Pediatric Out-of-Hospital Cardiac Arrest Resuscitation: Evaluation of IM Epinephrine (The PRIME Trial)

ACP/PCP Memo – Pre-Filled Syringes

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Study Synopsis:

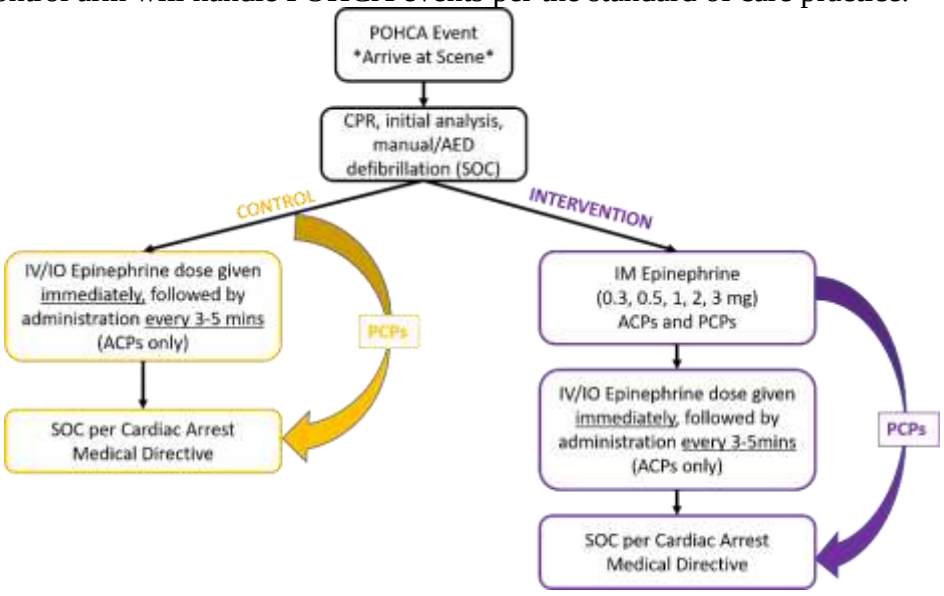
Paediatric out-of-hospital cardiac arrest (POHCA) is associated with extremely poor outcomes. **Survival rates of POHCA have been reported at only about 10%.** The few children who survive a POHCA event often have a significant new difficulty with tasks of daily living. Epinephrine has been shown to improve outcomes following cardiac arrest as it improves blood circulation to the heart and to the brain. Every minute delay in epinephrine is associated with an increased risk of death and poor neurological outcomes.

Current guidelines recommend epinephrine to be given via an intravenous (IV - in the vein) or intraosseous (IO – in the bone) route as soon as possible. However, there are delays in obtaining IV or IO access due to child's size and poor circulation, resulting in delayed epinephrine administration and worse outcomes. Furthermore, not all paramedics (i.e., Primary Care Paramedics, PCPs) in Ontario/Canada can administer IV/IO epinephrine to patients with cardiac arrest but they can give IM epinephrine for anaphylaxis (severe allergic reaction). We will be studying IM epinephrine for children with cardiac arrest, added to standard of care.

We believe it will result in more children with POHCA receiving epinephrine and may provide a more efficient means of providing the first epinephrine dose. This may improve the short- and long-term outcomes of these patients. There is an abundance of literature detailing the risk/benefit profile of IM epinephrine use in anaphylaxis; however, there is no human pediatric data on IM epinephrine for cardiac arrest. Animal models show that earlier epinephrine administration in cardiac arrest increases survival with no increased risk of harm. As well, a recent adult cardiac arrest study has shown that IM epinephrine administration is feasible and significantly decreases the time to initial epinephrine administration compared to IV or IO. This study will be the first Randomized Controlled Trial (RCT) to examine the role of IM epinephrine in cardiac arrest in children.

Study Design:

You are a participating paramedic service site. All participating sites will begin in the Control arm. The Control arm will handle POHCA events per the standard of care practice.



Sites will be randomized (like a flip of the coin) into the Intervention arm. The Intervention arm will introduce the use of pre-filled needle/syringe IM epinephrine as the first dose administered by ACP/PCP followed by the standard of care per cardiac arrest medical directive.

Eligibility Criteria:

Inclusion

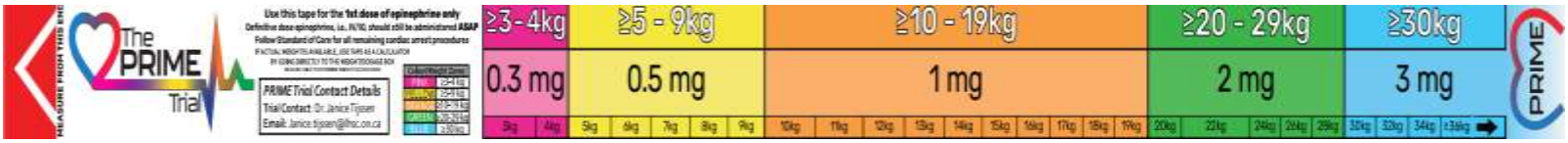
- Children aged 1day to 17 years who experience OHCA

Exclusion

- Cardiac arrest is in response to a trauma

Paramedic Instructions:

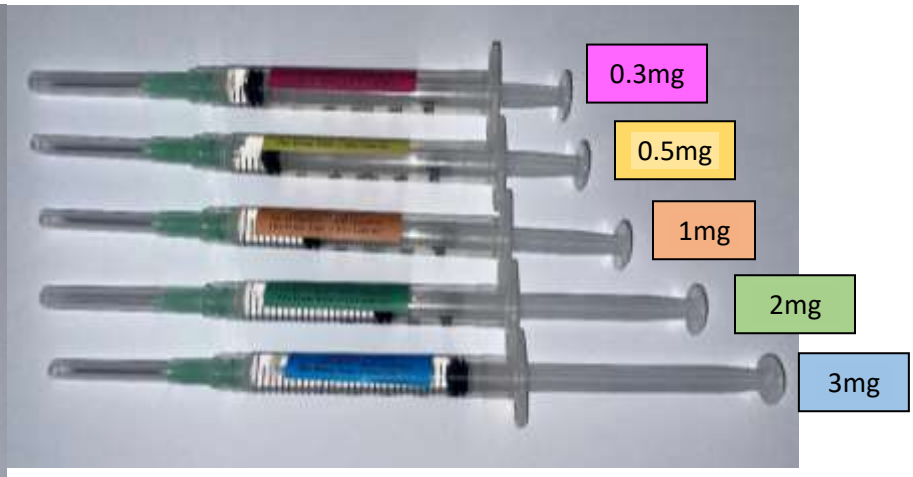
1. Identify weight category of patient using study specific Pediatric Measurement Tape (image not to scale)

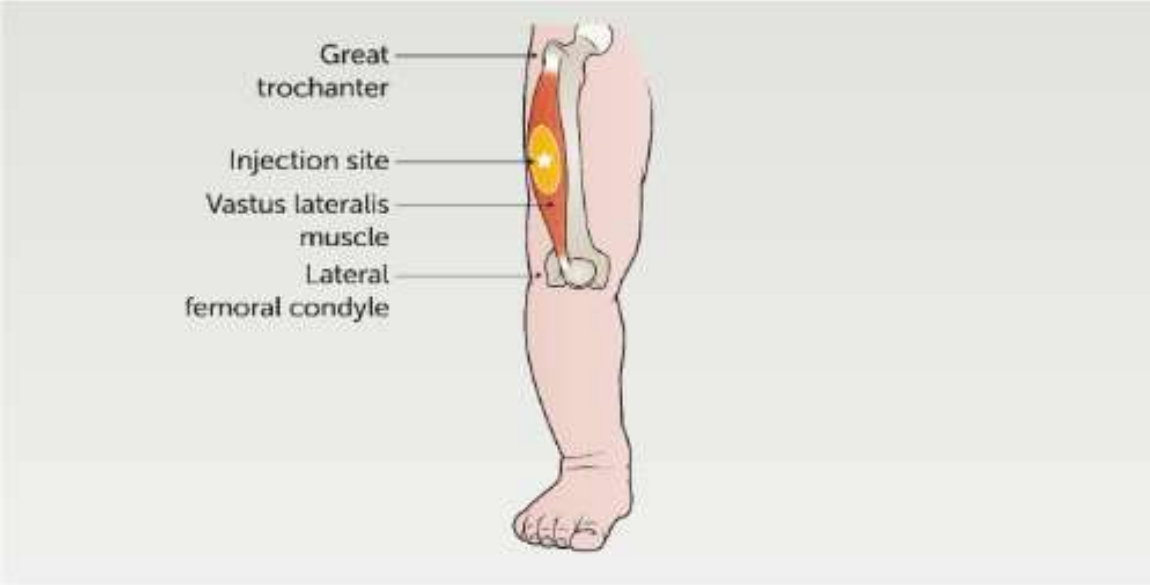


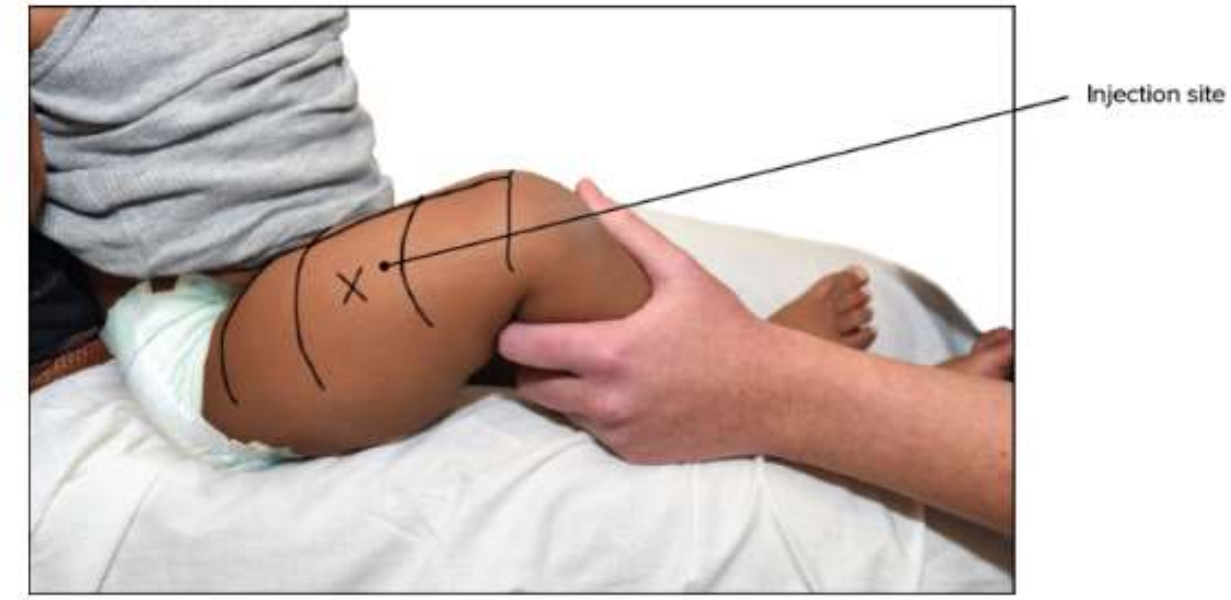
2. Select one pre-filled needle/syringe from study kit based on colour-coded weight category.

Estimated weight range (Kg)	Anticipated Dose Administered (mg)
≥3-<5	0.3
≥5-<10	0.5
≥10-<20	1.0
≥20-<30	2.0
≥30	3.0

a. The pre-filled syringes will be colour coordinated to match the Pediatric Measurement Tape for each weight range. The syringes will be in a box. Please identify the corresponding syringe.
b. Attach the needle to syringe and administer full injection **FAST** to the outer side of the thigh. **This is for IM injection ONLY.** Please administer the injection to the vastus lateralis muscle on the outer thigh (see images). Only use one pre-filled needle/syringe based on patient weight.







Study Medication Labels:

The pre-filled syringes will have the following label information attached:

1. **Syringe Label Example**

The PRIME Trial || Trio Lab Inc.
FOR IM USE ONLY
Pre-filled syringe contains:
Epinephrine (1mg/1ml) 0.3mg/0.3ml
LOT: EPI20240101 – **BUD:** 2024-04-01
Weight Range: ≥3-4kg
Administration: One time intramuscular (IM) injection **FAST** in anterolateral thigh

2. Outer Packaging Label

The PRIME Trial || Trio Lab Inc.
Principal Investigator: Dr. Janice Tijssen
Children's Hospital – London Health Sciences Centre
800 Commissioners Rd. E. London, ON N6A 5W9 519-685-8500

Pre-filled epinephrine syringes **FOR IM USE ONLY** – injection **FAST** in anterolateral thigh

Epinephrine Syringes: 0.3mg/0.3ml; 0.5mg/0.5ml; 1.0mg/1.0ml; 2.0mg/2.0ml; 3.0mg/3.0ml (weight dependent)
LOT: EPI20240101 – **BUD:** 2024-04-01

Study Medication: To be used for research purposes only by participating paramedic services as delegated by qualified investigator
Storage: Room temperature (15-30°C)

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Seringue d'épinéphrine préremplie **POUR UTILISATION IM SEULEMENT** – injection **RAPIDE** dans la cuisse antérolatérale

Seringue d'épinéphrine: 0.3mg/0.3ml; 0.5mg/0.5ml; 1.0mg/1.0ml; 2.0mg/2.0ml; 3.0mg/3.0ml (En fonction du poids)
LOT : EPI20240101 – **Date d'utilisation:** 2024-04-01

Médicament à l'étude: À utiliser à des fins de recherche uniquement par les services paramédicaux participants, délégués par un chercheur qualifié
Entreposage: Conserver à la température ambiante (15-30°C)

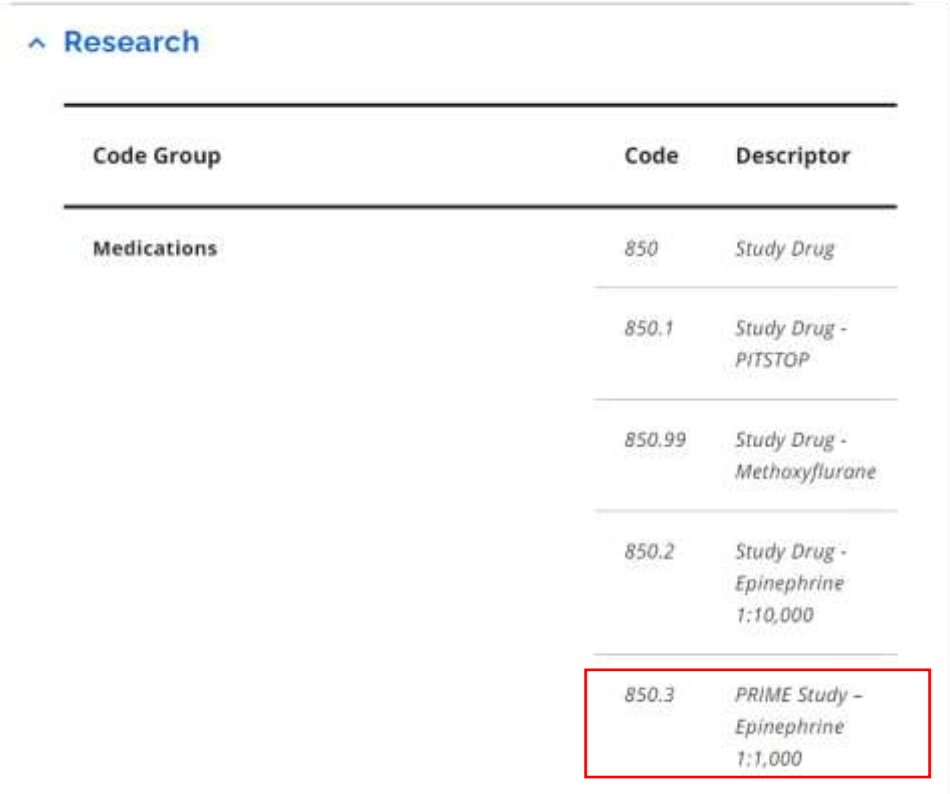
Research Study CODE:

A new code for the Ambulance Call Report has been requested as follows. Please familiarize with these codes.

Code 932.6 Study Enrollment – PRIME Trial

Code 850.3 Study Drug – Epinephrine 1:1,000 OR 850.3 PRIME Study – Epinephrine 1:1,000

You can find these codes on the ACR codes page on the Ministry of Health's website under the Research tab (https://www.ontario.ca/page/ambulance-call-report-codes). Please see the below screenshots of the codes in red outline.



Research

Code Group	Code	Descriptor
Medications	850	Study Drug
	850.1	Study Drug - PITSTOP
	850.99	Study Drug - Methoxyflurane
	850.2	Study Drug - Epinephrine 1:10,000
	850.3	PRIME Study – Epinephrine 1:1,000

Enrollment	*931*	*Study Enrollment - C-Spine Study*
	932	*Study Enrollment*
	932.1	*Study Enrollment - FIRST*
	932.2	*Study Enrollment - PITSTOP*
	932.3	*Study Enrollment - DOSE VF*
	932.4	*Study Enrollment - Palliative Care*
	932.5	*Study Enrollment - EPIDose*
	932.6	*Enrollment – PRIME Trial*

Recruiting Patients for Control and Intervention Arms

1. If you attend a POHCA event and recruit the child in to the PRIME Trial, complete your ACR forms as you normally would.
2. If recruiting under intervention arm:
    a. Time of pre-filled syringe will be defined as: time of when needle injection is administered to thigh.
3. Your service study champion will notify research personnel at Children's Hospital - LHSC for when a patient is recruited. Data will be collected by research personnel.
4. The study team will be collecting your event documentation and will record the details in the study data forms. Please document the event as best as you can!

Point of Contact:

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Thank you for your help in conducting this research project!

The PRIME Trial Team