

EpiDOSE

Epinephrine Dose: Optimal vs Standard Evaluation

Principal Investigators:

Paul Dorian MD MSc

Steve Lin MD MSc

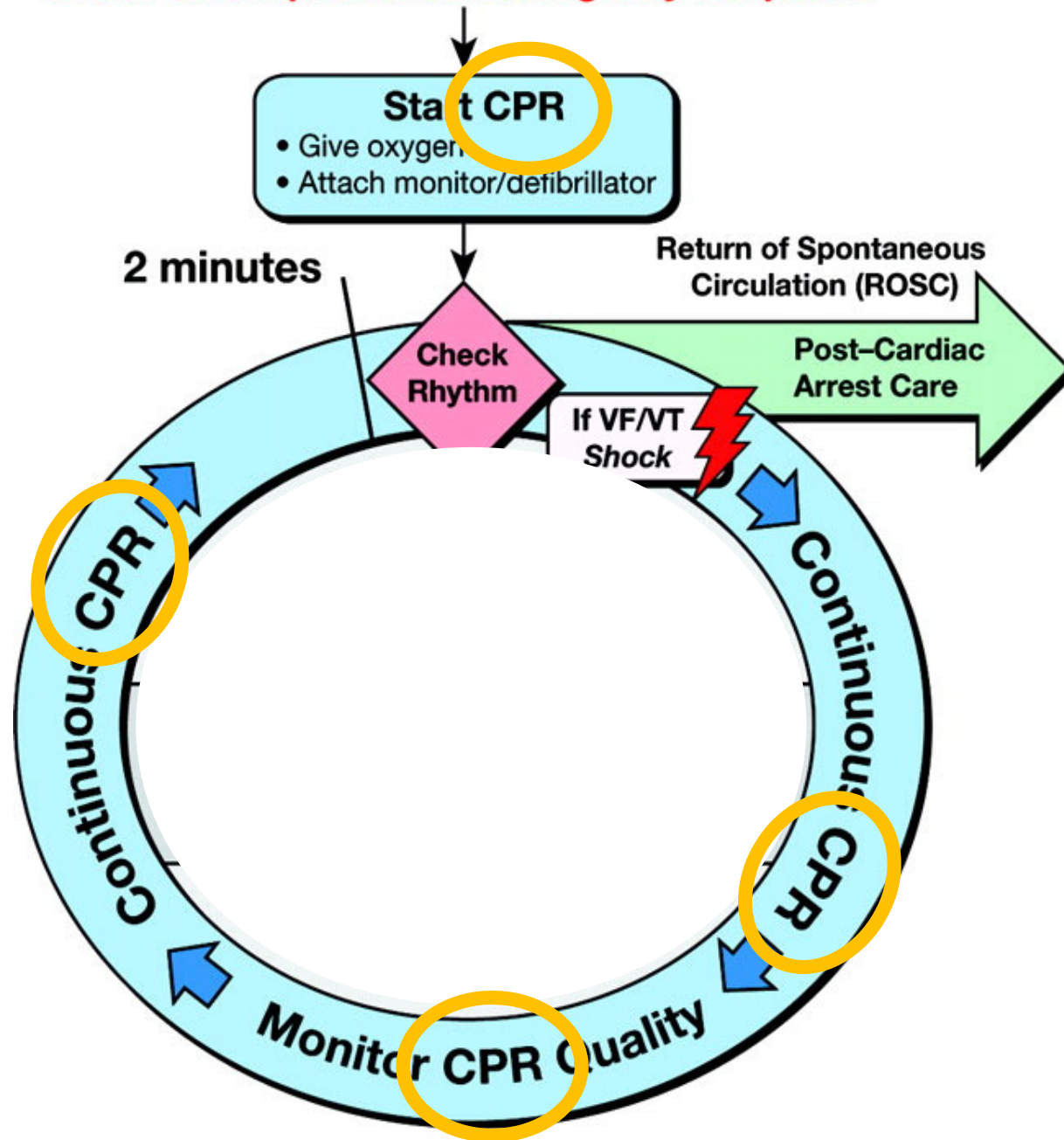
SPEAKER DISCLOSURES



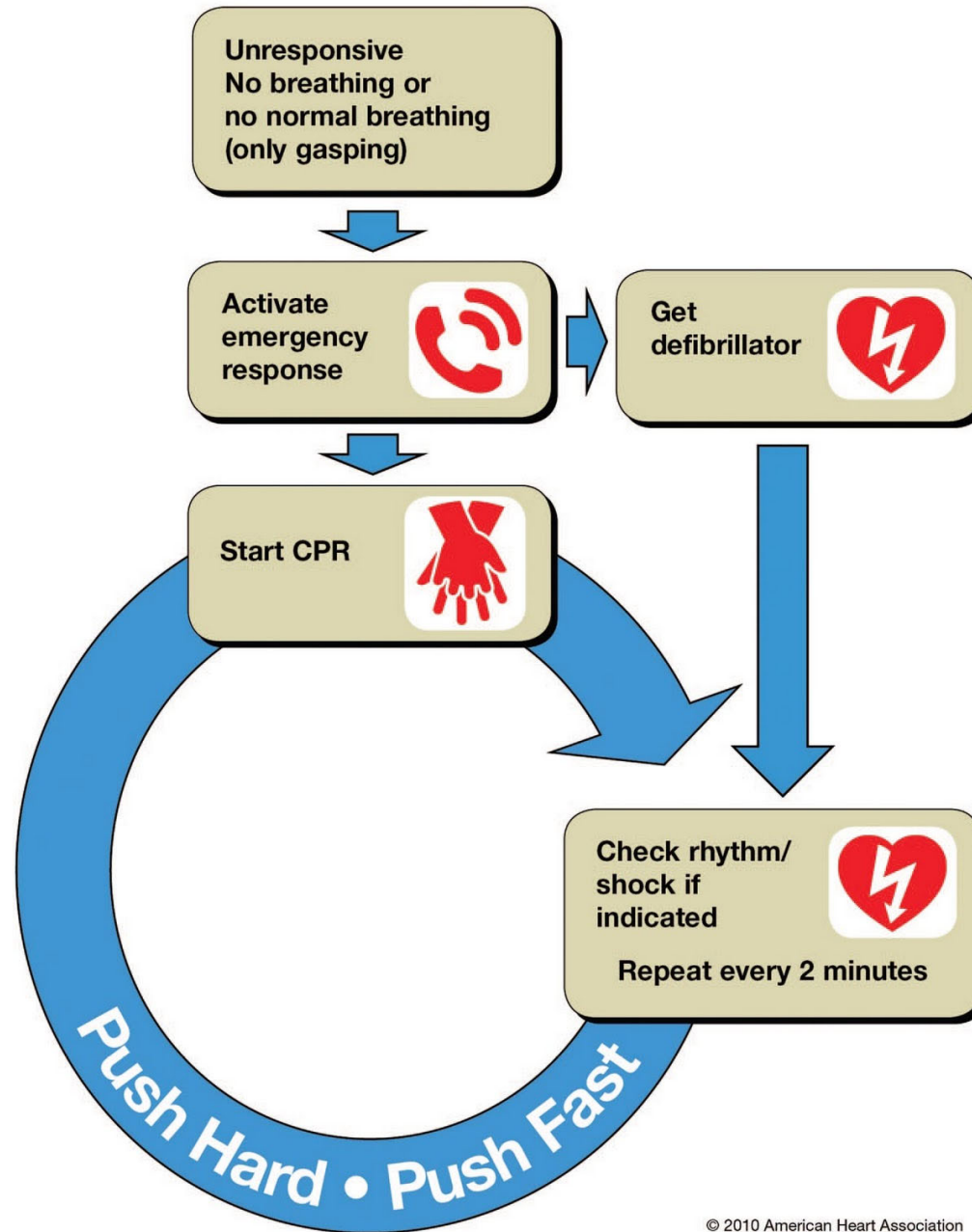
- Co-PI of CanROC EpiDOSE Trial
- Co-PI of the CANet-CanROC Collaboration
- Evidence Reviewer for ILCOR
- Author on AHA Resuscitation Guidelines and Scientific Statements



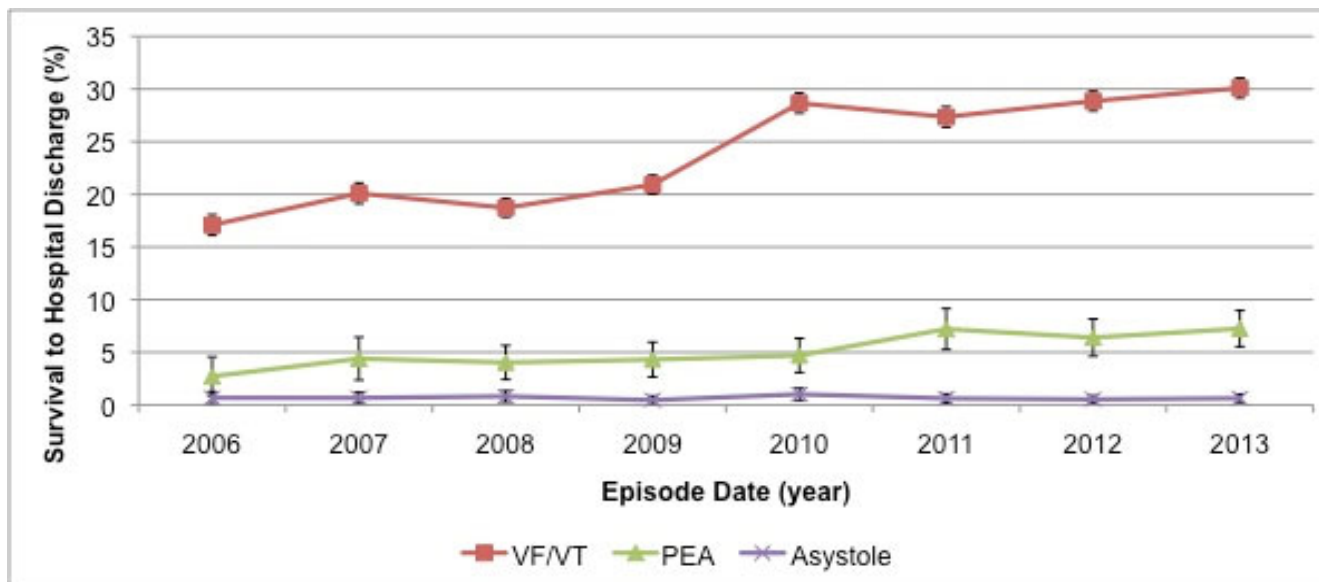
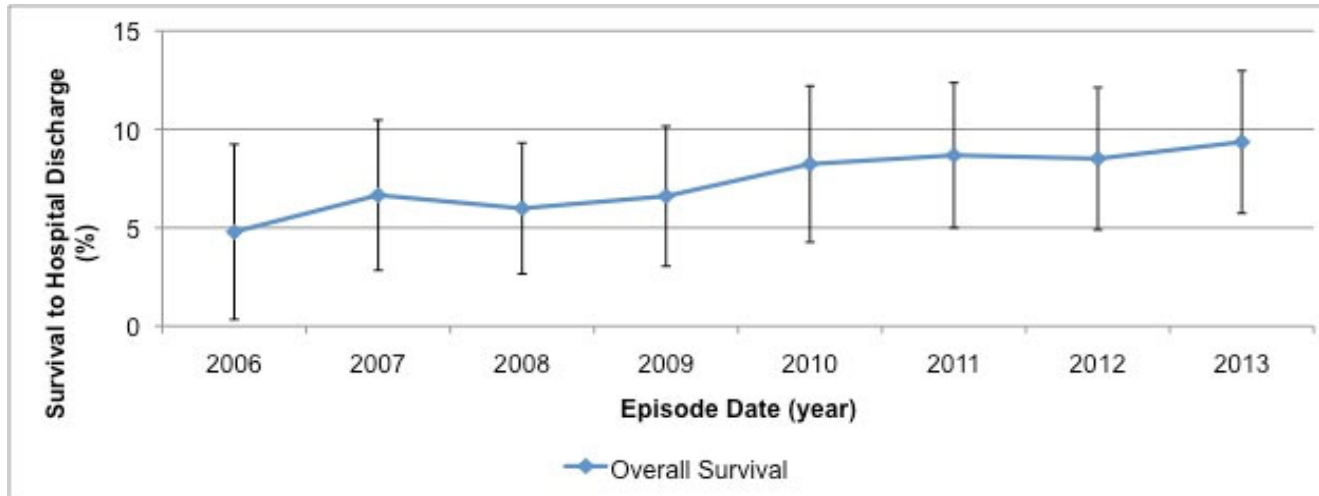
Shout for Help/Activate Emergency Response



Simplified Adult ~~BLS~~ *ACLS*



Survival Trends in Southern Ontario

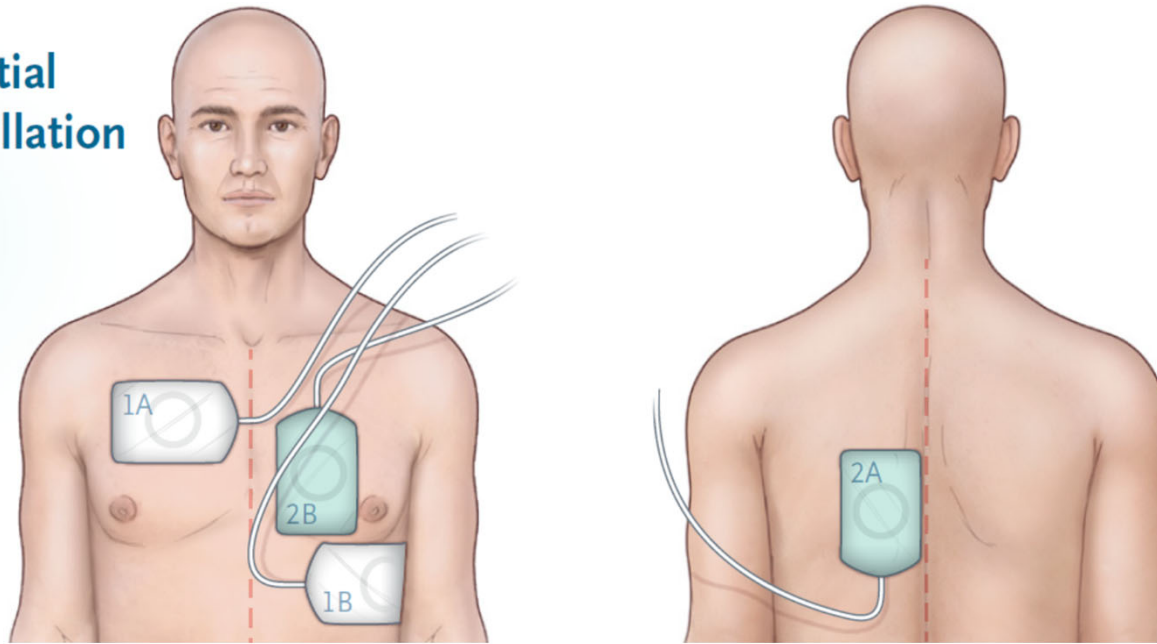


High CPR Quality

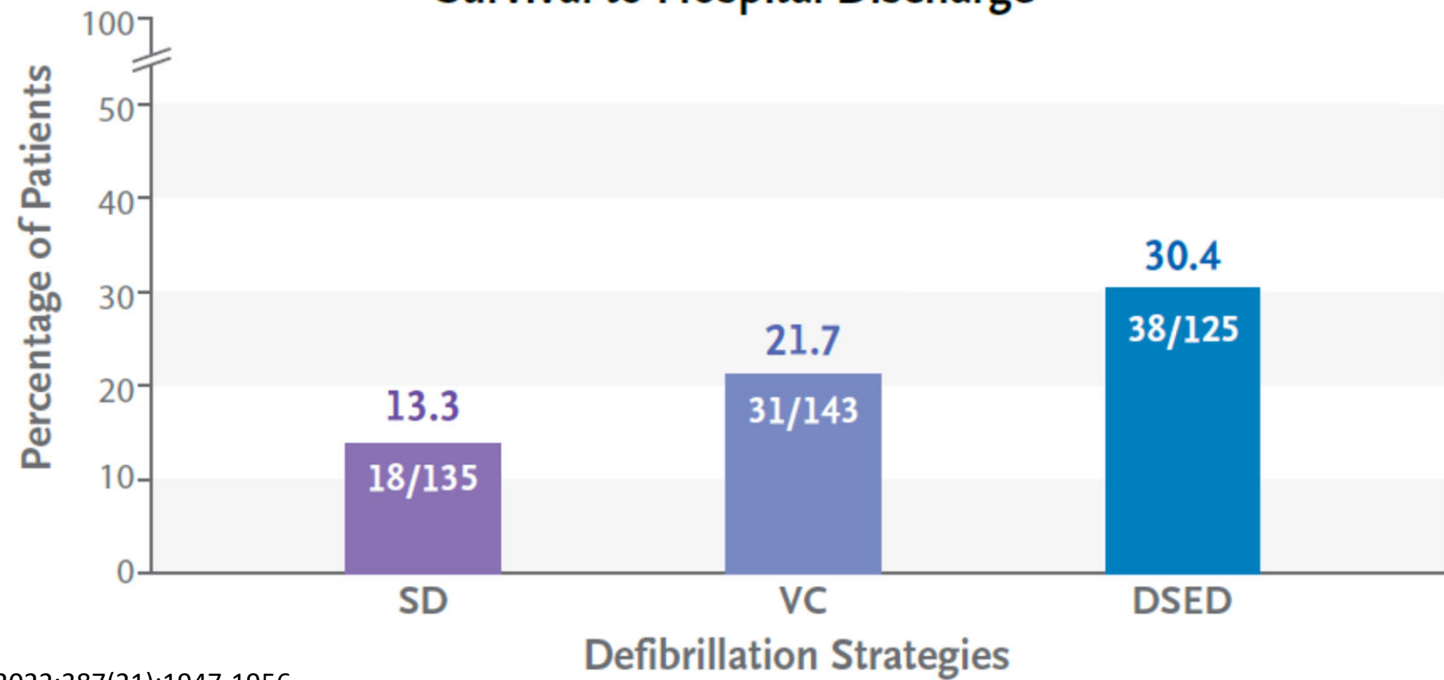
LOTS OF IT!



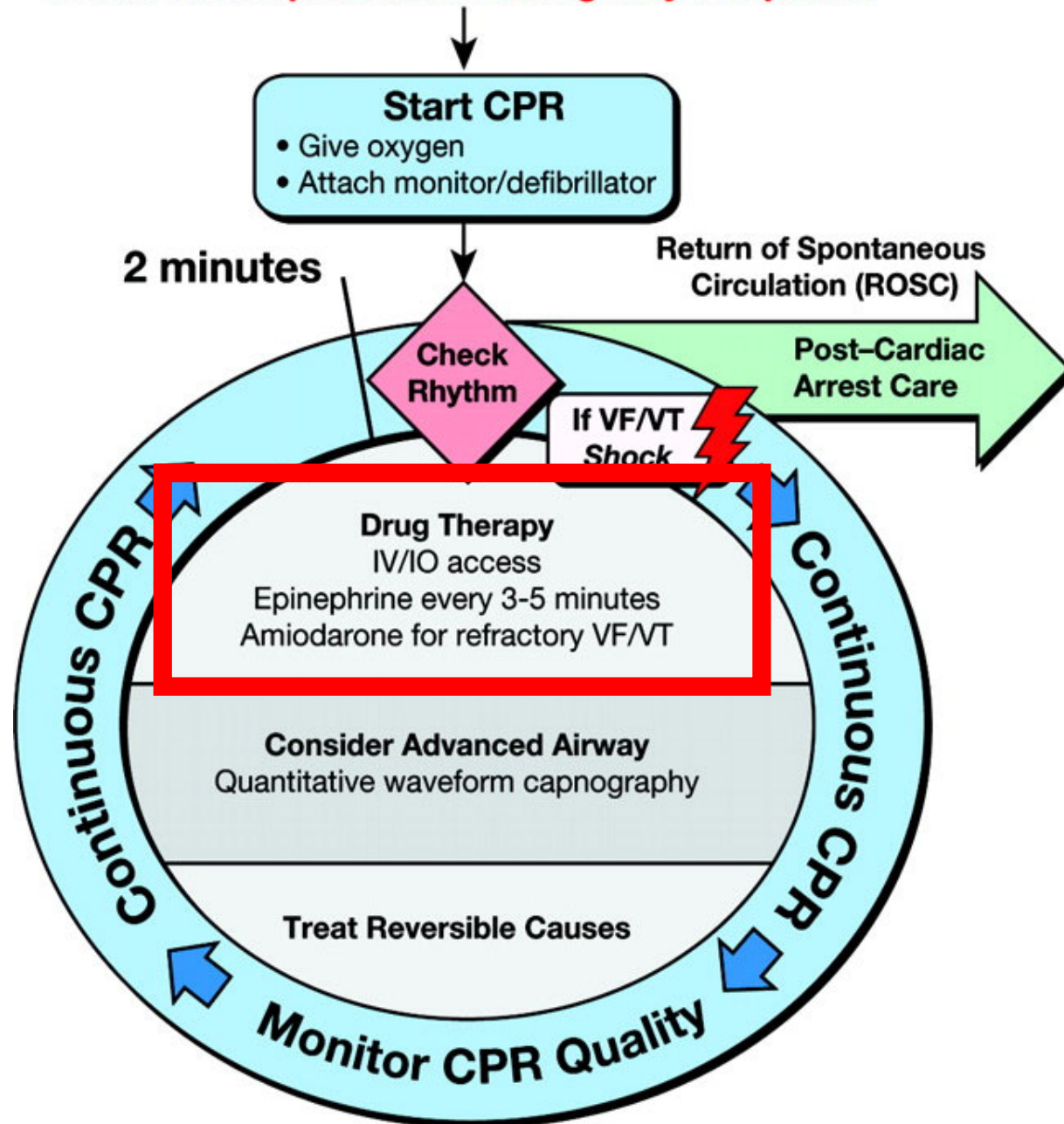
Double Sequential External Defibrillation



Survival to Hospital Discharge



Shout for Help/Activate Emergency Response





10 mL
NDC 008-437-34

EPINEPHRINE
Injection, USP

1 mg (0.1 mg/mL)

PROTECT FROM LIGHT

Lixfield®

Glass
AGB0JCT®
Unit of Use Syringe
With metal jaw lock
adapter and 26 gauge
needle

Rx only
Injecta

LOT: 10E2303
EXP: 10E2303

PRESS AND PULL TO OPEN

A COMPARISON OF STANDARD-DOSE AND HIGH-DOSE EPINEPHRINE IN CARDIAC ARREST OUTSIDE THE HOSPITAL

CHARLES G. BROWN, M.D., DANIEL R. MARTIN, M.D., PAUL E. PEPE, M.D., HARLAN STUEVEN, M.D.,
RICHARD O. CUMMINS, M.D., EDGAR GONZALEZ, PHARM.D., MICHAEL JASTREMSKI, M.D.,
IRINE STUDY GROUP*

**A Randomized Clinical Trial of
High-Dose Epinephrine and
Norepinephrine vs Standard-Dose
Epinephrine in Prehospital Cardiac Arrest**

Michael Callahan, MD; Christophe
Charles E. Saunders, MD; James F

A COMPARISON
OF EPINEPHRINE

PIERRE-YVES GUEZENNEC,
PIERRE

15mg!!

REPEATED STANDARD DOSES
OUTSIDE THE HOSPITAL

DICK GOLDSTEIN, M.D., EMMANUEL PHAM, M.D.,
VERGNION, M.D., PAUL PETIT, M.D.,

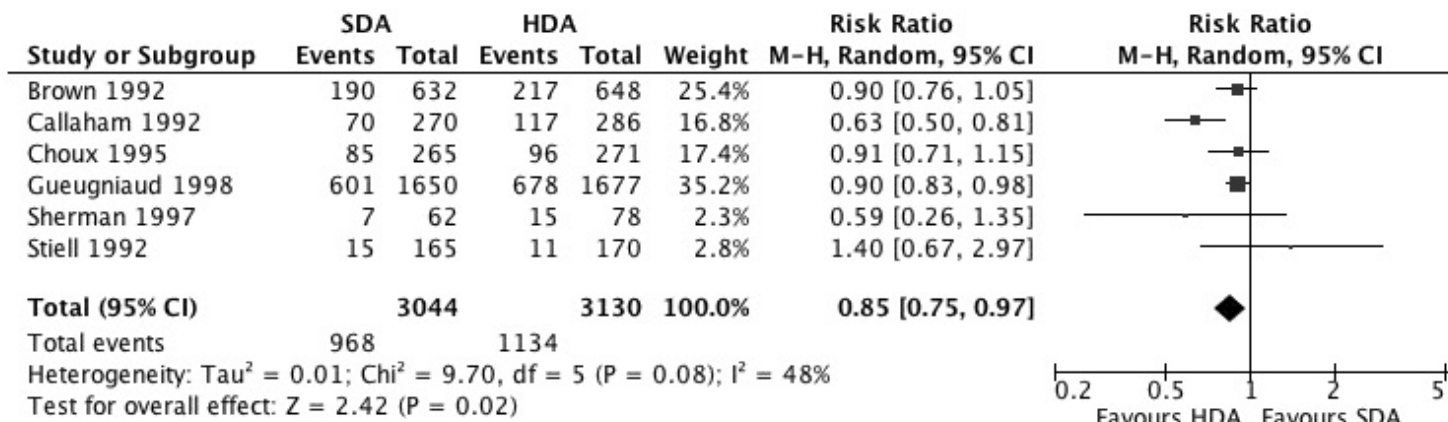
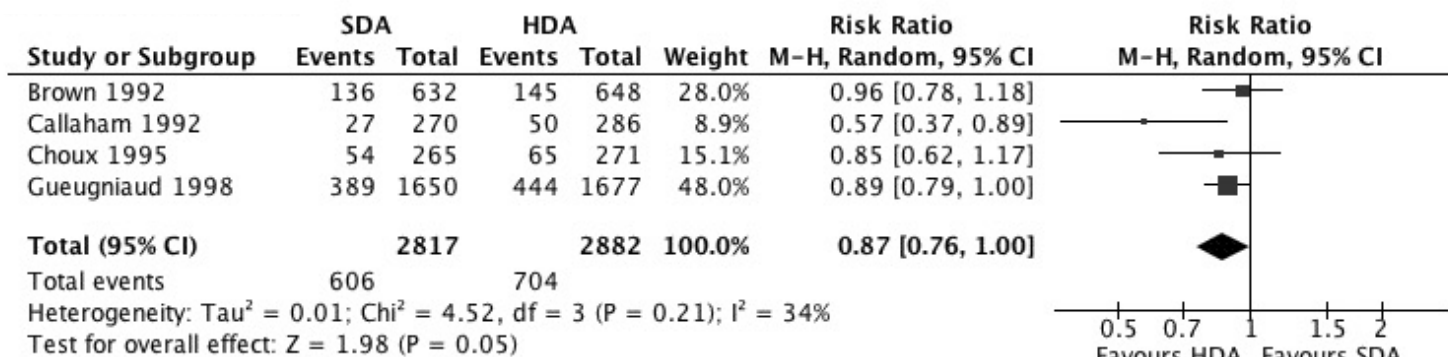
**High-Dose versus Standard-Dose Epinephrine Treatment
of Cardiac Arrest after Failure of Standard Therapy**

Bruce W. Sherman, M.D., Mark A. Munger, Pharm.D., Garrett E. Foulke, M.D.,
William E. Burchard, M.D., and Edward A. Berman, M.D.

HIGH-DOSE EPINEPHRINE IN ADULT CARDIAC ARREST

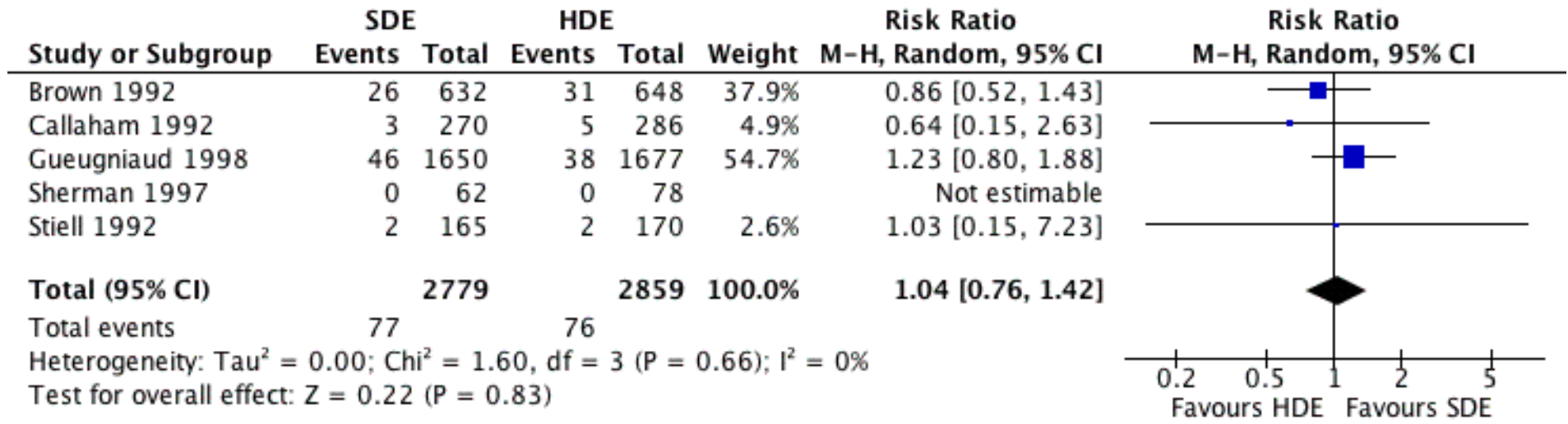
IAN G. STIELL, M.D., PAUL C. HEBERT, M.D., BRIAN N. WEITZMAN, M.D., GEORGE A. WELLS, PH.D.,
SANKARANARAYANAN RAMAN, PH.D., RYAN M. STARK, M.Sc., LYALL A.J. HIGGINSON, M.D.,
JAN AHUJA, M.D., AND GARTH E. DICKINSON, M.D.

ROSC / ADMISSION

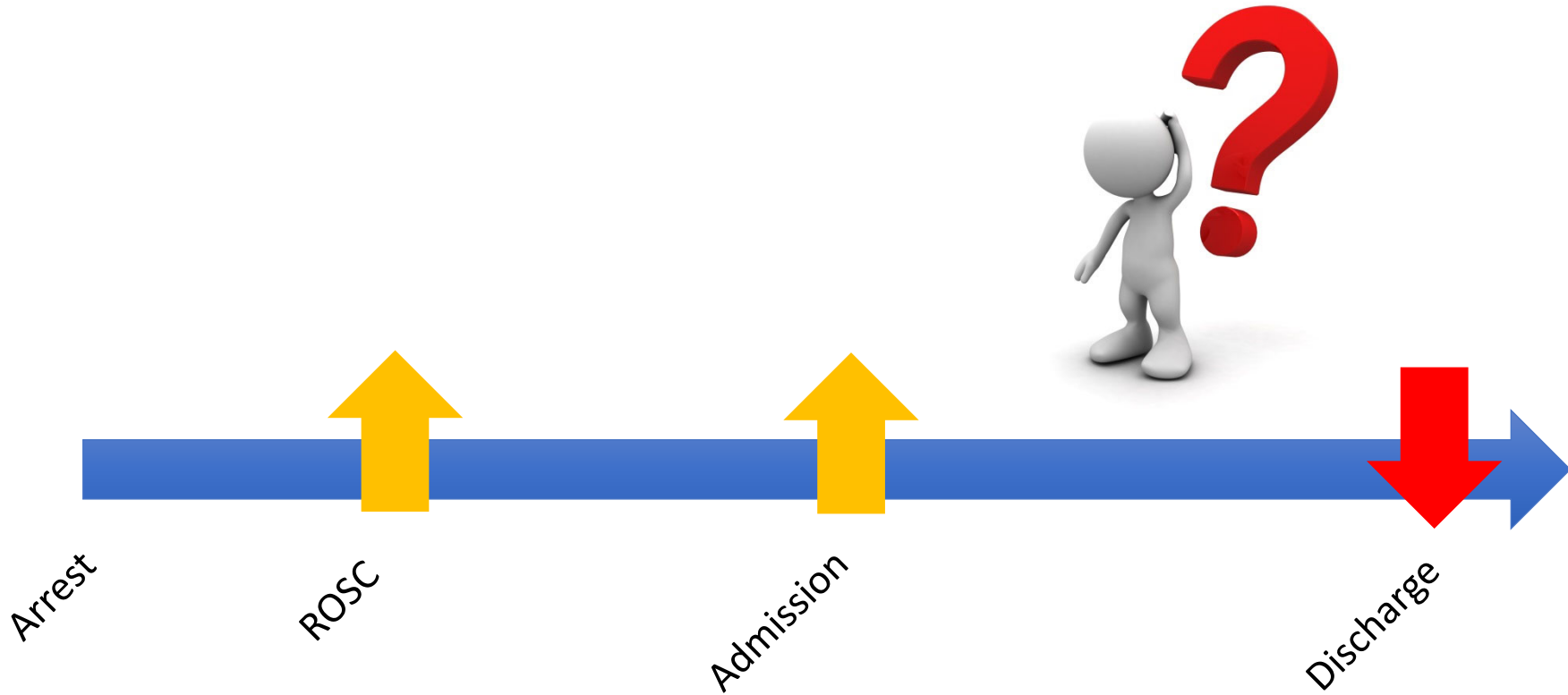


INCREASES

SURVIVAL



NO DIFFERENCE



EPINEPHRINE



UK Trial of 8000 patients!

Standard Epinephrine vs Placebo

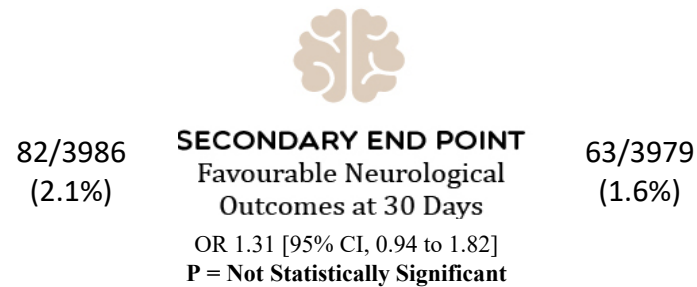
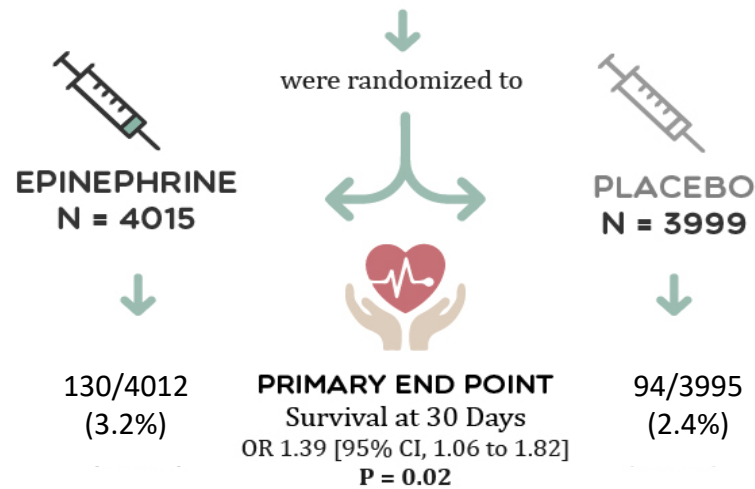
EPINEPHRINE IN OUT-OF-HOSPITAL CARDIAC ARREST - THE PARAMEDIC2 TRIAL

Multicenter, Double-blind, Randomized, Placebo-controlled Trial



STUDY OBJECTIVE: To Assess the use of epinephrine as a treatment for out-of-hospital cardiac arrest

8014 Adults who sustained out-of-hospital cardiac arrest for which ACLS was provided by trial-trained paramedics





Early recognition of cardiac arrest and call for help is
10 TIMES MORE EFFECTIVE



Cardiopulmonary resuscitation (CPR) is
8 TIMES MORE EFFECTIVE

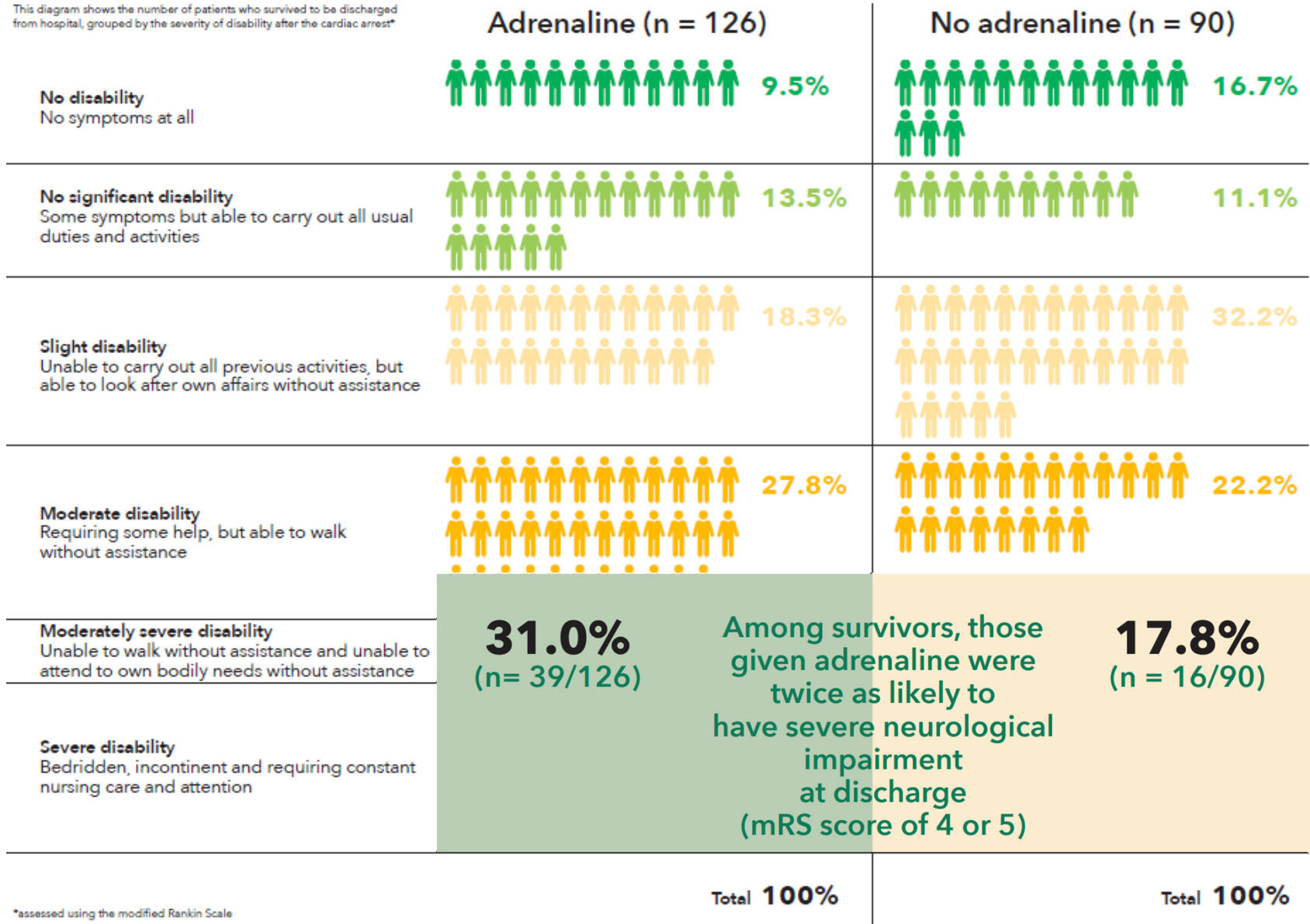


Defibrillation (electric shock) is
20 TIMES MORE EFFECTIVE



Adrenaline

This diagram shows the number of patients who survived to be discharged from hospital, grouped by the severity of disability after the cardiac arrest*



*assessed using the modified Rankin Scale



The Guardian

Routine treatment for cardiac arrest doubles risk of brain damage - study

Landmark trial likely to change the way cardiac arrest has been treated in the UK for more than half a century

Daily **Mail**
.com

Giving adrenaline to people who have had a cardiac arrest barely increases their survival chances - but **DOUBLES their risk of brain damage, major trial finds**



BRAIN RESUSCITATION



CIHR IRSC

CanROC
Canadian Resuscitation Outcomes Consortium
Consortium Canadien de Recherche en Réanimation

Will adrenaline continue to be used?



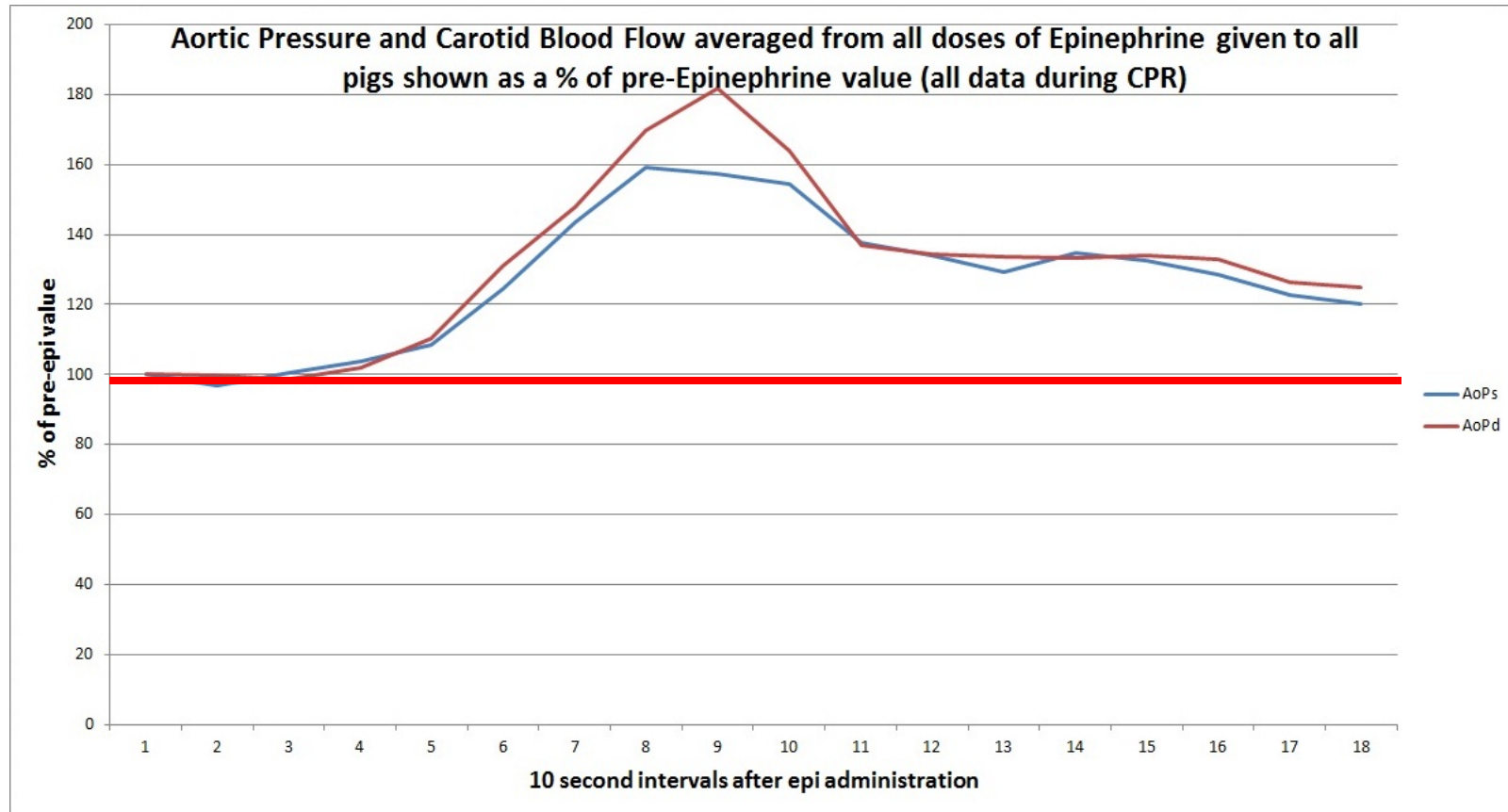
**ALL OR NONE?!
What about all in between?**

...and International
...tion (ILCOR) produce
...help paramedics decide

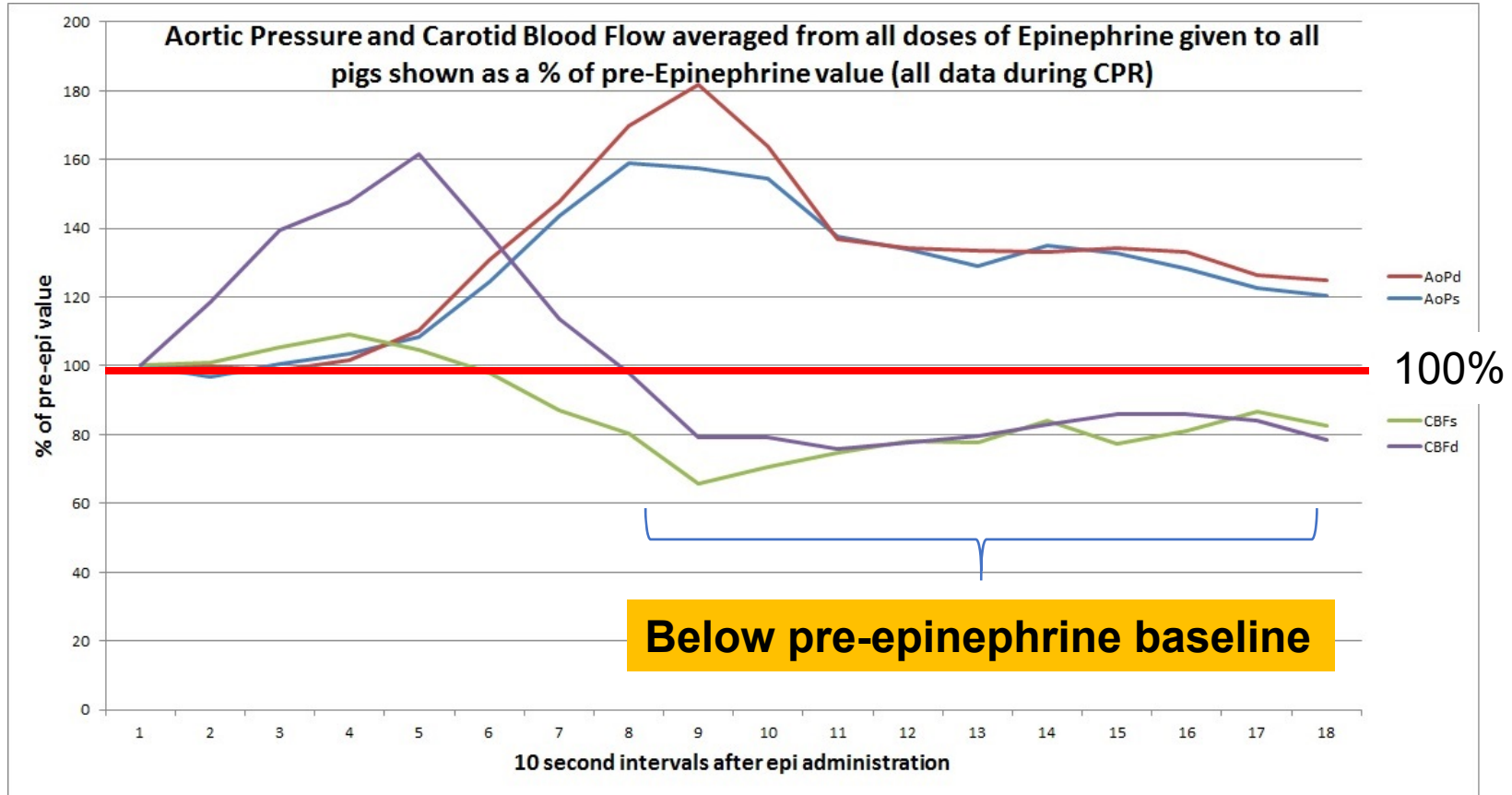
...provides definitive evidence about the
...of adrenaline in out-of-hospital cardiac
...st. The results will need to be evaluated by these
...organisations in the context of all available evidence
...and the values and preferences of patients and the
...wider community.

Clinicians and the public should continue to prioritise
evidence based treatments - high quality CPR and
prompt defibrillation.

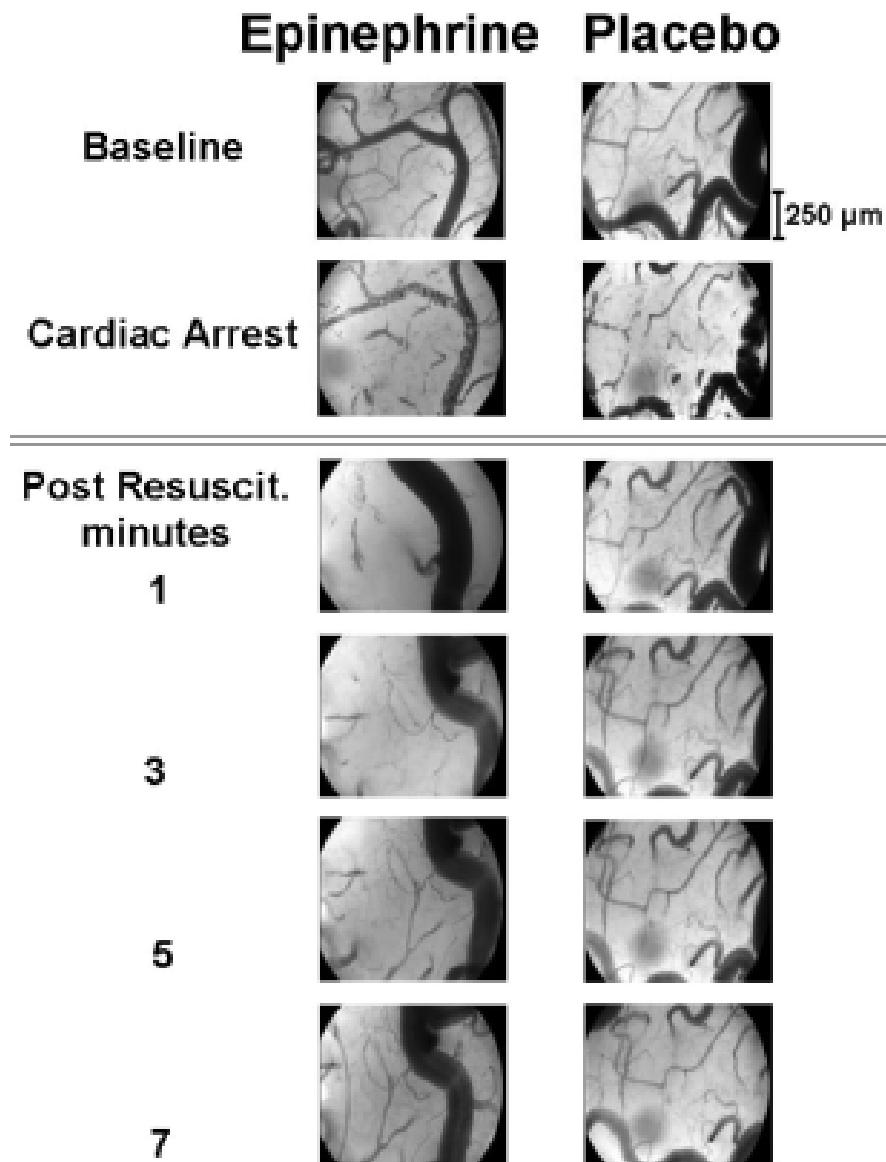
Porcine Model



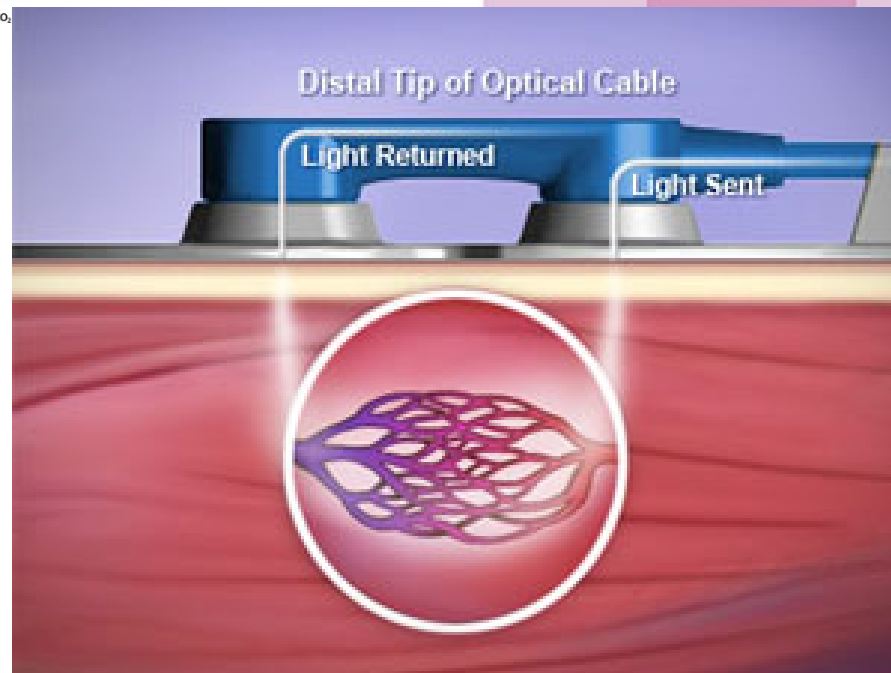
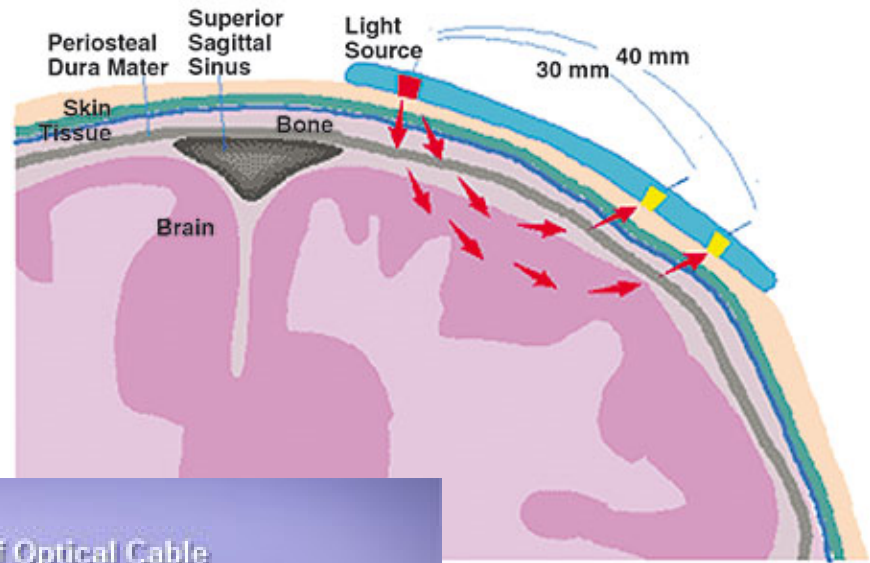
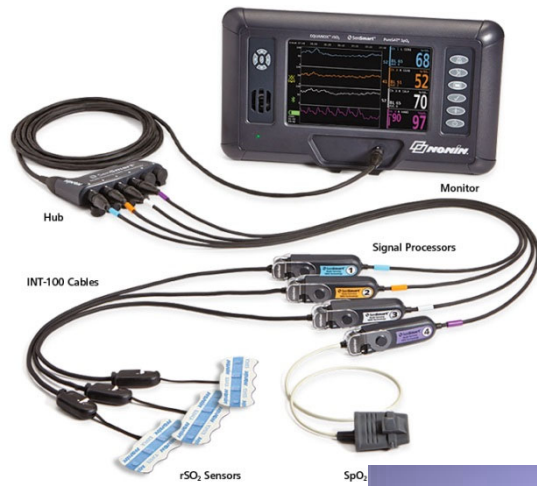
Porcine Model

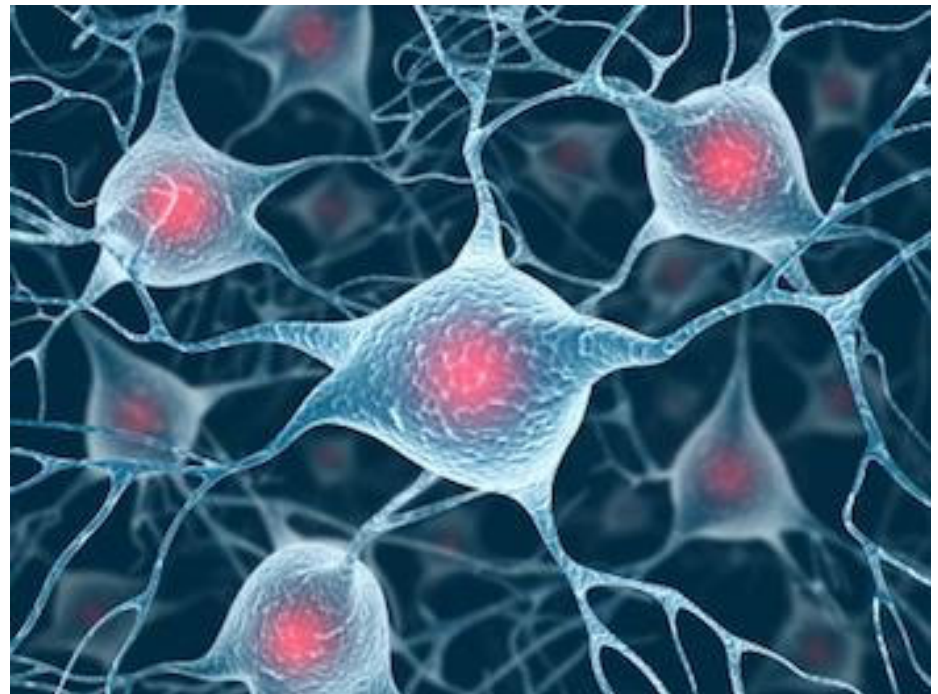
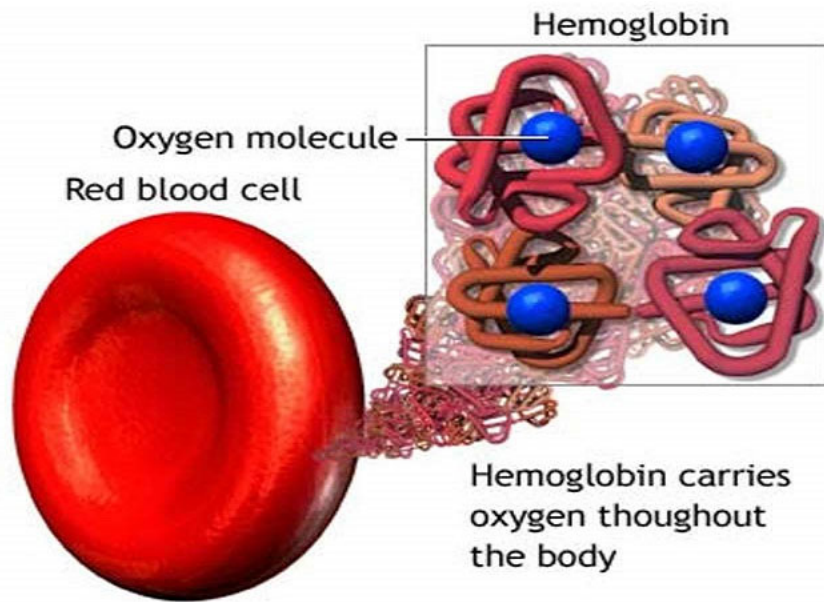


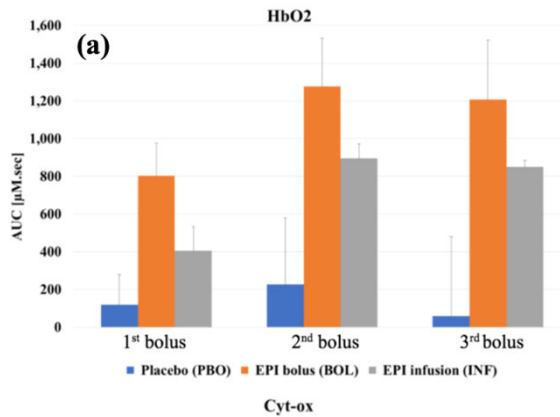
Epinephrine reduces cerebral perfusion during cardiopulmonary resuscitation*



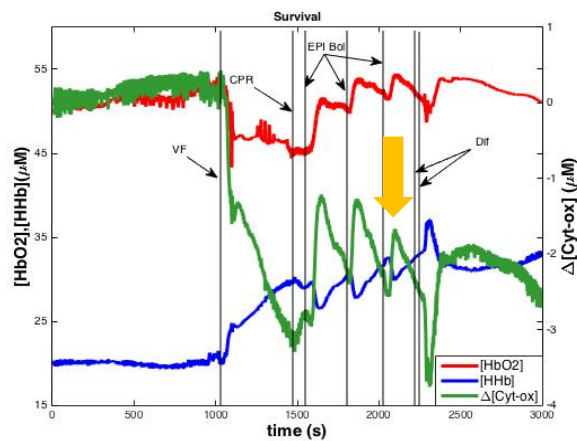
NEAR INFRARED SPECTROSCOPY





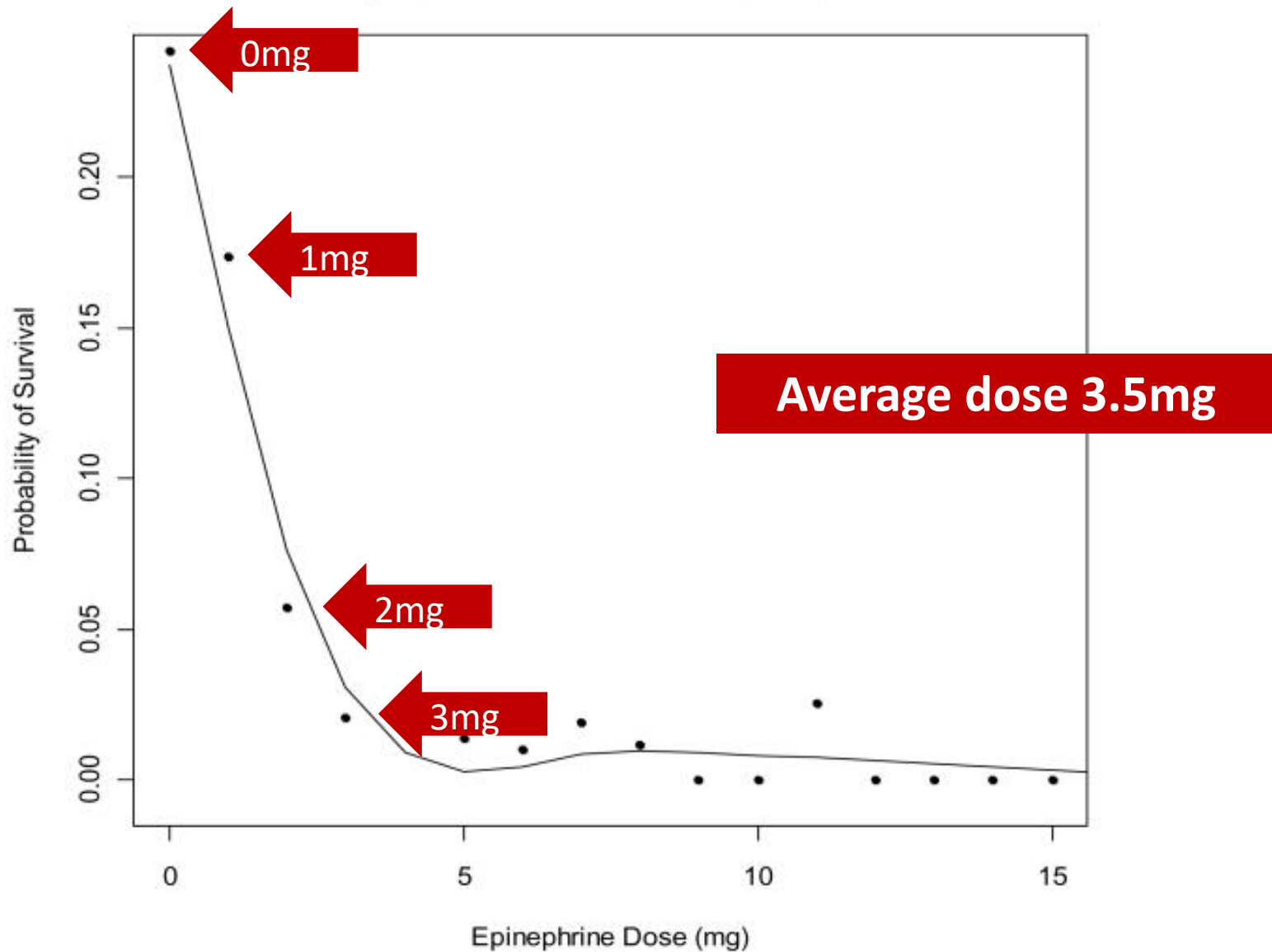


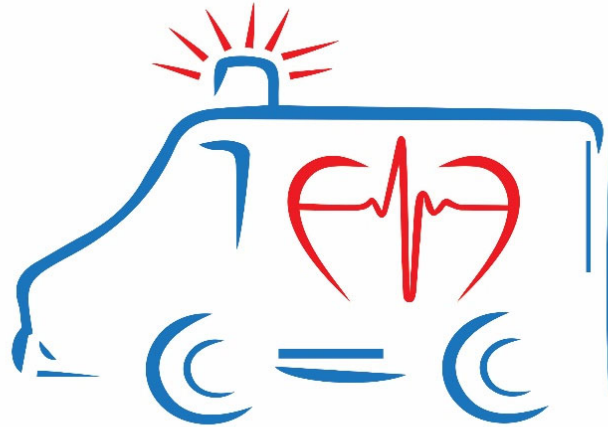
Brain oxygen **INCREASES**
with 2 doses



Brain cell metabolism
DECREASES after
3 doses

Smoothing Spline of Survival on Epinephrine Dose





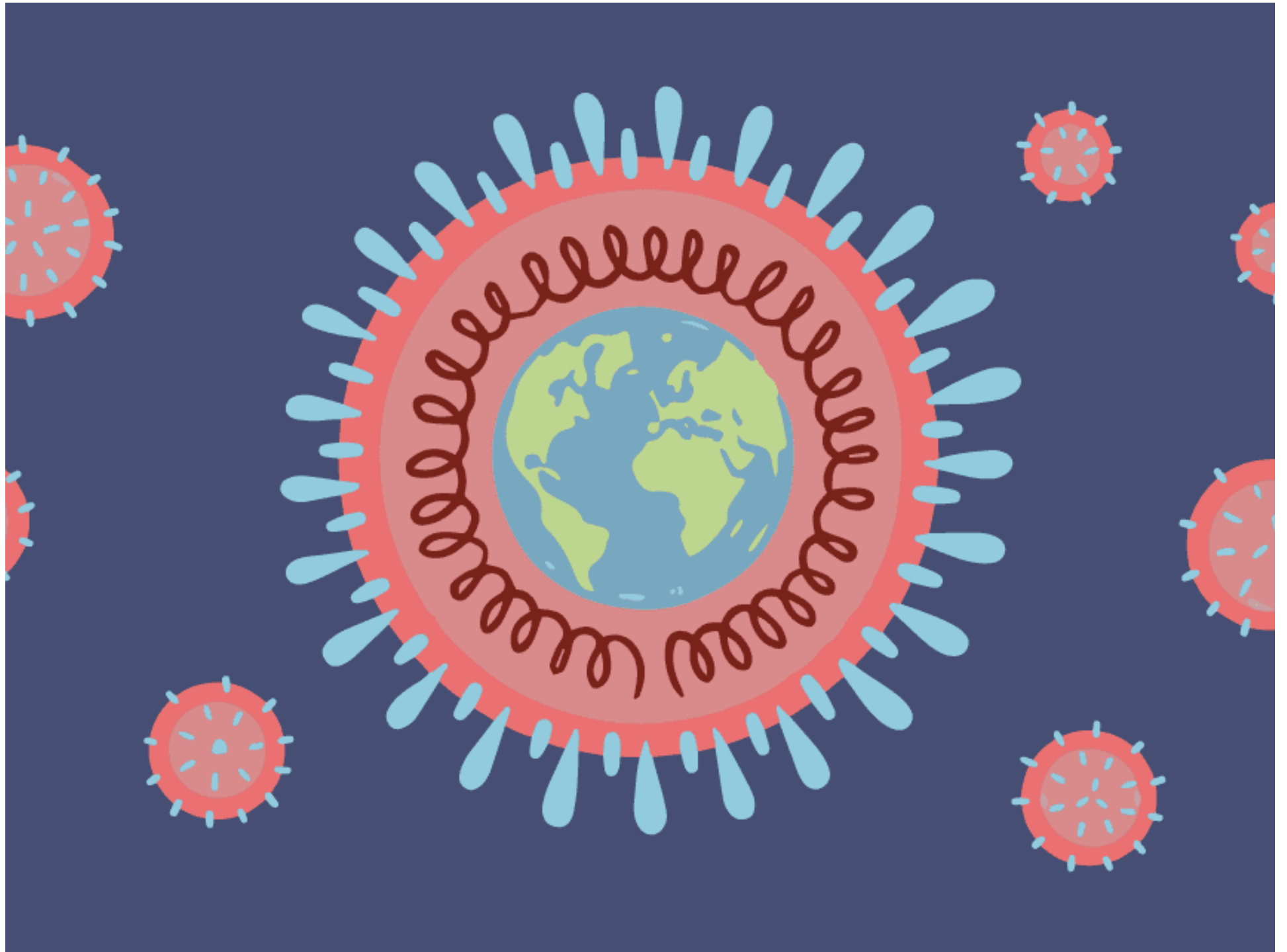
EpiDOSE

Epinephrine Dose: Optimal vs Standard Evaluation

Principal Investigators:

Paul Dorian MD MSc

Steve Lin MD MSc



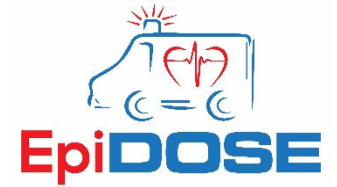


**Prospective, pragmatic,
multicentre RCT**

**Low dose (up to 2mg total)
“optimal”**

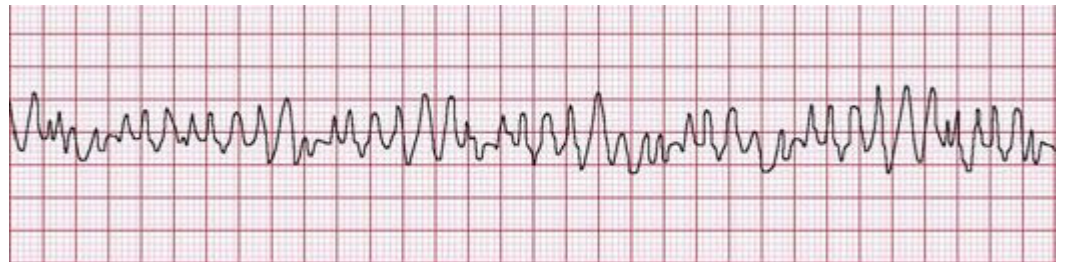
Standard dose (up to 6mg total)

STUDY PATIENTS



Inclusion Criteria:

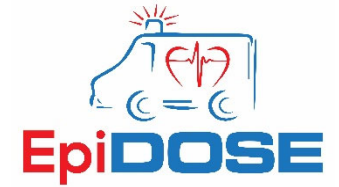
- Treated OHCA - presumed cardiac
- Initial rhythm of VF or VT
- IV access



Exclusion Criteria:

- Age <18 years
- Initial rhythm of PEA or asystole
- Non-cardiac etiology
- Prior IV or IM epinephrine

INTERVENTION ARMS



Initial VF/VT or AED shock on first analysis
witnessed or administered by EMS



Low dose



Standard dose



OUTCOMES



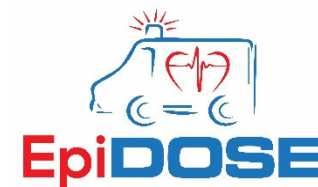
Primary Outcomes:

- Survival to hospital discharge

Secondary Outcomes:

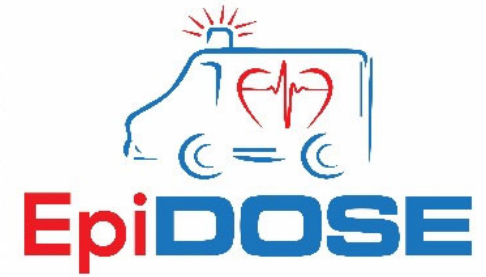
- Survival at 1 year
- Neurologic function at 1 year
- Global quality of life at 1 year

SAMPLE SIZE



Population	Number Per Arm
Per Protocol (secondary analysis)	1671
Modified Intention-to-Treat (primary analysis)	1705
Intention-to-Treat (secondary analysis)	1895
Total patients needed	3790

Based on a 2-sided alpha of 0.05 and 85% power to detect an improvement in survival to hospital discharge from 16% (standard dose epinephrine) to 20% (low dose epinephrine)



**First RCT
Low Dose
Epinephrine**

**Largest
Cardiac
Arrest Trial
in Canada**

**Rolling EMS
launches**

Who is Involved?

Halton

Paramedic Services

Launched May 24, 2023



Ottawa

Paramedic Services

Launched December 4, 2023



British Columbia Emergency



Health Services

Launched July 17, 2023



**Middlesex London
Paramedic Services**

Launched August 20, 2024

Essex-Windsor

Paramedic Services

Launched November 7, 2024



Superior North

Paramedic Services

Launched September 11, 2024



Peel

Paramedic Services

Launched December 9, 2024

**Launching
Soon**



**Medavie Health
Services West
(Saskatoon)**



@EpiDOSEtrial



@EpiDOSE_Trial

QUESTIONS



Steve Lin – steve.lin@unityhealth.to
Paul Dorian – paul.dorian@unityhealth.to
Theresa Aves – theresa.aves@unityhealth.to