, Facebook, Twitter, etc.)	Press release (template provided by CC)
Mailings (including email circulars/bursts and direct paper mailings)	
Booth/Table Community event	
Outdoor advertising (placards, bus ads, billboards, etc.)	
Television and radio ads (broadcast advertising)	
Newspaper advertisement (and similar print advertising)	
News stories, interviews (print, radio, or TV)	
Newsletters (articles or informational ads, print or electronic)	
Brochures, flyers, handouts, bulletin boards	
Radio or TV PSA (public service announcements)	

Community Consultation – Example Recs.

Community Consultation Menu

A (Optional)	B (Required)
A presentation and discussion by an investigator visiting a meeting of an existing group (visits to existing meetings)	Web-based survey (provided by coordinating center)
Focus group (moderated small group session)	In-person solicited survey e.g. waiting room (template provided by coordinating center)
In-person individual interviews or meetings	
A booth or table at community events involving interactive discussions (not just surveys)	
Meetings convened by the investigators inviting the targeted audience (preferably with RSVP)	
Social media messaging	

Respect For Persons – CC Goals

- Key Ethical Principle in the Belmont Report
- Allows community members to be informed in advance
- Allows for communities to provide meaningful input to overseeing IRB before approval
- Gives time for community leaders to identify concerns within its members
- Should include members of the community who are potentially at risk of conditions of the study
- Information is accessible and should be provided at places where the community is already gathered when able

Opting Out

-Must be pathways in place for community members to “opt-out” if they do not wish to participate in the trial

-Typically, have come in the form of a bracelet to wear

-Patients admitted wearing the bracelet will be considered excluded from the trial

Trauma Population – Our Community

County	City	Trauma Population	%White	% Black	% Asian	% Hispanic	% Other
Hamilton(OH)	Cincinnati, Harrison, Norwood, Cleves	3524	52.9%	41.5 %	0.8%	3.3%	1.6%
Butler(OH)	Hamilton, Middletown, Fairfield, Liberty Township	579	79.1%	12.6 %	2.2%	3.5%	2.4%
Clermont(OH)	Amelia, Batavia	477	96.0%	1.5%	0.6%	0.6%	1.0%
Brown(OH)	Ripley, Fayetteville, Mount Orb	191	95.8%	2.6%	0.5%	0.0%	1.0%
Boone(KY)	Florence, Burlington, Union, Walton	212	84.4%	3.8%	1.4%	6.1%	4.2%
Campbell(KY)	Newport, Ft. Thomas, Alexandria, California, Belleview	209	92.8%	6.7%	0.0%	0.5%	0.0%
Kenton(KY)	Covington, Erlanger, Independence	369	87.5%	6.8%	0.3%	2.7%	2.7%
Warren(OH)	Lebanon, Loveland, Mason, Franklin	135	85.2%	3.7%	5.2%	5.2%	2.2%
Dearborn(IN)	Lawrenceburg, Aurora, Greendale, Hidden Valley	203	98.5%	0.0%	0.0%	1.0%	0.5%
Franklin(IN)	Brookville, Laurel, Metamora, Oldenburg, New Trenton, Mount Carmel	78	98.7%	0.0%	0.0%	1.3%	0.0%

Putting Together a Plan

Budget

Many events cost money to book. Resources should be spent on events and ads that are most likely to reach more people.

Time

Requires study staff to work nights and weekends

Representative

Events should be diverse and target different pockets of our community so that all groups are included.

Accessible

Opportunities to learn about the study should be well advertised or a part of events that are where the community is already gathered

PAIN STUDY

Sponsor: Department of Defense
Local PI: Jason McMullan, MD

Background

- Providing analgesia as soon as practicable is humane, reduces suffering, moderates physiologic complications of trauma, and may mitigate incidence of long term sequelae such as chronic pain and PTSD
- Opioids associated with the highest rate of adverse events among analgesics (hypotension, respiratory depression)
- Previous studies show promise in ketamine as an alternative

Prehospital Analgesia Intervention Trial

- Multisite, prehospital, randomized, double-blind, clinical trial
- Fentanyl vs Sub-Dissociative Ketamine for pain management
- Trauma patients transported from scene by Ground EMS
- Males ≥ 18, Females ≥ 50
- **Primary Aim: Determine if among prehospital trauma patients with compensated shock (SI ≥ 0.9) and an indication for pain management, treatment with sub-dissociative IV ketamine as compared to IV fentanyl reduces mortality at 24 hours following admission**

LITES
Linking Investigations in Trauma and Emergency Services

UCMC trial for safer pain management for trauma patients

Researchers at the College of Medicine will join the Prehospital Analgesia INtervention (PAIN) Trial to determine if giving fentanyl or low-dose ketamine to trauma patients in pain affects health outcomes. The medication will be given while in an ambulance to the hospital. The principal investigator for this trial is **Jason McMullen, MD**, professor in the Department of Emergency Medicine.

Fentanyl is widely recognized as a highly potent and deadly street drug, but it does serve a medical purpose as an effective emergency pain management medication for severely injured trauma patients. However, its side effects can include the suppression of breathing. Ketamine, another anesthetic, relieves pain without affecting breathing. McMullen emphasizes that the "relief of pain and suffering is an important part of prehospital care. The PAIN study will help us determine what is safe and effective so that we can treat our patients in the best way possible."

The three-year, multi-center trial will begin this fall and will assess if ketamine is a safer option than fentanyl for patients in pain. It will enroll about 1,200 trauma patients (randomized to fentanyl or ketamine) from nine health care sites in the LITES Network in the United States.

Anyone may opt out of the study by contacting the research team at 1-800-664-0557 or emailing PAINStudy@uc.edu to receive an opt-out "NO PAIN Study" bracelet. Opting out will not prevent trauma patients from receiving pain medication, only from enrollment in the study. This research is supported by Department of Defense (DoD) contract W81XWH-16-D-0024 W81XWH-19-F-0539. Any opinions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the DoD.

LiTES

Linking Investigations in Trauma and Emergency Services

Research study looks at pain management in trauma patients

FOR MORE INFORMATION:

www.litesnetwork.org/pain/

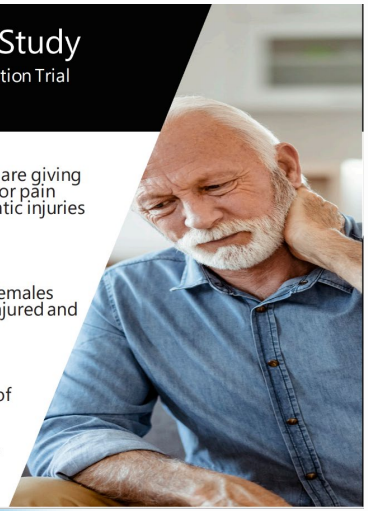
PAINStudy@uc.edu

513-558-6332

Trauma Research Study

Prehospital Analgesia INtervention Trial

PAIN



What

The purpose of this study is to compare giving fentanyl or ketamine through an IV for pain management in patients with traumatic injuries before they arrive at the hospital.

Who

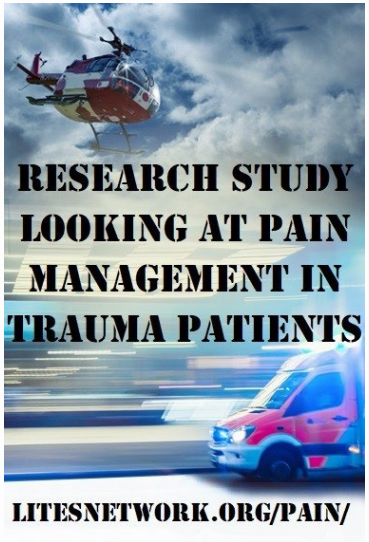
Adult males 18 years and older and females age 50 and older, who are severely injured and require pain medication through IV.

Details

For more information or to opt-out of this study, contact the PAIN Study Hotline at (513) 558-6332 or PAINstudy@uc.edu.

UC Health

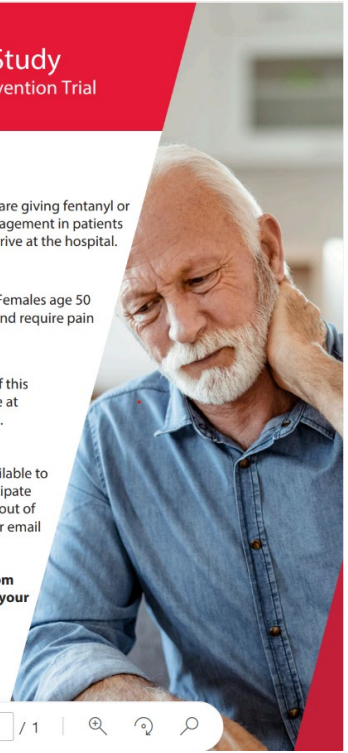
IRB# 2022-0960



Trauma Research Study

Prehospital Analgesia INtervention Trial

PAIN



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For more information or to opt-out of this study, contact the PAIN Study Hotline at (513) 558-6332 or PAINstudy@uc.edu.

How to "opt-out" of this study?

Bracelets and wallet cards will be available to individuals who do not wish to participate in this study. If you would like to opt-out of the study, please call 513-558-6332 or email PAINstudy@uc.edu.

Opting out will not prevent you from getting pain medication as part of your normal care.

UC Health

Social Media

Survey

This research study, called: "Prehospital Analgesia INtervention Trial" (PAIN), will look at whether giving ketamine or fentanyl to people who have traumatic injuries and need treatment for pain will help them survive better than normal care.

Normally when a person has a severe traumatic injury, fentanyl is given through an IV for pain management. Fentanyl is an opioid used to treat pain. New information suggests that giving ketamine, which is not an opioid, may avoid side effects of opioids such as very low blood pressure, low oxygen level, or the need to insert a breathing tube to help the patient breathe.

For the study, severely injured patients will receive either fentanyl or ketamine through an IV for pain treatment by EMS providers. Researchers will look at both groups of people and see if one group did better than the other. We'll also collect information from health records for both groups as part of the study.
People who are included in studies needing emergency treatments like this one are very sick and cannot give permission beforehand. However, we must tell the person as soon as we can that they are in the study and give them a chance to decide if they want to keep participating.

Emergency studies must follow special rules. One rule is that before we do the study, we must talk to community members like you to make sure people know about the study and to see what the community thinks about it. This survey is one way for us to do that. The following questions will help us determine your views concerning the PAIN study. There will be an opportunity at the end of this questionnaire for you to add any additional comments you may have. Thank you for your input.

Survey (cont.)

1. What is the purpose of the PAIN study?

- To see if giving platelets will help slow or stop severe bleeding from getting worse
- To see if giving oxygen helps trauma patients
- To compare different ways of controlling pain after injury
- To determine the effect of blood transfusions on people with diabetes

reset

2. If you were severely injured and needed pain medication, would you want to be entered into this research study, even though you couldn't give consent?

We would still try to get consent for continued participation after your arrival to the hospital.

- Yes
- No
- I don't know
- I don't want to answer

reset

Survey (cont.)

4. If one of your family members was severely injured and needed treatment for pain, would you want them to be entered into the research study, even if they or you couldn't give consent?

We would still try to get consent for continued participation after their arrival to the hospital.

- Yes
- No
- I don't know
- I don't want to answer
- Not applicable (respondent doesn't have family members)

reset

6. Do you believe that emergency medical research is necessary?

- Yes
- No
- I do not know
- I do not want to answer

reset

7. Do you believe that this study should be done in this community?

- Yes
- No

reset

TOWAR

Sponsor: Department of Defense
Local PI: Michael Goodman, MD

Background

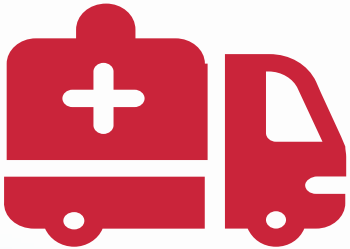
- Initiation of damage control resuscitation early, in prehospital setting, has potential to reduce downstream complications attributable to hemorrhage by intervening closer to time of injury
- Prior to development of coagulopathy, irreversible shock, and ensuing inflammatory response
- Previous study showed patients receiving red cells AND plasma had better adjusted survival than receiving crystalloids alone.

Type O Whole Blood and Assessment of Age during Prehospital Resuscitation

- Severely Injured patients who have lost a lot of blood (hemorrhagic shock)
- Patients transported to our hospital by helicopter
- Whole blood transfusion (O+) versus Standard of Care components (pRBC and FFP)

TROOP

Sponsor: National Heart, Lung and Blood Institute (NHLBI)
Local PI: Michael Goodman, MD



Background

- Trauma is leading cause of death in adults (below age 46), and blood transfusion is an essential part of resuscitation
- Current standard is to transfuse a balanced administration of equal ratios of blood components, effectively trying to reconstitute whole blood
- Components have a volume of preservatives and anticoagulants that when summed is not inconsequential

Trauma Resuscitation with Low - Titer Group O Whole Blood or Products

- Multicenter, Bayesian, group-sequential, combined non-inferiority/ superiority, randomized clinical trial
- Trauma patients, estimated > 15, taken directly to hospital from scene of injury and…
    - Have traumatic injury with confirmed or suspected acute major bleeding
    - Require a large volume blood transfusion, or activation of Massive Transfusion Protocol (MTP)
- MTP Coolers supplied with whole blood or components and patient is enrolled when cooler is opened bedside

TAP

Sponsor: CSL Behring
Local PI: Michael Goodman, MD

Background

- Even with improved resuscitation methods in the administration of blood products to patients in hemorrhagic shock, exsanguination continues to be a leading cause of traumatic mortality
- Kcentra used for urgent reversal of acquired coagulation factor defieciency induced by Warfarin therapy
- Meta-analysis of studies involving Kcentra show possibility that the effects of the drug extend beyond coagulopathy reversal
- Zeeshan et al. showed Kcentra as an adjunct to FFP was associated with improved survical and reduction in transfusion requirements.

Trauma and Prothrombin Complex Concentrate Trial

- Multicenter, Randomized, Double-Blind, Placebo Controlled Trial
- Evaluates use of BE (Kcentra) to improve survival in patients with traumatic injury and acute major bleeding
- Patients estimated ≥ 15 years who…
    - Have traumatic injury with confirmed or suspected acute major bleeding
    - Require a large volume blood transfusion, or activation of Massive Transfusion Protocol (MTP)
- Infusion of Investigational Product must begin within 90 minutes of arrival

THANKS!

DO YOU HAVE ANY QUESTIONS?

wakefidm@ucmail.uc.edu
513-558-7247

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COLLEGE OF MEDICINE

REFERENCES

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