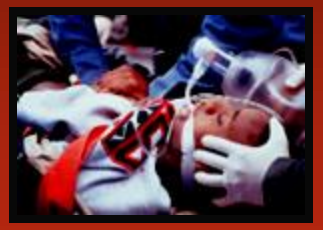
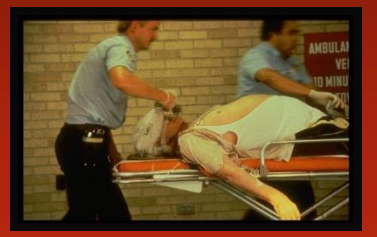
EBM vs. EBM

Why We Need Both Evidence-Based and *Experienced-Based* Medicine *!*



Paul E. Pepe, MD, MPH, FAEMS, MACP, MCCM

Professor of Management, Policy & Community Health

The University of Texas Health Sciences Center in Houston (TX), USA

Volunteer Professor of Surgery, **Univ. of Miami Miller School of Medicine, Miami (FL), USA**

Medical Director, **Dallas County Emergency Medical Services & Public Safety, Dallas (TX), USA**

Medical Director for Special Operations, **Broward County, Palm Beach County**

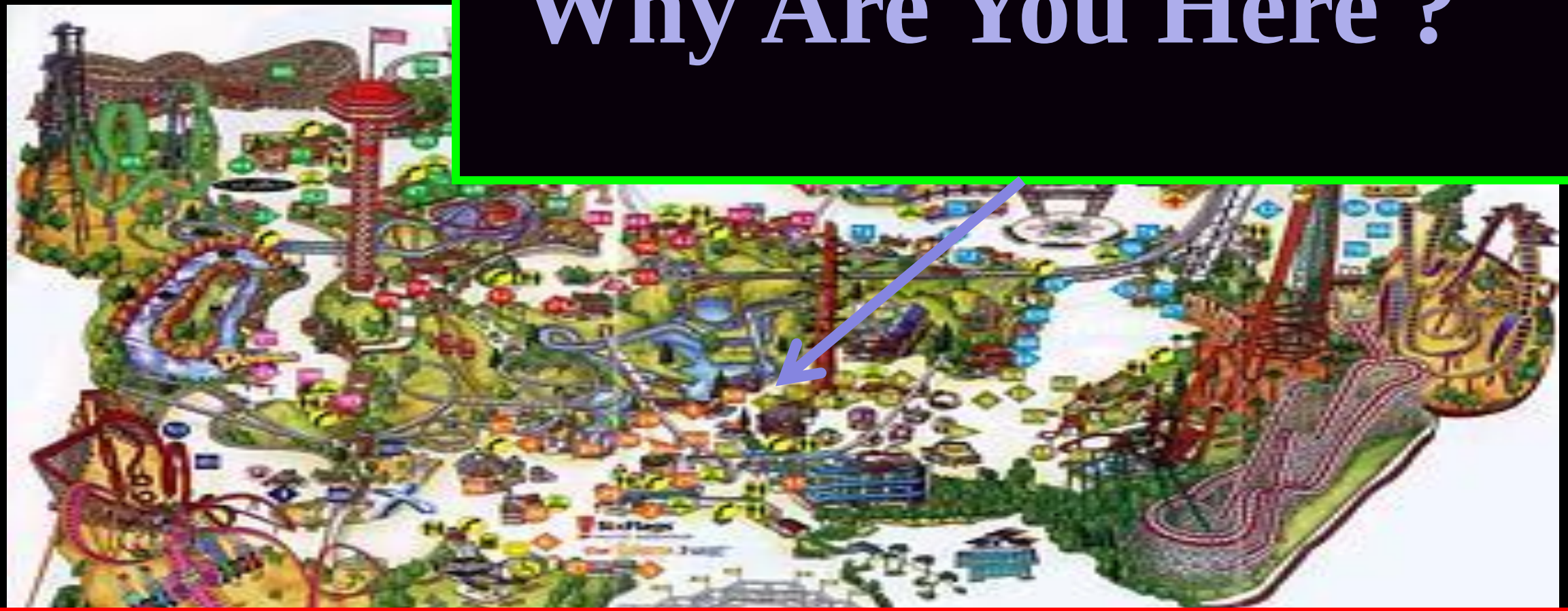
& Numerous Other South Florida Jurisdictions including Coral Springs-Parkland Fire Department

The Patient Has a Fractured Fibula….
…on a Mild Sedative…. Can Go Home Tomorrow …

Organizers Get Assistance Finding Today's Speaker…

Existential Fun Park…

Why Are You Here ?

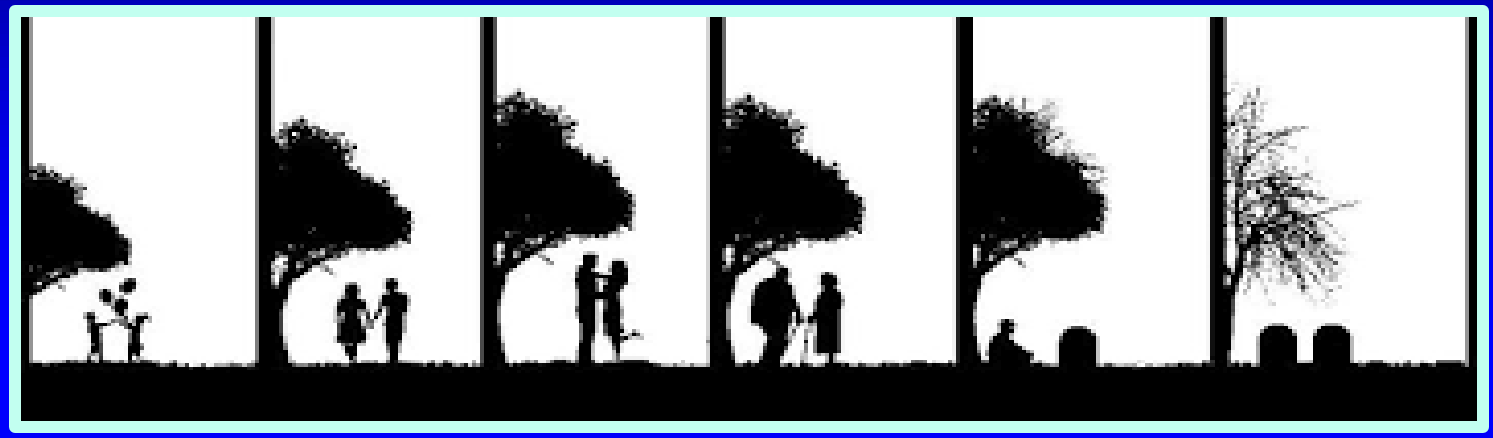


Don't Believe Everything You Think …

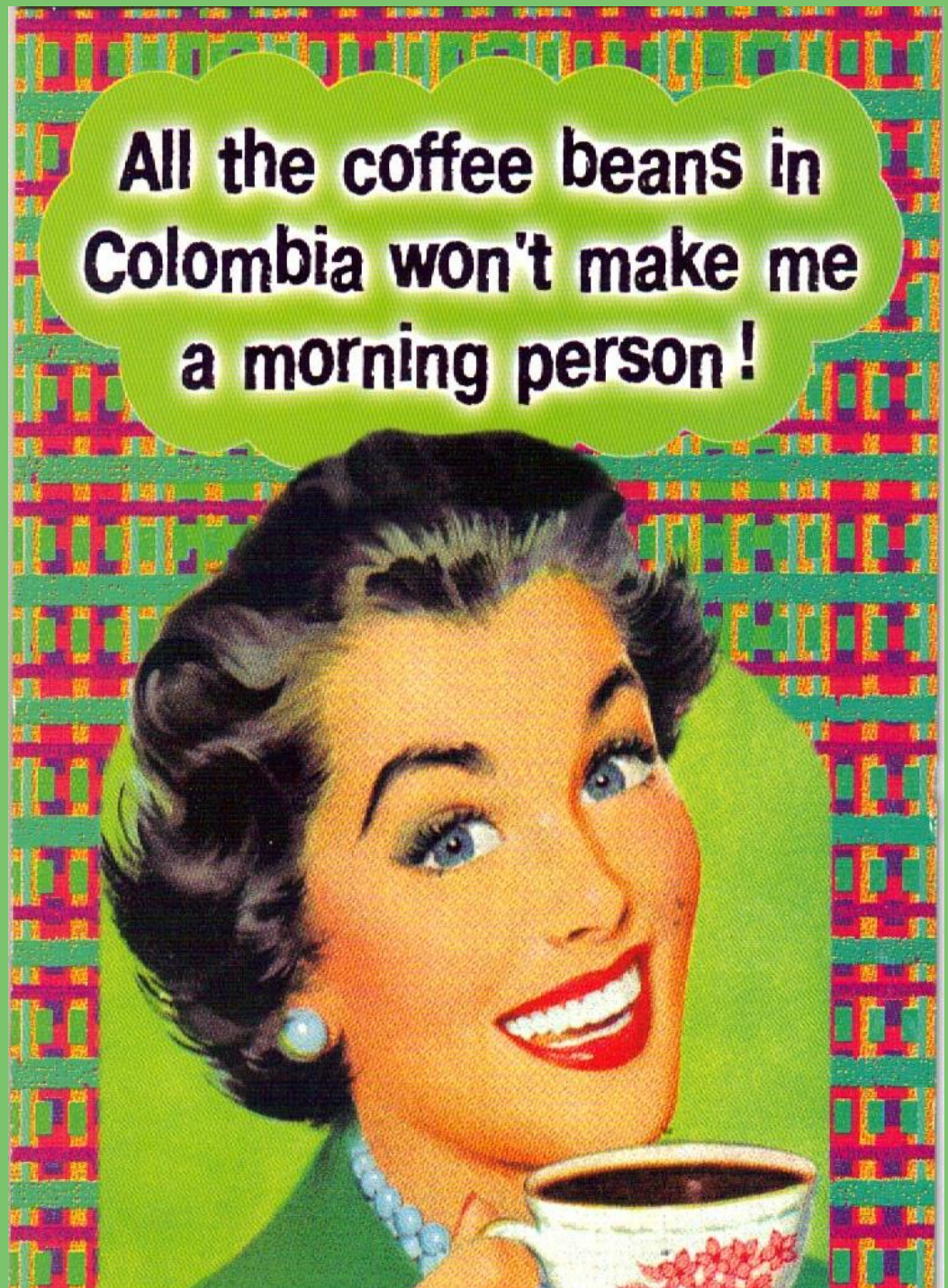
Before We Get Started …

The 4 Inevitabilities of Life …

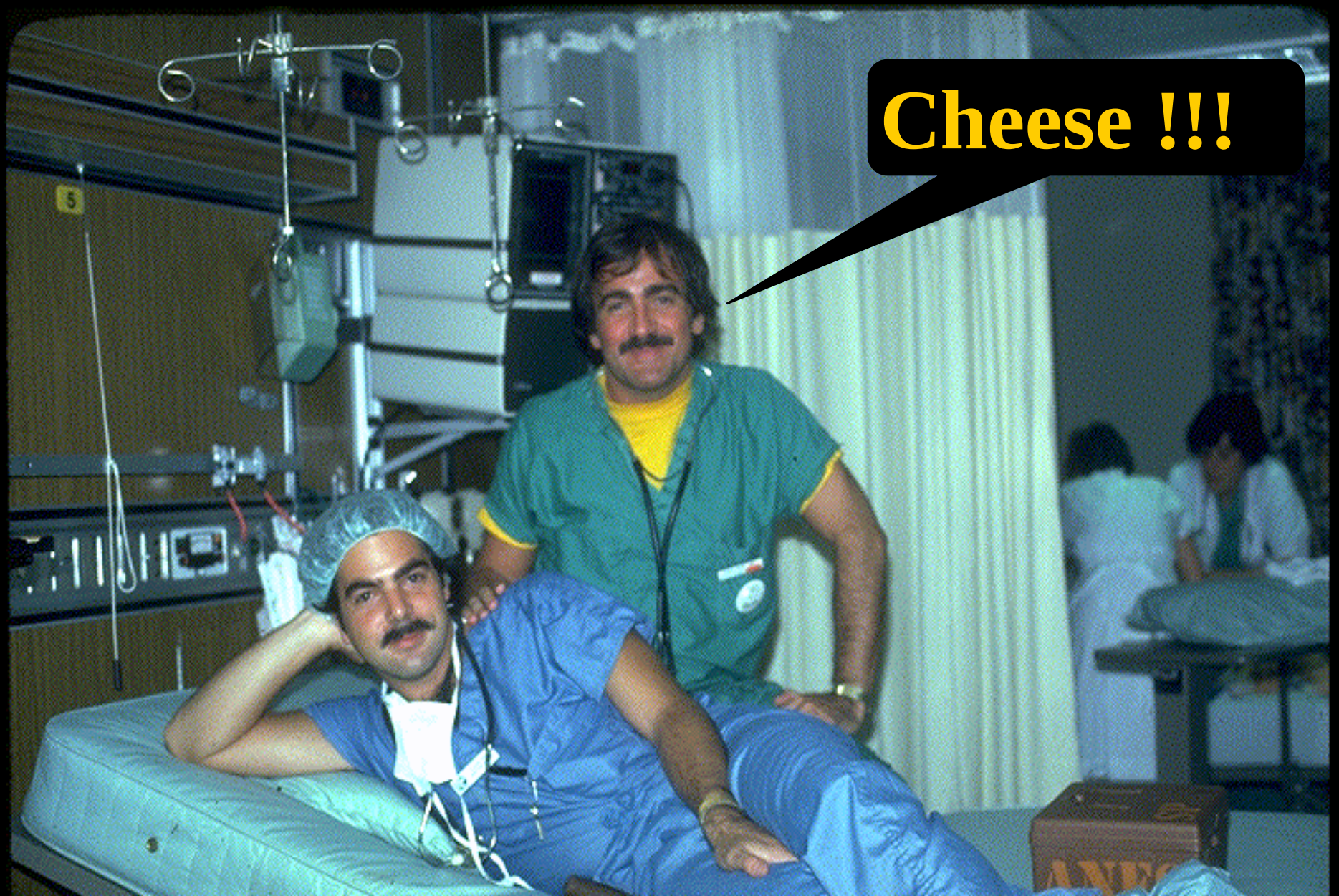
- Death
- Taxes
- Kale (California)
- Disclosures



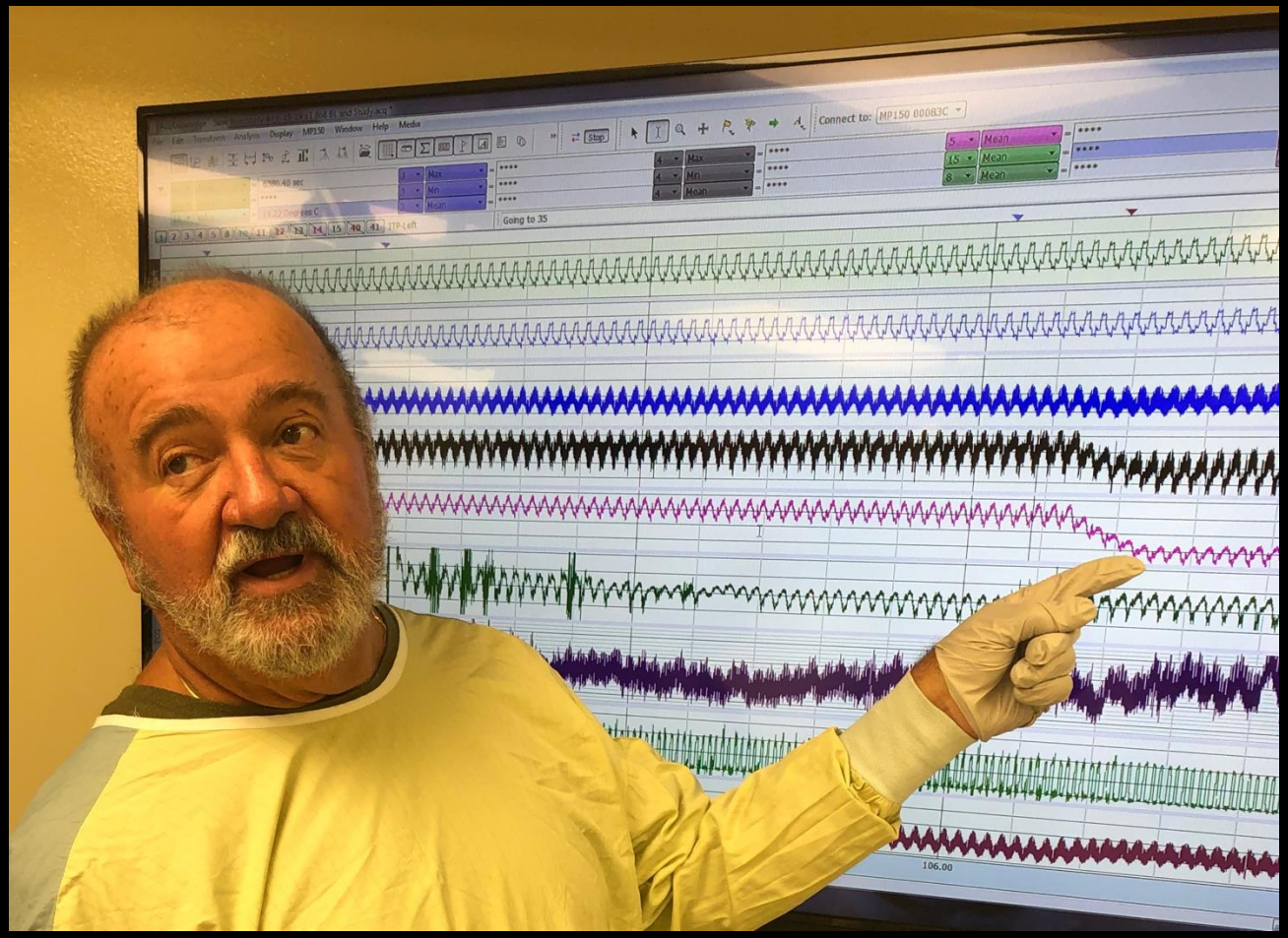
I am *NOT*
a Morning Person…

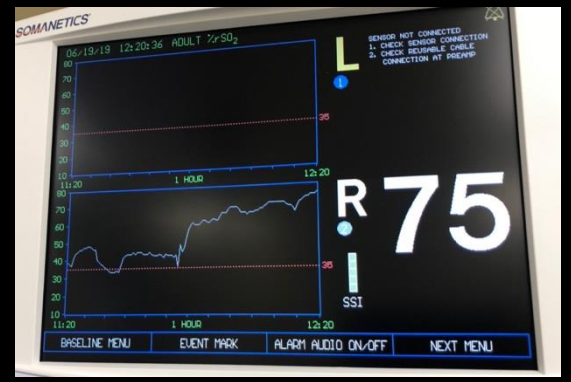


….. at University of Miami / Jackson Memorial Trauma Center – **40 Years Ago This Month!**

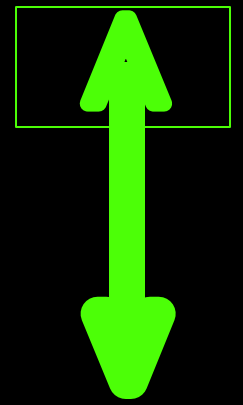


Still a Lab Rat….

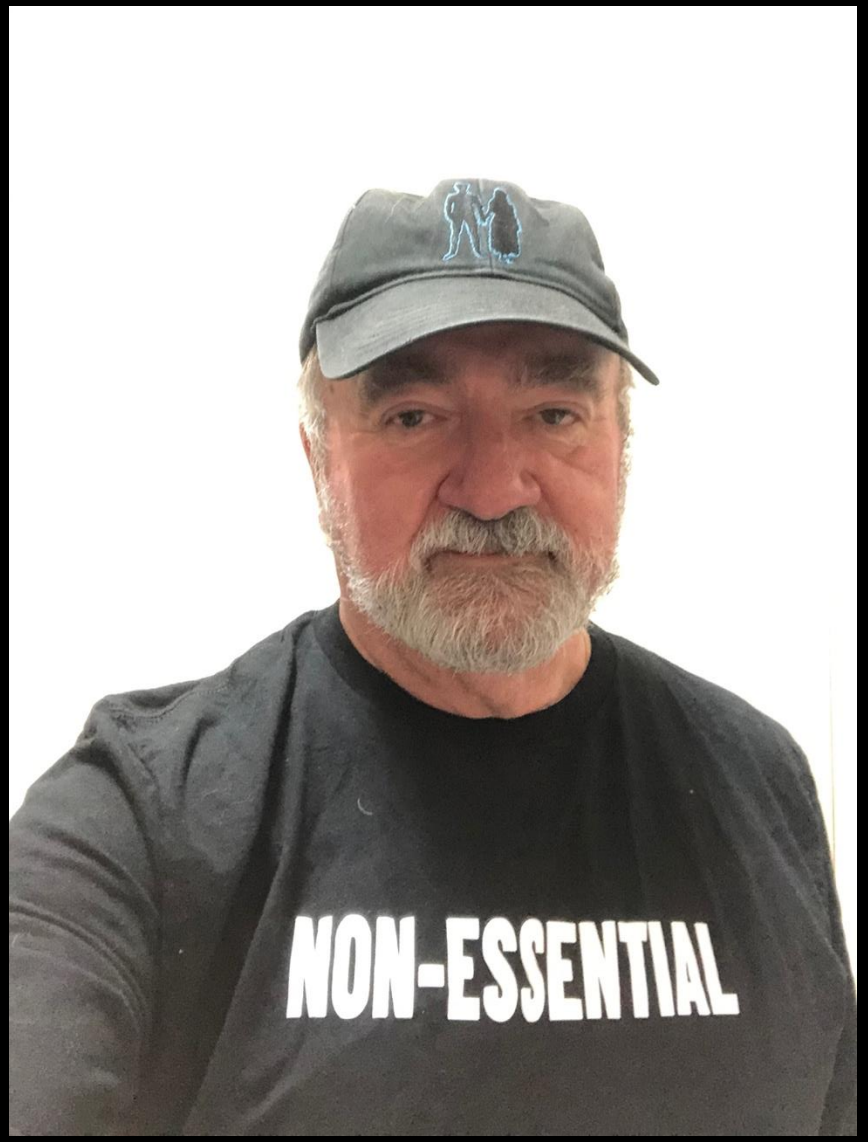




Up



Flat


NON-ESSENTIAL

29 Prehospital Resuscitation with Low Titer O+ Whole Blood by Civilian EMS Teams: Rationale and Evolving Strategies for Use

P. E. Pepe, J. P. Roach, and C. J. Winckler

29.1 Introduction: Civilian Setting Resuscitation Strategies for Bleeding over the Past Half Century

For the Life of all flesh, is the blood thereof. (Leviticus 17:14, the Bible)

Most modern out-of-hospital emergency medical services (EMS) systems, as we have come to recognize them today, were established in the 1960s and 1970s when a cadre of intrepid physicians ventured into the streets and later published their successful experiences with lifesaving approaches to managing acute coronary syndromes, trauma care, and cardiopulmonary arrest on-scene [1–3]. These lifesaving

NONMECHANICAL HEMOSTASIS IN TRAUMA CARE

Part I: Evolving prehospital practices and the role of TXA

By Paul E. Pepe, MD, MPH, FAEMS, MCCM; Jonathan Jui, MD, MPH, FACEP, FAEMS; and John B. Holcomb, MD, FACS

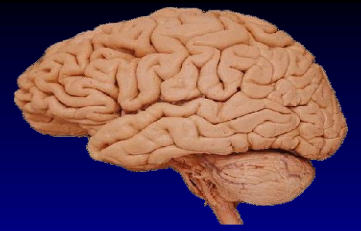
Resident Eagle is a monthly column profiling the work of top EMS physicians and medical directors from the Metropolitan EMS Medical Directors Global Alliance (the "Eagles"), who represent America's largest and key international cities.

TENTATIVE DATES FOR GATHERING OF EAGLES 2021: JUNE 14–18, HOLLYWOOD, FLA. FOR MORE SEE USEAGLES.ORG.

Modern trauma systems were created more than a half century ago to enable severely injured patients to reach a facility where surgeons were standing by around-the-clock ready to rapidly achieve anatomical hemostasis (physical bleeding control) for internal hemorrhage and/or evacuate blood and control further bleeding within the intracranial vault.[1]

Time is of the essence. Physically clamping and repairing damaged blood vessels within the chest, abdomen, or skull must be achieved before exsanguination or fatal CNS compromise. A person's own blood is equipped with optimal clotting factors and functioning platelets. It is the ultimate medium for sustaining human life minute to minute with delivery of oxygen to vital organs. While timely transfusions can be

Cognitive Roadmap



- First Tell You Why I Became the Apostle, Paul, Zealously Preaching the Gospel of the RCT, and Pushing Envelopes for EFIC & Funding for RCTs
- Then, Using Our Experience with Heavily-Resourced RCTs for Out-of-Hospital Cardiac Arrest, Will Give Examples of Why I Came to Appreciate That We Were Putting Too Much Faith in RCTs
- Finally – Will Warn You to Beware of the Binaries & Let You Know What We Are Now Doing for OHCA & Maybe Also Consider for Trauma Interventions

déjà vu ...

... All Over Again

EBM vs. EBM

EBM vs. EBM: combining evidence-based and experienced-based medicine in resuscitation research

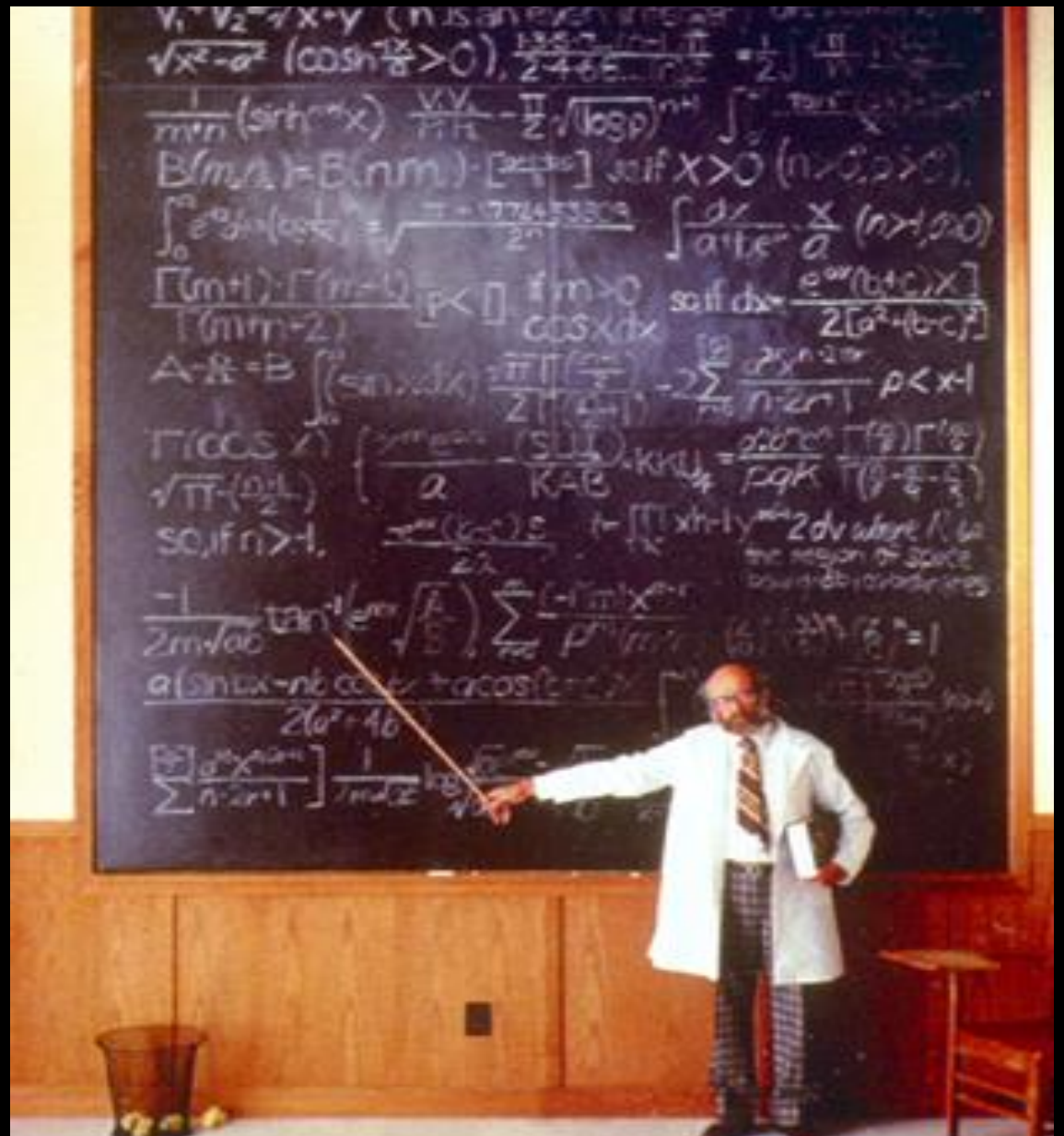
Paul E. Pepe[a] and Tom P. Aufderheide[b]

Purpose of review
To discuss the clear rationale for evidence-based medicine (EvBM) in the challenging realms of resuscitation research, yet also provide case examples in which even the well designed, multicentered randomized clinical trial may have had unrecognized limitations, and thus misleading results. This is where experienced-based medicine (ExBM) helps to resolve the issue.

Recent findings
Recent publications have brought to task the conclusions drawn from various clinical trials of resuscitative interventions. These articles have indicated that some major clinical trials that later determined the universal guidelines for resuscitative protocols may have been affected by unrecognized confounding variables, effect modifiers and other problems such as delayed timing. Many interventions, deemed to be ineffective because of these study factors, may actually have lifesaving effects that would have been confirmed had the proper circumstances been in place. With the right mindset, the clinician-researcher can often identify and address those situations.

Summary
When clinical trials indicate ineffectiveness of an intervention that worked very well in other circumstances, both preclinical and clinical, clinician-investigators should continue to re-search the issues and not always take conclusions at face value.

Some New Information ...



Before We Begin the Main Dyscourse …

PUBLIC USE OF AUTOMATED EXTERNAL DEFIBRILLATORS

SHERRY L. CAFFREY, E.M.T.-P., PAULA J. WILLOUGHBY, D.O., M.H.P.E., PAUL E. PEPE, M.D., M.P.H., AND LANCE B. BECKER, M.D.

ABSTRACT

Background Automated external defibrillators save lives when they are used by designated personnel in certain public settings. We performed a two-year prospective study at three Chicago airports to assess whether random bystanders witnessing out-of-hospital cardiac arrests would retrieve and successfully use automated external defibrillators.

Methods Defibrillators were installed a brisk 60-to-90-second walk apart throughout passenger terminals at O'Hare, Midway, and Meigs Field airports, which together serve more than 100 million passengers per year. The use of defibrillators was promoted by public-service videos in waiting areas, pamphlets, and reports in the media. We assessed the time from notification of the dispatchers to defibrillation, survival rate at 72 hours and at one year among persons with cardiac arrest, their neurologic status, and the characteristics of rescuers.

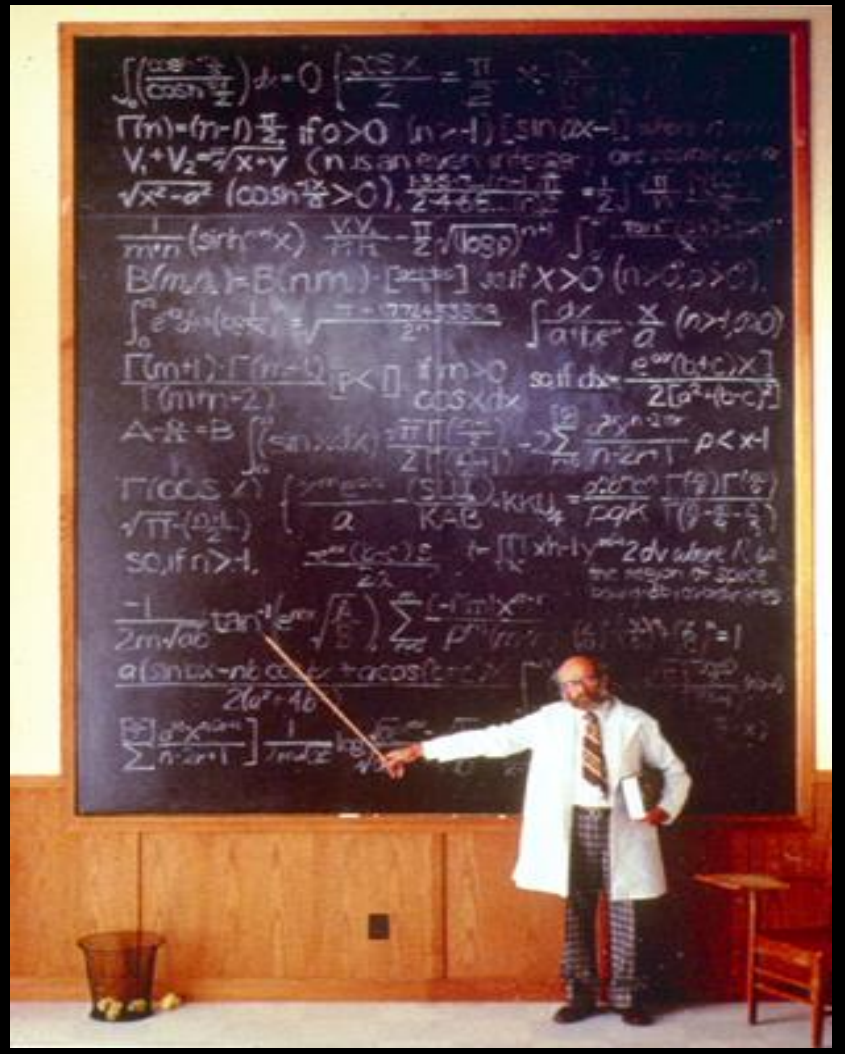
Results Over a two-year period, 21 persons had nontraumatic cardiac arrest, 18 of whom had ventricular fibrillation. With two exceptions, defibrillator operators were good Samaritans, acting voluntarily. In the case of four patients with ventricular fibrillation, defibrillators were neither nearby nor used within five minutes, and none of these patients survived. Three others remained in fibrillation and eventually died, de-

CARDIOVASCULAR disease remains the most common cause of death in the United States and most other Western nations.[1-4] Among these deaths, sudden, out-of-hospital cardiac arrest claims approximately 1000 lives each day in the United States alone.[3] Most of these cardiac arrests are due to ventricular fibrillation.[4-7] Though highly reversible with the rapid application of a defibrillator, ventricular fibrillation is otherwise fatal within minutes, even when cardiopulmonary resuscitation is provided immediately.[7-11] The overall survival rate in the United States is estimated to be less than 5 percent.[4,5,7,12-14]

Recent developments in automated-external-defibrillator technology have provided a means of increasing the rate of prompt defibrillation after out-of-hospital cardiac arrest.[15] After minimal training, nonmedical personnel (e.g., flight attendants and casino workers) are able to use defibrillators in the workplace, with life-saving effects.[16-20] Nonetheless, such programs have involved designated personnel whose job description includes assisting persons who have had sudden cardiac arrest. Data are still lacking on the success of programs in which automated external defibrillators have been installed in public places to be used by persons

Just Keep That One in Mind …

So Let's Begin ...



Time to Fasten Your Seatbelts…

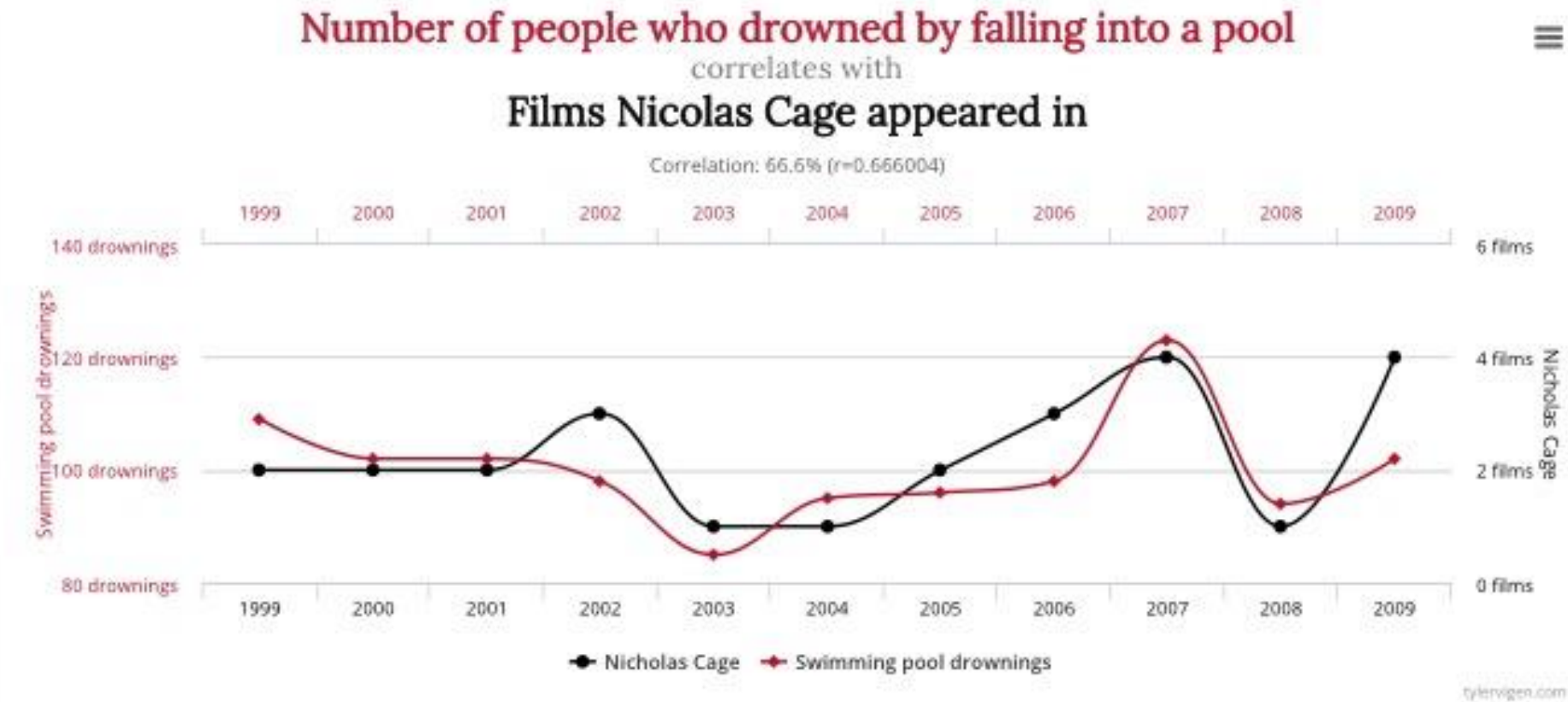
My Bias -- EBM is:

Clearly Essential,

Cost-Effective…

… and Even Life-Saving


THE
INDEX



Data Source: Centers for Disease Control and Prevention and Internet Movie Database

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(OBVIOUS) CONCLUSION:

"With the exception of '*Moonstruck*', Nicholas Cage movies were apparently so bad that many people drowned themselves (by falling into a pool) ….

… Further study is needed"

Randomized, Controlled Clinical Trials Have Always Been Considered

The Gold Standard In Evidenced-Based Medicine

Unique Challenges

Clinical trials in the out-of-hospital setting: Rationale and strategies for successful implementation

Paul E. Pepe, MD, MPH, MACP, FCCM, FACEP; Michael K. Copass, MD; George Sopko, MD, MPH

Cardiopulmonary arrest and trauma are two of the major epidemics of our time. In most cases, the final outcome is altered, for better or for worse, by how interventions are provided in the prehospital setting, making that venue critical for lifesaving community research efforts. In certain venues, out-of-hospital emergency medical services personnel are highly skilled at managing resuscitations and routinely operate under strict, highly scrutinized protocols, resulting in extraordinary study compliance. Larger patient enrollment derived from population-based investigations can lead to faster study completion, less selection bias, higher-powered data, and enhanced subgroup analysis. Most importantly, the concomitant training, expert protocol development, and rigid scrutiny all lead to improved patient outcomes, regardless of study intervention. For successful implementation, emergency medical services personnel should be involved in study design, and utilize routine, automated data collection. Technologies should be provided that simplify tasks and diminish confounding variables. Considering that exception to informed consent is a critical component, prospective education and involvement of the medical community, community leaders, employee groups and the media, long before protocol implementation, is essential. Such efforts should be led by respected, academically authoritative, grassroots emergency medical services medical directors and trauma chiefs, preferably those based at the main trauma centers or public receiving facilities. (Crit Care Med 2009; 37[Suppl.]:S91–S101)

Key Words: resuscitation; trauma; injury; research; clinical trials; outcomes data; cardiac arrest; cardiopulmonary resuscitation; CPR; sudden death; emergency medical services; EMS; survival rates; informed consent; exception to consent; ethics; community consultation; population-based research out-of-hospital; prehospital

In many aspects of medicine, the earlier a medical intervention is provided, the better the results. In resuscitation medicine, not only are the intervals to various therapies inversely correlated with survival, but with current techniques, patients rarely survive if pulses are not restored within minutes (1–8). Furthermore, the prehospital venues, with immediate provision of basic cardiopulmonary resuscitation (CPR) by bystanders soon followed by EMS defibrillation, long-term survival rates now have exceeded 60% for witnessed cases of ventricular fibrillation, the major etiology of out-of-hospital sudden death (1, 4). Recent out-of-hospital research has shown that in certain public settings, costs as well (14). Considering that, in the United States alone, sudden death accounts for nearly a thousand premature deaths each day, the profound value of these study efforts has become very compelling and they are now a focus on federal research agendas in North America (1, 14–16). In addition, for many of the reasons described in detail later in

Food and Drug Administration Public Hearing on the Conduct of Emergency Clinical Research: Testimony of Dr. Pepe—Defending the Rights of All Individuals to Have Access to Potential Life-saving Therapies and Resuscitation Studies

Paul E. Pepe, MD, MPH, FACEP, FCCM, FACP

Using average life expectancy as an arbitrary benchmark, a great percentage of those Americans who will die prematurely today will be those who lose their lives to sudden cardiac arrest and severe traumatic injury.[1–5] Despite the grim annual toll, many of these deaths are fully preventable when certain immediate interventions are provided.[1,6–8] In most cases, the ultimate outcome, good or bad, will be decided in the out-of-hospital setting in the first few minutes after the precipitating event.[1,6–11] As a result, resuscitation medicine has now become a mainstream focus in the house of medicine, not only clinically but also in terms of national research priorities.[12,13] This evolution is best exemplified by recent creation of the Resuscitation Outcomes Consortium by the National Institutes of Health and

lection constraints because resuscitation trials generally involve an entire community and dozens of hospitals. As a result, despite the existence of many promising therapies that have been elegantly demonstrated in the laboratory and supported in preliminary clinical studies,[17,29,31] efforts to provide the world with definitive clinical trials generally have ended in significant gridlock. A large part of the gridlock has been due to ethical anxieties, provocative media stories, and political pressures that have emanated, understandably, from concerns over the protection of an individual's right to consent to treatment, along with unfaded memories of secretive human experimentation, ranging from Dachau to Tuskegee.[32]

In contrast to those infamous scenarios, well-designed

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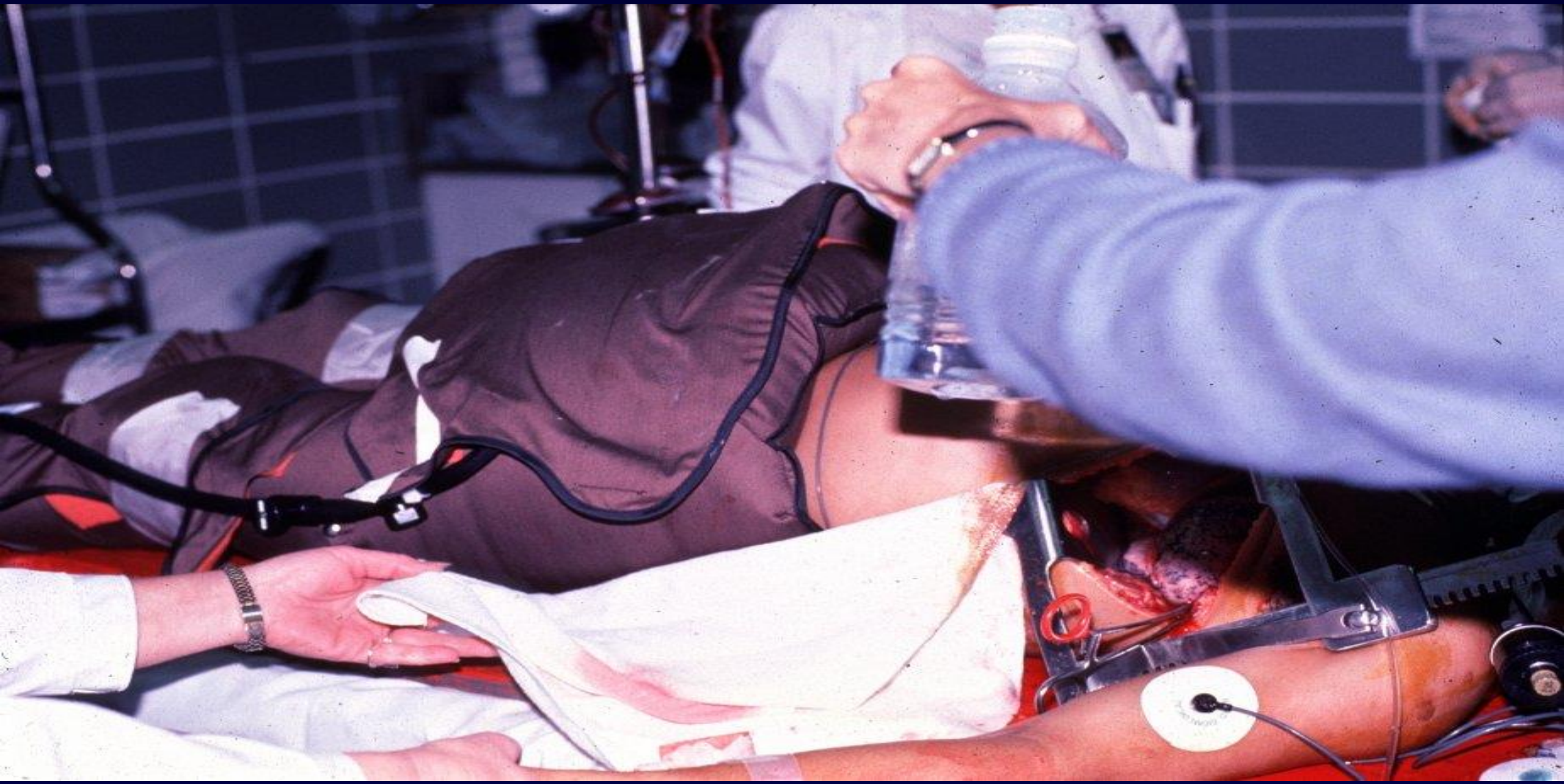

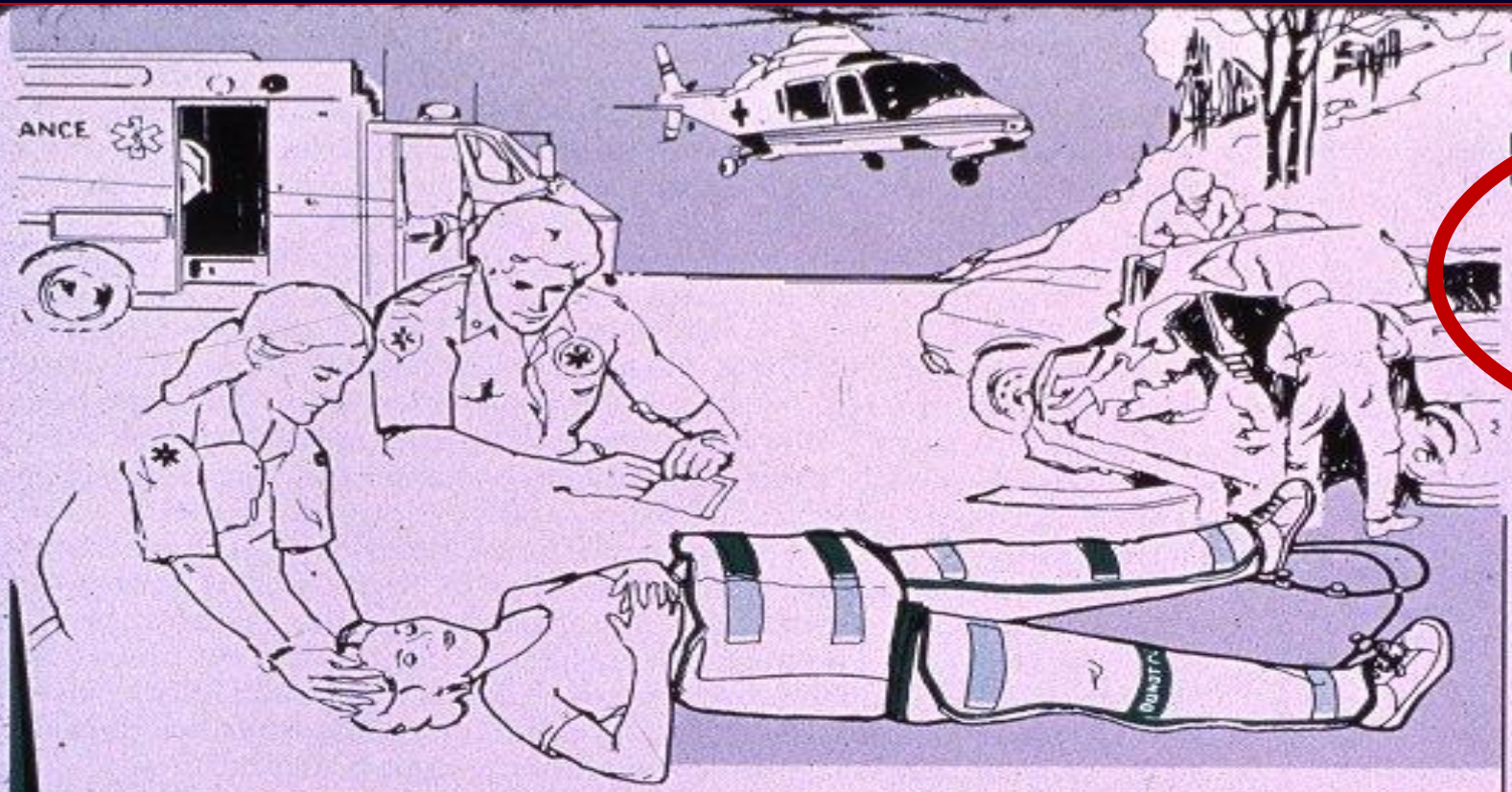

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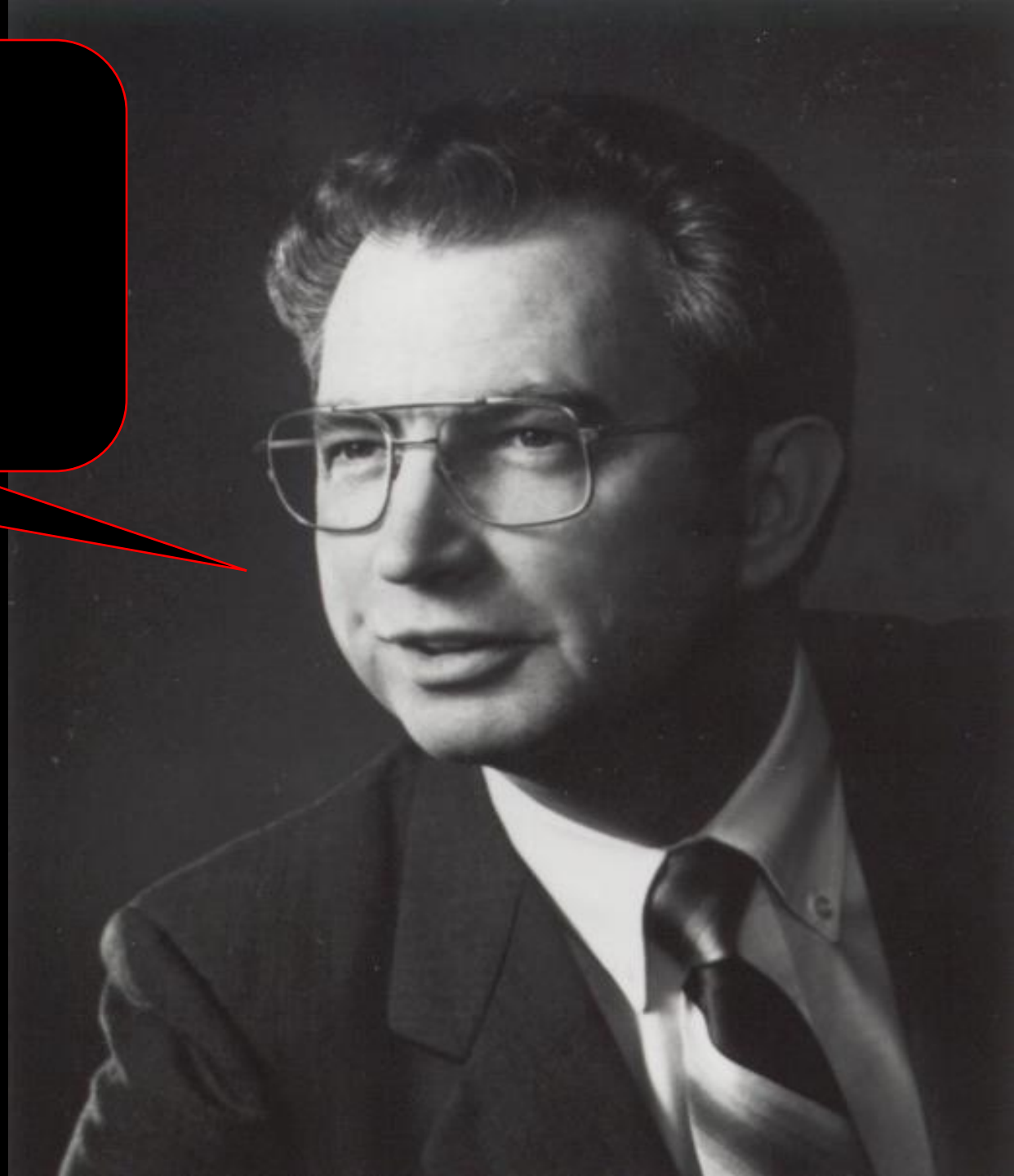

The PASG

Actually Had Worse Outcomes !

And the Control Groups Had Better Outcomes Than the Historical Levels…

>>> Clinical Trials Save Lives

>>> Beware of Historical Controls

The New England
Journal of Medicine

Volume 331 OCTOBER 27, 1994 Number 17

IMMEDIATE VERSUS DELAYED FLUID RESUSCITATION FOR HYPOTENSIVE PATIENTS WITH PENETRATING TORSO INJURIES

WILLIAM H. BICKELL, M.D., MATTHEW J. WALL, JR., M.D., PAUL E. PEPE, M.D., R. RUSSELL MARTIN, M.D., VICTORIA F. GINGER, M.S.N., MARY K. ALLEN, B.A., AND KENNETH L. MATTOX, M.D.

Abstract *Background.* Fluid resuscitation may be detrimental when given before bleeding is controlled in patients with trauma. The purpose of this study was to determine the effects of delaying fluid resuscitation until the time of operative intervention in hypotensive patients with penetrating injuries to the torso.

Methods. We conducted a prospective trial comparing immediate and delayed fluid resuscitation in 598 adults with penetrating torso injuries who presented with a pre-

Results. Among the 289 patients who received delayed fluid resuscitation, 203 (70 percent) survived and were discharged from the hospital, as compared with 193 of the 309 patients (62 percent) who received immediate fluid resuscitation ($P = 0.04$). The mean estimated intraoperative blood loss was similar in the two groups. Among the 238 patients in the delayed-resuscitation group who survived to the postoperative period, 55 (23 percent) had one or more complications (adult respiratory distress syn-

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Paul E. Pepe, MD, MPH, FACEP, FCCM, FACP

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Unfortunately, to date, only a few interventions have lection constraints because resuscitation trials generally involve an entire community and dozens of hospitals. As a result, despite the existence of many promising therapies that have been elegantly demonstrated in the laboratory and supported in preliminary clinical studies,[17,29,31] efforts to provide the world with definitive clinical trials generally have ended in significant gridlock. A large part of the gridlock has been due to ethical anxieties, provocative media stories, and political pressures that have emanated, understandably, from concerns over the protection of an individual's right to consent to treatment, along with unfaded memories of secretive human experimentation, ranging from Dachau to Tuskegee.[32]

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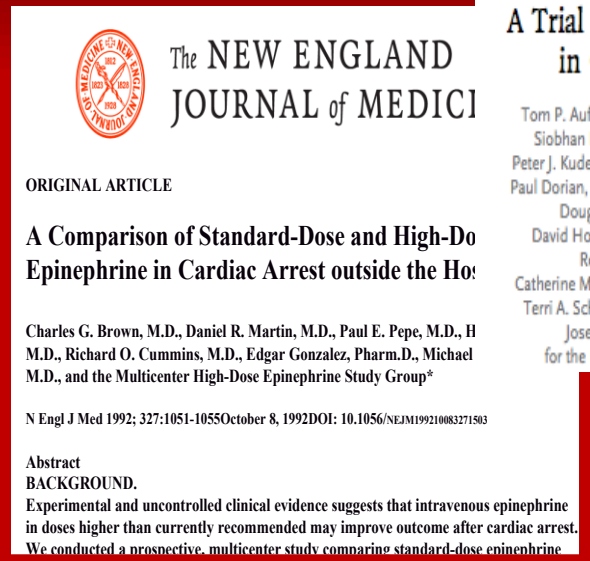
EBM is:

Clearly Essential,

Cost-Effective…

… and Even Life-Saving

Problem:



The NEW ENGLAND JOURNAL of MEDICI

ORIGINAL ARTICLE

A Comparison of Standard-Dose and High-Do
Epinephrine in Cardiac Arrest outside the Ho

Charles G. Brown, M.D., Daniel R. Martin, M.D., Paul E. Pepe, M.D., H
M.D., Richard O. Cummins, M.D., Edgar Gonzalez, Pharm.D., Michael
M.D., and the Multicenter High-Dose Epinephrine Study Group*

N Engl J Med 1992; 327:1051-1055October 8, 1992DOI: 10.1056/NEJM199210083271503

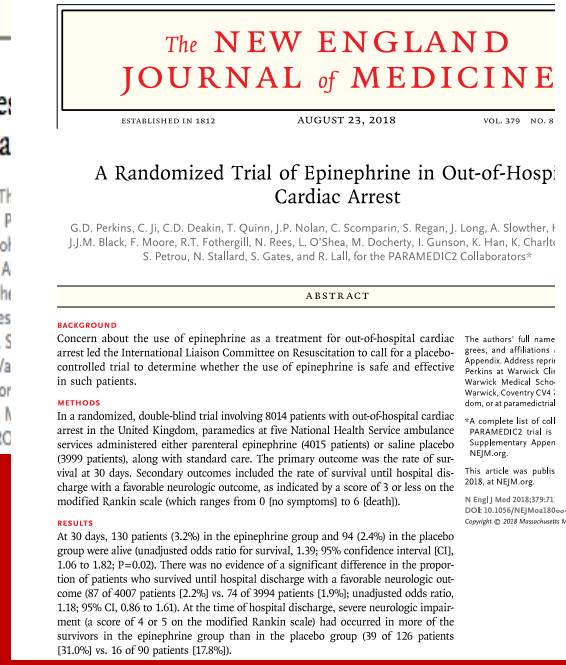
Abstract
BACKGROUND.
Experimental and uncontrolled clinical evidence suggests that intravenous epinephrine
in doses higher than currently recommended may improve outcome after cardiac arrest.
We conducted a prospective, multicenter study comparing standard-dose epinephrine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of an Impedance Thres
in Out-of-Hospital Cardia

Tom P. Aufderheide, M.D., Graham Nichol, M.D., Th
Siobhan P. Brown, Ph.D., Brian G. Leroux, Ph.D., P
Peter J. Kudenchuk, M.D., Jim Christenson, M.D., Mol
Paul Dorian, M.D., Clifton W. Callaway, M.D., Ph.D., A
Douglas Andrusiek, M.Sc., Shannon W. Stephe
David Hostler, Ph.D., Daniel P. Davis, M.D., James
Ronald G. Pirrallo, M.D., M.H.S.A., Ian G. S
Catherine M. Clement, R.N., Alan Craig, M.S., Lois Va
Terri A. Schmidt, M.D., Henry E. Wang, M.D., Myror
Joseph P. Ornato, M.D., and George Sopko, M
for the Resuscitation Outcomes Consortium (RO



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2018 VOL. 379 NO. 8

A Randomized Trial of Epinephrine in Out-of-Hosp
Cardiac Arrest

G.D. Perkins, C. Ji, C.D. Deakin, T. Quinn, J.P. Nolan, C. Scomparin, S. Regan, J. Long, A. Slowther, H
J.J.M. Black, F. Moore, R.T. Fothergill, N. Rees, L. O'Shea, M. Docherty, I. Gunson, K. Han, K. Charlt
S. Petrou, N. Stallard, S. Gates, and R. Lall, for the PARAMEDIC2 Collaborators*

ABSTRACT

BACKGROUND
Concern about the use of epinephrine as a treatment for out-of-hospital cardiac arrest led the International Liaison Committee on Resuscitation to call for a placebo-controlled trial to determine whether the use of epinephrine is safe and effective in such patients.

METHODS
In a randomized, double-blind trial involving 8014 patients with out-of-hospital cardiac arrest in the United Kingdom, paramedics at five National Health Service ambulance services administered either parenteral epinephrine (4015 patients) or saline placebo (3999 patients), along with standard care. The primary outcome was the rate of survival at 30 days. Secondary outcomes included the rate of survival until hospital discharge with a favorable neurologic outcome, as indicated by a score of 3 or less on the modified Rankin scale (which ranges from 0 [no symptoms] to 6 [death]).

RESULTS
At 30 days, 130 patients (3.2%) in the epinephrine group and 94 (2.4%) in the placebo group were alive (unadjusted odds ratio for survival, 1.39; 95% confidence interval [CI], 1.06 to 1.82; P=0.02). There was no evidence of a significant difference in the proportion of patients who survived until hospital discharge with a favorable neurologic outcome (87 of 4007 patients [2.2%] vs. 74 of 3994 patients [1.9%]; unadjusted odds ratio, 1.18; 95% CI, 0.86 to 1.61). At the time of hospital discharge, severe neurologic impairment (a score of 4 or 5 on the modified Rankin scale) had occurred in more of the survivors in the epinephrine group than in the placebo group (39 of 126 patients [31.0%] vs. 16 of 90 patients [17.8%]).

The authors' full name
grees, and affiliations
Appendix. Address repri
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*A complete list of coll
PARAMEDIC2 trial is
Supplementary Appen
NEJM.org.

This article was publis
2018, at NEJM.org.

N Engl J Med 2018;379:71
DOI: 10.1056/NEJMoa180xxxx

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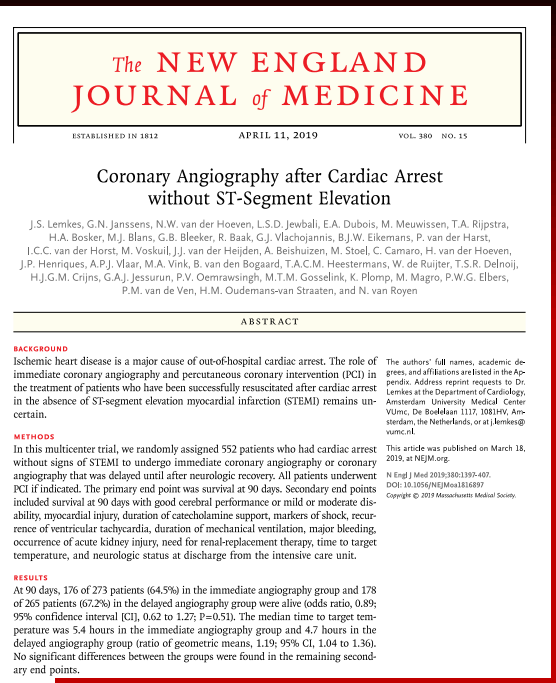

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 11, 2019 VOL. 380 NO. 15

Coronary Angiography after Cardiac Arrest
without ST-Segment Elevation

J.S. Lemkes, G.N. Janssens, N.W. van der Hoeven, L.S.D. Jewbali, E.A. Dubois, M. Meuwissen, T.A. Rijpstra, H.A. Bosker, M.J. Blans, G.B. Bleeker, R. Baak, G.J. Vlachojannis, B.J.W. Eikemans, P. van der Harst, I.C.C. van der Horst, M. Voskuil, J.J. van der Heijden, A. Beishuizen, M. Stoel, C. Camaro, H. van der Hoeven, J.P. Henriques, A.P.J. Vlaar, M.A. Vink, B. van den Bogaard, T.A.C.M. Heestermans, W. de Ruijter, T.S.R. Delnoij, H.J.G.M. Crijns, G.A.J. Jessurun, P.V. Oemrawsingh, M.T.M. Gosselink, K. Plomp, M. Magro, P.W.G. Elbers, P.M. van de Ven, H.M. Oudemans-van Straaten, and N. van Royen

ABSTRACT

BACKGROUND
Ischemic heart disease is a major cause of out-of-hospital cardiac arrest. The role of immediate coronary angiography and percutaneous coronary intervention (PCI) in the treatment of patients who have been successfully resuscitated after cardiac arrest in the absence of ST-segment elevation myocardial infarction (STEMI) remains uncertain.

METHODS
In this multicenter trial, we randomly assigned 552 patients who had cardiac arrest without signs of STEMI to undergo immediate coronary angiography or coronary angiography that was delayed until after neurologic recovery. All patients underwent PCI if indicated. The primary end point was survival at 90 days. Secondary end points included survival at 90 days with good cerebral performance or mild or moderate disability, myocardial injury, duration of catecholamine support, markers of shock, recurrence of ventricular tachycardia, duration of mechanical ventilation, major bleeding, occurrence of acute kidney injury, need for renal-replacement therapy, time to target temperature, and neurologic status at discharge from the intensive care unit.

RESULTS
At 90 days, 176 of 273 patients (64.5%) in the immediate angiography group and 178 of 265 patients (67.2%) in the delayed angiography group were alive (odds ratio, 0.89; 95% confidence interval [CI], 0.62 to 1.27; P=0.51). The median time to target temperature was 5.4 hours in the immediate angiography group and 4.7 hours in the delayed angiography group (ratio of geometric means, 1.19; 95% CI, 1.04 to 1.36). No significant differences between the groups were found in the remaining secondary end points.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Lemkes at the Department of Cardiology, Amsterdam University Medical Center VUmc, De Boelelaan 1117, 1081HV, Amsterdam, the Netherlands, or at j.lemkes@vumc.nl.

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Over the Past Four Decades:

Numerous (in fact, Most) Cardiac Arrest Clinical Trials Had Disappointing Results

So Why Are OHCA Clinical Trials Compromised?

- **Many Interwoven Interdependent Variables …**
- **Ventilatory Techniques Affect Blood Flow**
- **CPR Quality Affected By Numerous Factors**
- **Drugs or Devices Don’t Work If Too Late**
- **Interventions Needed at One Point in Time …**
  …. Not Needed at Another Point in Time
- **Individual Device or Intervention Effectiveness**
  Requires Other Coordinated Interventions

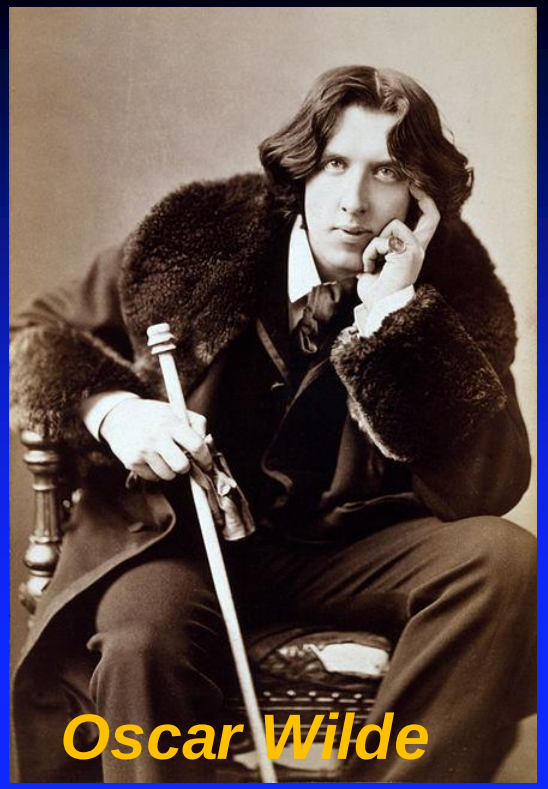
Pivotal ITD Study

The 2011 NIH ROC NEJM study…
Elegant Study, Impressive Design

150 EMS Agencies in U.S. and Canada

OUTCOME ???

N.S.D.



The Truth is Rarely Pure …
… and Never Simple

THE LANCET

Volume 377 · Number 9762 · Pages 271–352 · January 22–28, 2011 www.thelancet.com

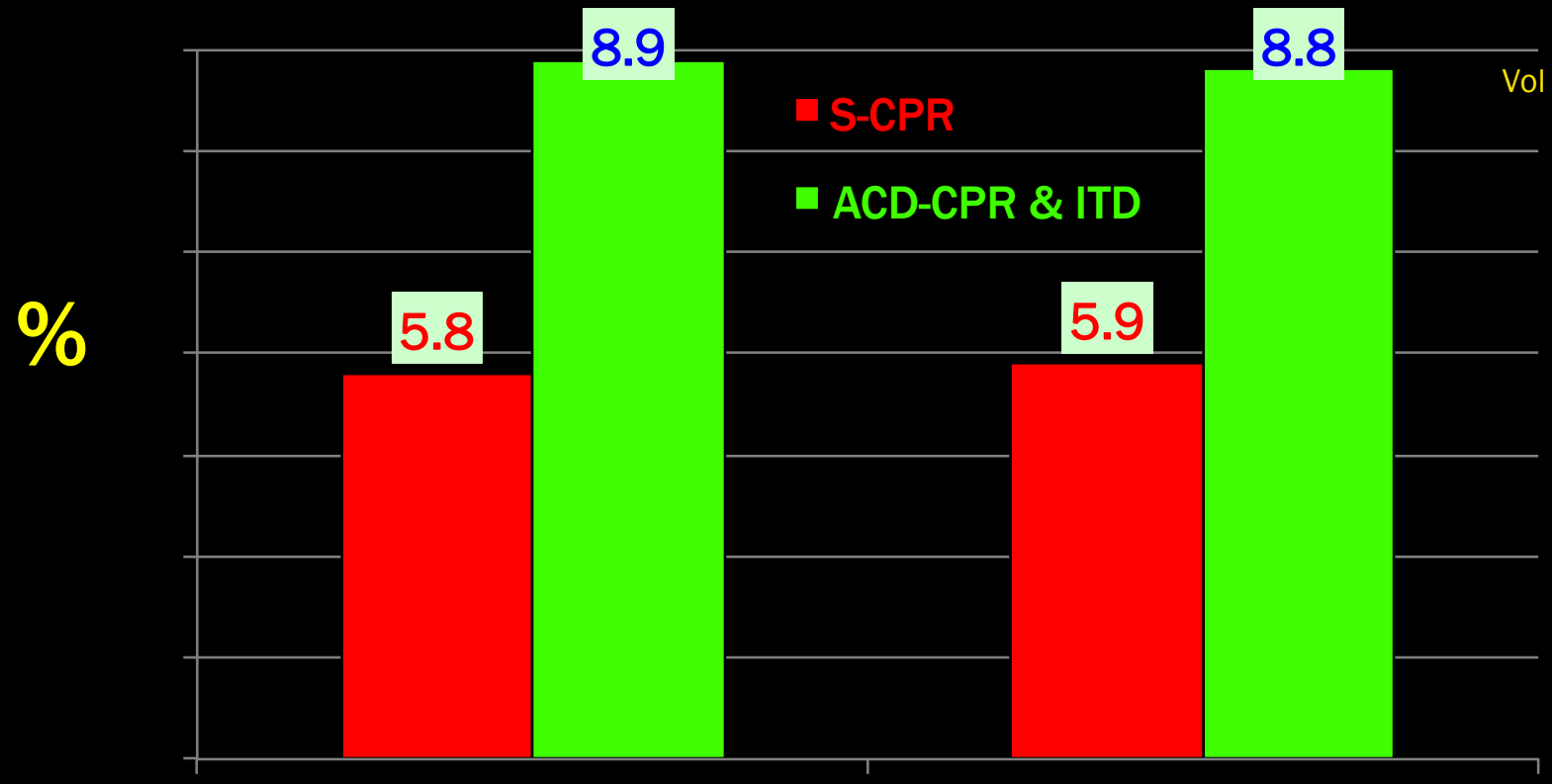
"Cardiopulmonary resuscitation with augmentation of negative intrathoracic pressure should be considered as an alternative to standard CPR to increase long-term survival after cardiac arrest."

Active Compression-- Decompression

+

ACD Device

Improved Long-Term Survival with Favorable Neurologic Outcome

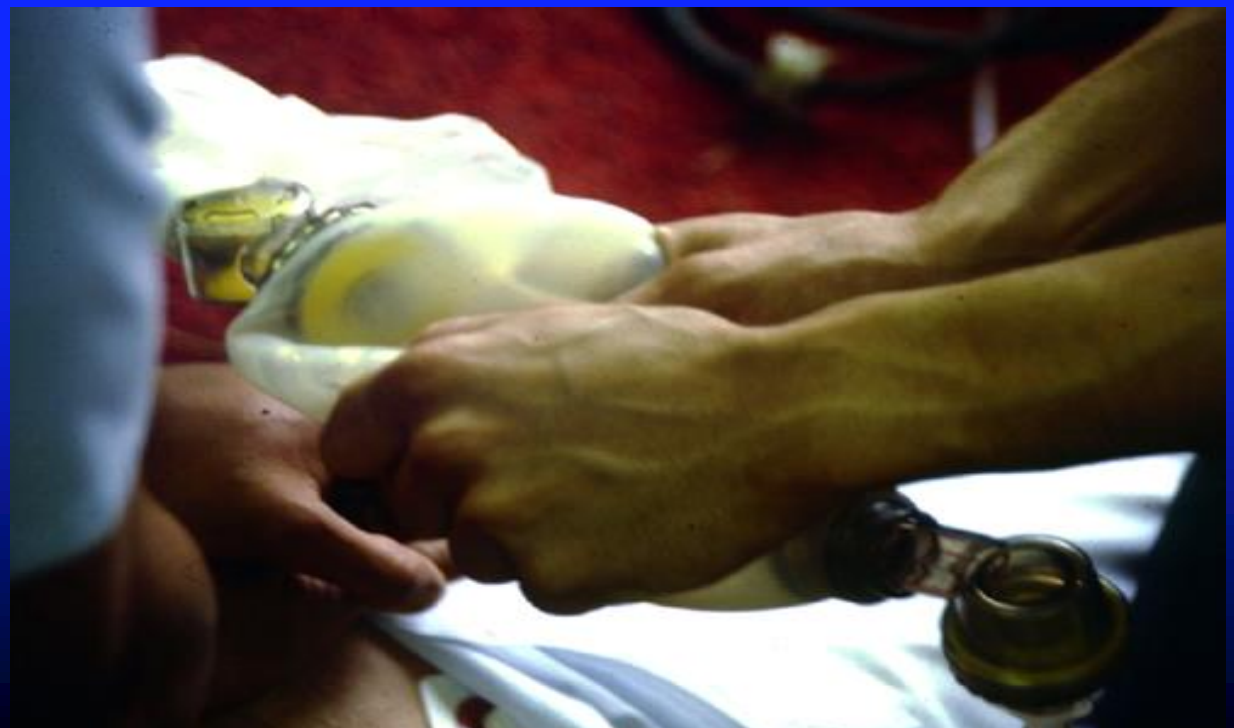


Aufderheide et al.
Lancet 2011;
Vol .377(9762):301-311

So Why the Discrepancy ?

Could It Be the Quality of the CPR ?

Or Some Other Effect Modifier ?



Clinical Paper

Quality of CPR: An important effect modifier in cardiac arrest clinical outcomes and intervention effectiveness trials☆

Demetris Yannopoulos[a,*], Tom P. Aufderheide[b], Benjamin S. Abella[c], Sue Duval[a], Ralph J. Frascone[a], Jeffrey M. Goodloe[d], Brian D. Mahoney[e], Vinay M. Nadkarni[f], Henry R. Halperin[g], Robert O'Connor[h], Ahamed H. Idris[i], Lance B. Becker[b], Paul E. Pepe[j]

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JAMA Cardiology | Original Investigation

Optimal Combination of Compression Rate and Depth During Cardiopulmonary Resuscitation for Functionally Favorable Survival

Sue Duval, PhD; Paul E. Pepe, MD, MPH; Tom P. Aufderheide, MD, MS; Jeffrey M. Goodloe, MD; Guillaume Debaty, MD, PhD; José Labarère, MD, PhD; Atsushi Sugiyama, MD, PhD; Demetris Yannopoulos, MD

Invited Commentary

IMPORTANCE Previous studies of basic cardiopulmonary resuscitation (CPR) indicate that both chest compression rate (CCR) and chest compression depth (CCD) each are associated with survival probability after out-of-hospital cardiac arrest. However, an optimal CCR-CCD combination has yet to be identified, particularly with respect to age, sex, presenting cardiac rhythm, and CPR adjunct use.

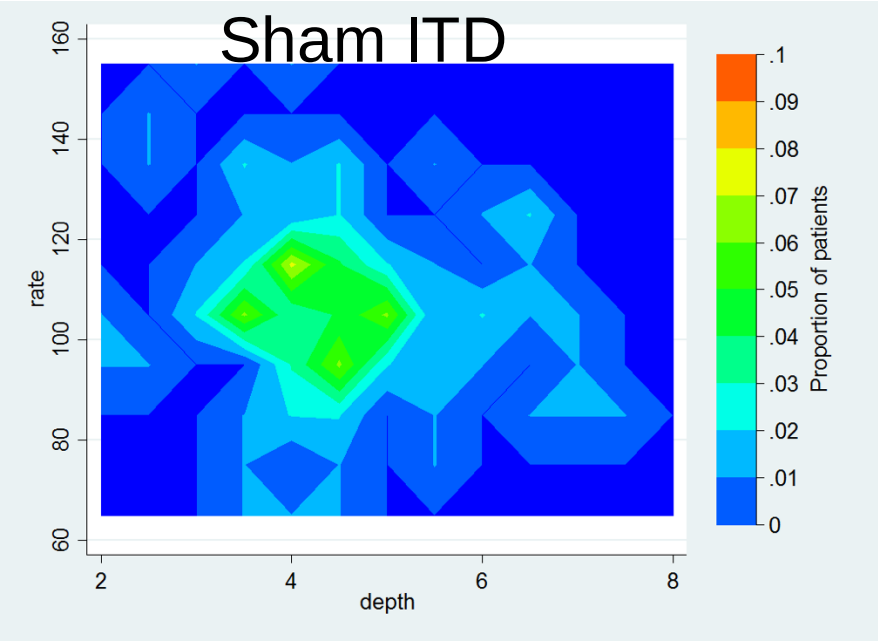
OBJECTIVES To identify an ideal CCR-CCD combination associated with the highest

The Sweeter Spot for Neurologically-Sound Survival

Witnessed Arrests

Contour Plots Using Proportion of Good Survivors in Each Cell

Canonical Analysis for Optimization



The Sweeter Spot for Neurologically-Sound Survival

Witnessed Arrests

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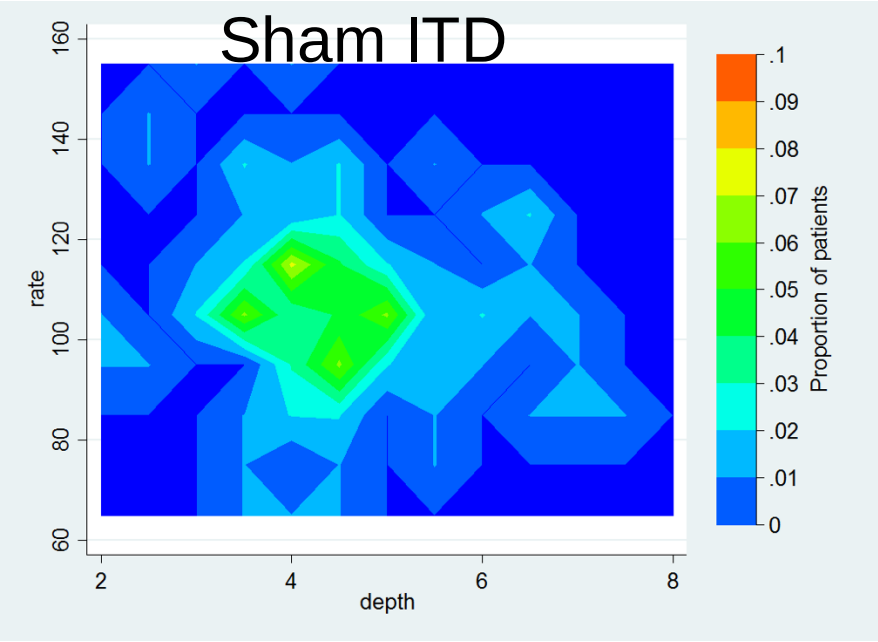
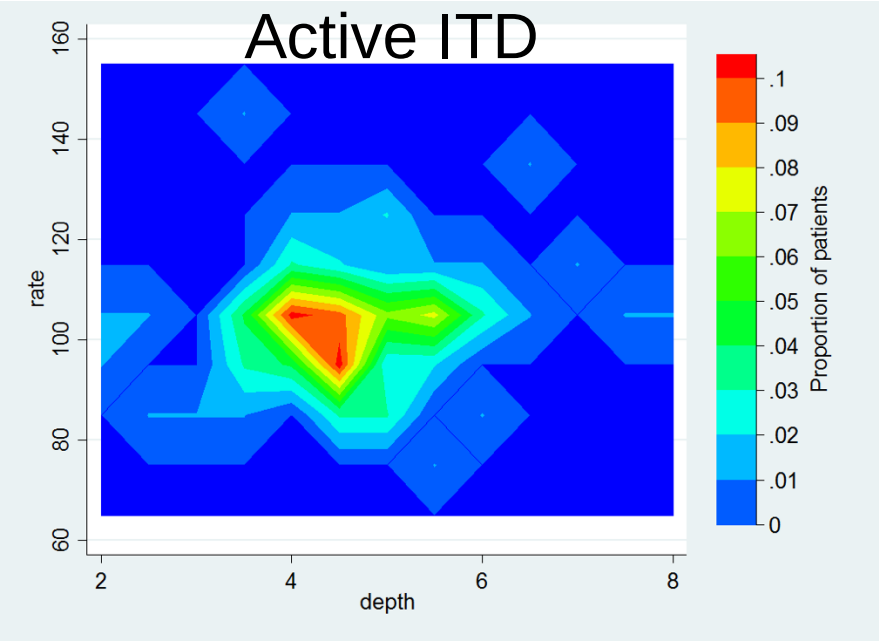
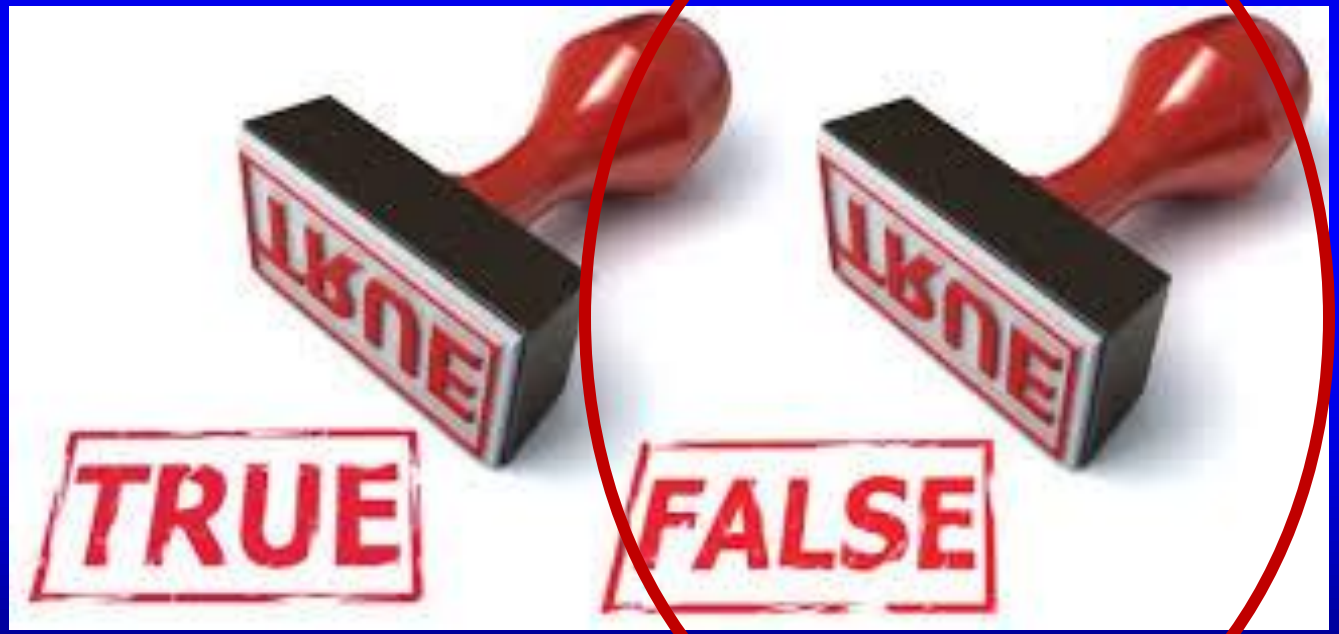




Duval et al 2015

Don't Judge Too Quickly …



An Intervention is Not Simply Good or Bad

Med 2011;365:798-806

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of an Impedance Threshold Device in Out-of-Hospital Cardiac Arrest

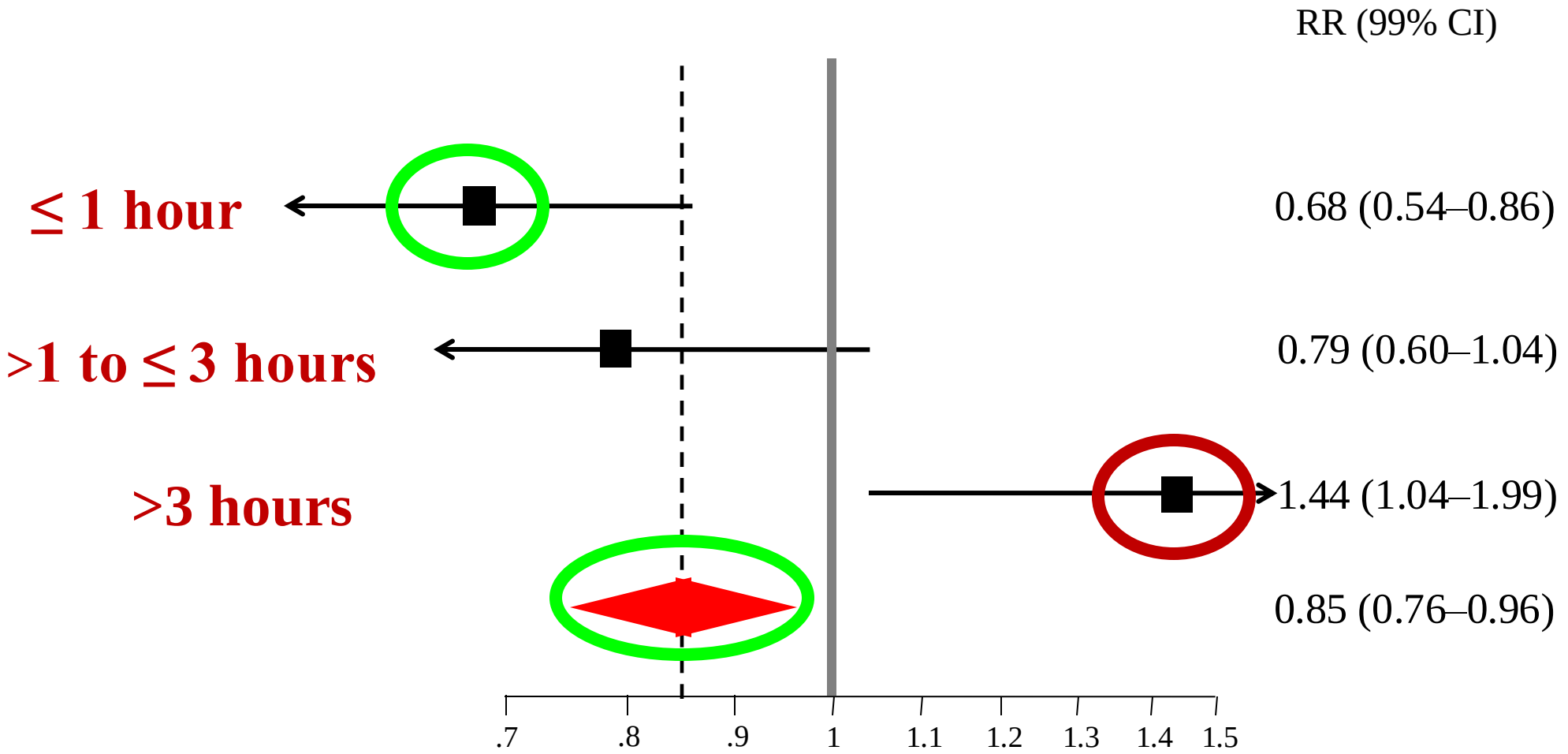
Tom P. Aufderheide, M.D., Graham Nichol, M.D., Thomas D. Rea, M.D., Siobhan P. Brown, Ph.D., Brian G. Leroux, Ph.D., Paul E. Pepe, M.D., Peter J. Kudenchuk, M.D., Jim Christenson, M.D., Mohamud R. Daya, M.D., Paul Dorian, M.D., Clifton W. Callaway, M.D., Ph.D., Ahamed H. Idris, M.D., Douglas Andrusiek, M.Sc., Shannon W. Stephens, E.M.T.-P., David Hostler, Ph.D., Daniel P. Davis, M.D., James V. Dunford, M.D.,

ACCURATE -- *But Only Within the Context of the Study* …

BUT NOT NECESSARILY "THE TRUTH"

For Bleeding Deaths –

Early TXA Treatment is Better



BETTER OUTCOME

WORSE OUTCOME

p=0.000008

These Are Just Examples of Why So-Called "Evidenced-Based" Studies Can Be So Conflicting …

Especially For Those Who Still Think in a "Binary" Pattern

(i.e., "Works" or "Doesn't Work" !)

BUT – it Really DEPENDS ..

… and Binaries Can Get So Contentious About Things …

ONLY A SITH DEALS IN ABSOLUTES ….

ONLY A SITH DEALS IN ABSOLUTES

Why we need both evidence-based & experience-based thinking in resuscitation research

By Paul E. Pepe, MD, MPH, FAEMS, MCCM, MACP

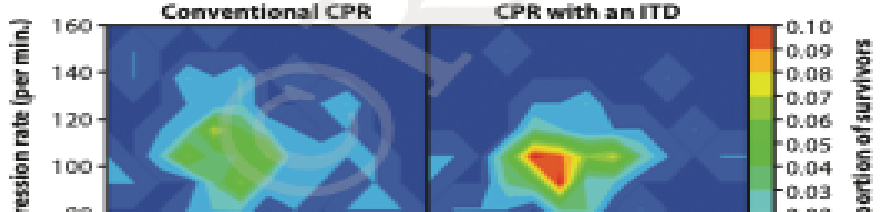
& Tom P. Aufderheide, MD, MS, FACEP, FACC, FAHA

For decades, reported survival rates and studies of interventions for out-of-hospital cardiac arrest (OHCA) have remained disappointing.[1–3] To improve outcomes, many respected organizations have developed widely adopted guidelines for both basic and advanced interventions, emphasizing an "evidence-based" process using published peer-reviewed literature.[4,5] Although these processes have had clear value, they also have their limitations.

Publications forming the evidence often have had conflicting information, statistical limitations, and even a lack of adherence to intended protocols, all leading to inconclusive findings.[6] Traditional controlled trials that test a singular intervention at a time may be one of the main reasons.[7]

Examining simple binary outcomes (i.e., effective or not) are affected by the time-dependent and multifactorial nature of OHCA cases.[8–14] For example, a single intervention (e.g., drug, AED) that's highly effective when provided within minutes, may not be so helpful if too many minutes have elapsed.

Proper chest compressions—minimally interrupted with optimal rate, depth and recoil—require proper coordination with the ventilatory variables that significantly impact circulation.[9,10,12] Effectiveness of interventions, including medications and CPR itself, can be compromised by these many interdependent factors that require the right timing and proper implementation.[5,8,9,10,14] (See Figure 1.)



All of these factors also need to be adjusted under certain conditions, particularly when flow-enhancing devices are used or when spontaneous circulation or respirations resume.[9,12,14] Accordingly, any proscribed "absolute" target or use for each of these circulatory, ventilatory, drug or procedural components, may need to be adjusted at any given time point and under different conditions.[11–13]

These complex dynamics have confounded many of our current evidence-based publications, even gold standard clinical trials.[10,14] Experience has now shown investigators that certain interventions deemed to be ineffective, or even harmful, in an evidence-based clinical trial (e.g., ITD, epinephrine, TXA) are actually very effective when quality CPR performance and/or physiologically sound ventilatory practices are used—or when the right patient population and timely intervention is used (e.g., TXA in severe traumatic brain injury).[10,12,14,15]

Important variables also include the populations served, residential infrastructures (e.g., many high-rises), traffic, geography, distances, climate, dispatch functions and the frequency and quality of early bystander CPR.[3–8,12,16,17] EMS system response configuration can significantly impact the skills of EMS personnel and therefore outcomes—as can the skills and resources of the receiving facilities.[14,16–24]

In essence, many interdependent components form a longitudinal (e.g., chain of survival) bundle of interdependent management for OHCA, where

The New England Journal of Medicine

PUBLIC USE OF AUTOMATED EXTERNAL DEFIBRILLATORS

SHERRY L. CAFFREY, E.M.T.-P., PAULA J. WILLOUGHBY, D.O., M.H.P.E., PAUL E. PEPE, M.D., M.P.H., AND LANCE B. BECKER, M.D.

ABSTRACT

Background Automated external defibrillators save lives when they are used by designated personnel in certain public settings. We performed a two-year prospective study at three Chicago airports to assess whether random bystanders witnessing out-of-hospital cardiac arrests would retrieve and successfully use automated external defibrillators.

Methods Defibrillators were installed a brisk 60-to-90-second walk apart throughout passenger terminals at O'Hare, Midway, and Meigs Field airports, which together serve more than 100 million passengers per year. The use of defibrillators was promoted by public-service videos in waiting areas, pamphlets, and reports in the media. We assessed the time from notification of the dispatchers to defibrillation, survival rate at 72 hours and at one year among persons with cardiac arrest, their neurologic status, and the characteristics of rescuers.

Results Over a two-year period, 21 persons had nontraumatic cardiac arrest, 18 of whom had ventricular fibrillation. With two exceptions, defibrillator operators were good Samaritans, acting voluntarily. In the case of four patients with ventricular fibrillation, defibrillators were neither nearby nor used within five minutes, and none of these patients survived. Three others remained in fibrillation and eventually died, de-

CARDIOVASCULAR disease remains the most common cause of death in the United States and most other Western nations.[1-4] Among these deaths, sudden, out-of-hospital cardiac arrest claims approximately 1000 lives each day in the United States alone.[3] Most of these cardiac arrests are due to ventricular fibrillation.[4-7] Though highly reversible with the rapid application of a defibrillator, ventricular fibrillation is otherwise fatal within minutes, even when cardiopulmonary resuscitation is provided immediately.[7-11] The overall survival rate in the United States is estimated to be less than 5 percent.[4,5,7,12-14]

Recent developments in automated-external-defibrillator technology have provided a means of increasing the rate of prompt defibrillation after out-of-hospital cardiac arrest.[15] After minimal training, nonmedical personnel (e.g., flight attendants and casino workers) are able to use defibrillators in the workplace, with life-saving effects.[16-20] Nonetheless, such programs have involved designated personnel whose job description includes assisting persons who have had sudden cardiac arrest. Data are still lacking on the success of programs in which automated external defibrillators have been installed in public places to be used by persons

Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial

*Nicholas Crombie, Heidi A Doughty, Jonathan R B Bishop, Amisha Desai, Emily F Dixon, James M Hancox, Mike J Herbert, Caroline Leech, Simon J Lewis, Mark R Nash, David N Naumann, Gemma Slinn, Hazel Smith, Iain M Smith, Rebekah K Wale, Alastair Wilson, Natalie Ives, Gavin D Perkins, on behalf of the RePHILL collaborative group**

Lancet Haematol 2022

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See Online/Comment
https://doi.org/10.1016/S2352-3026(22)00074-6

Summary

Background Time to treatment matters in traumatic haemorrhage but the optimal prehospital use of blood in major trauma remains uncertain. We investigated whether use of packed red blood cells (PRBC) and lyophilised plasma (LyoPlas) was superior to use of 0·9% sodium chloride for improving tissue perfusion and reducing mortality in trauma-related haemorrhagic shock.

Methods Resuscitation with pre-hospital blood products (RePHILL) is a multicentre, allocation concealed, open-label, parallel group, randomised, controlled, phase 3 trial done in four civilian prehospital critical care services in the UK.

Research

==> *Re-Search*

A Concept that Needs to Be Considered Integral to Excellence in Resuscitation Research

CONCLUSION #1

"Much of What is So-Called

'Evidenced-Based Medicine'

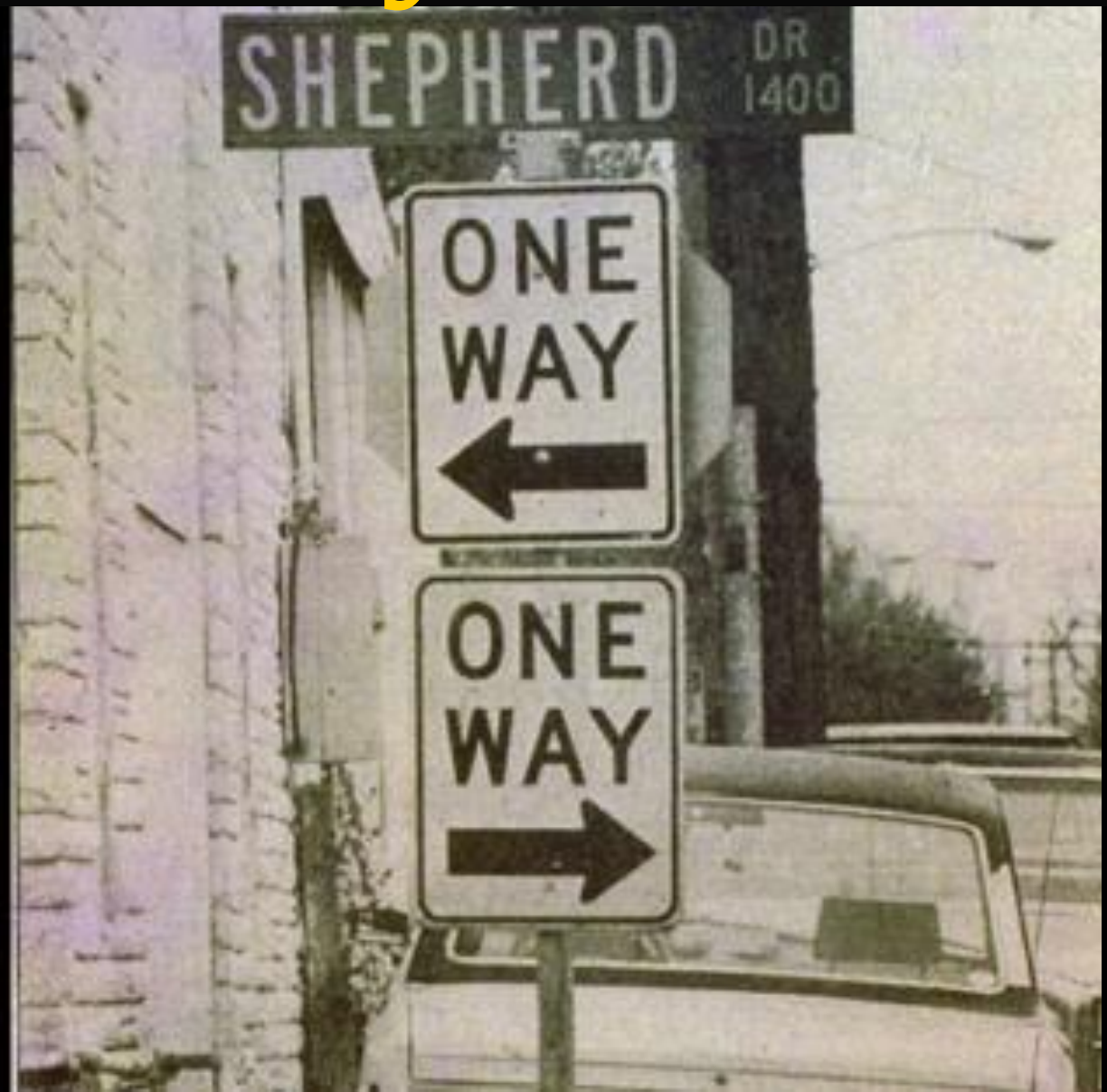
Is Not Always the 'Ultimate' Truth

Applicable to All Patients ..

... at All Times"

Obi Wan Kenobe

Which Way Do We Go ?



So Can We Suggest Any Alternatives to the RCT in OHCA?

…to advance science, care & save $$$$ after a quarter century of frustration

Classic Experimental Concept…

Reproducible Methodologies

… With Reproducible Results

Rationale and Strategies for Development of an Optimal Bundle of Management for Cardiac Arrest

Pepe PE, Aufderheide TP, Lamhaut L, Davis DP, Lick CJ, Polderman KH, Scheppke KA, Deakin CD, O'Neil BJ, Van Schuppen H, Levy MK, Wayne MA, Youngquist ST, Moore JC, Lurie KG, Bartos JA, Bachista KM, Jacobs MJ, Rojas-Salvador C, Grayson ST, Manning JE, Kurz MC, Debaty G, Segal N, MD, Antevy PM, Miramontes DA, Cheskes S, Holley JE, Frascone RJ, Fowler RL, Yannopoulos D, writing group for the International Resuscitation Collaborative. *Critical Care Explor* 2019; 2: (in press).

STAR Research Award Winner

#40 Novel Strategy for Identifying an Optimal Bundle of Management for Sudden Cardiac Arrest

RESUSCITATION 135 (2019) 162–167

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Early On-Scene Management of Pediatric Out-of-Hospital Cardiac Arrest Can Result in Improved Likelihood for Neurologically-Intact Survival

Paul R. Banerjee[a,b], *Latha Ganti*[b], *Paul E. Pepe*[a,c,*], *Amninder Singh*[b], *Abhishek Roka*[b], *Raf A. Vittone*[a]

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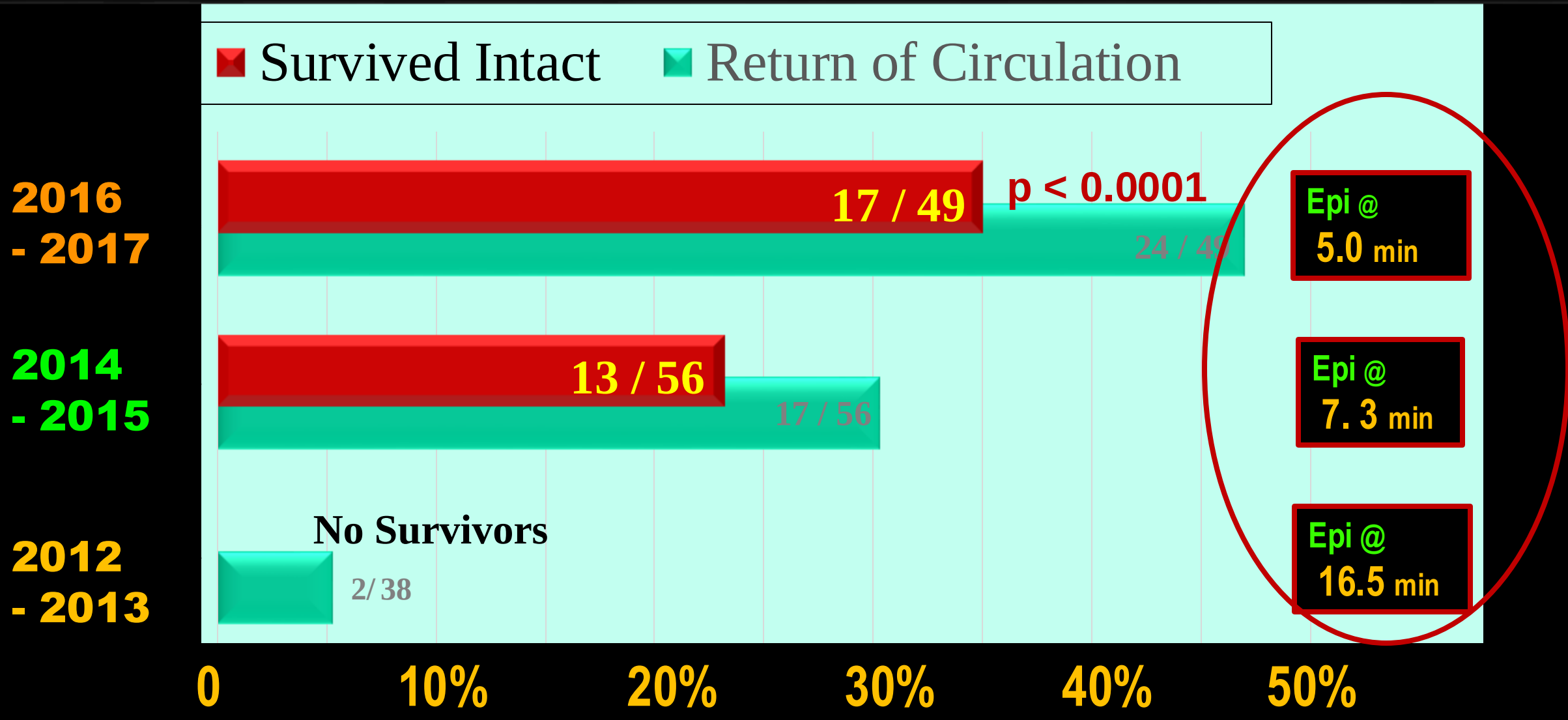
Abstract

Aim: To evaluate the frequency of neurologically-intact survival (SURV) following pediatric out-of-hospital cardiac arrest (POHCA) when comparing traditional early evacuation strategies to those emphasizing resuscitation efforts being performed immediately on-scene.

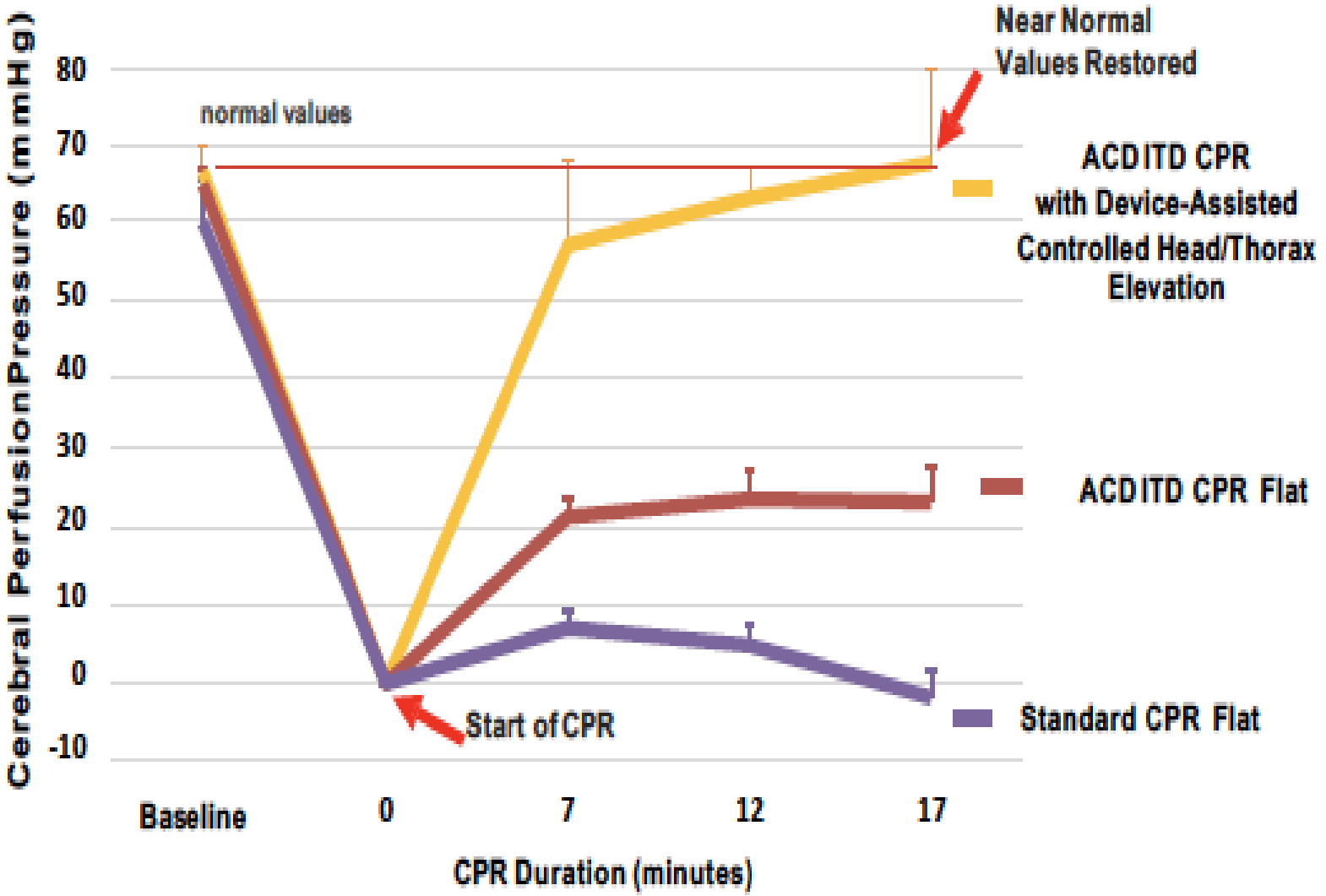
Methods: Before 2014, emergency medical services (EMS) crews in a county-wide EMS agency provided limited treatment for POHCA on-scene and rapidly transported patients to appropriate hospitals. After 2014, training strongly concentrated upon EMS provider comfort levels with on-scene resuscitation efforts including methods to expedite protocols on-site and control positive-pressure ventilation. Frequency of SURV (hospital discharge)

Pediatric Cardiac Arrest Survivors

Pre-Intervention (2012-13) vs. Phase I (2014-15) & Phase II (2016-17)



Let's Use *Neuroprotective CPR* as a More Recent Example



ACD - Active compression decompression CPR

ITD - Impedance Threshold Device

Critical Care Medicine
Society of Critical Care Medicine

STAR RESEARCH PRESENTATIONS: CARDIOVASCULAR

2: CLINICAL CONFIRMATION OF PROFOUND IMPROVEMENTS IN NEURO-INTACT SURVIVAL USING THE HEAD-UP CPR BUNDLE

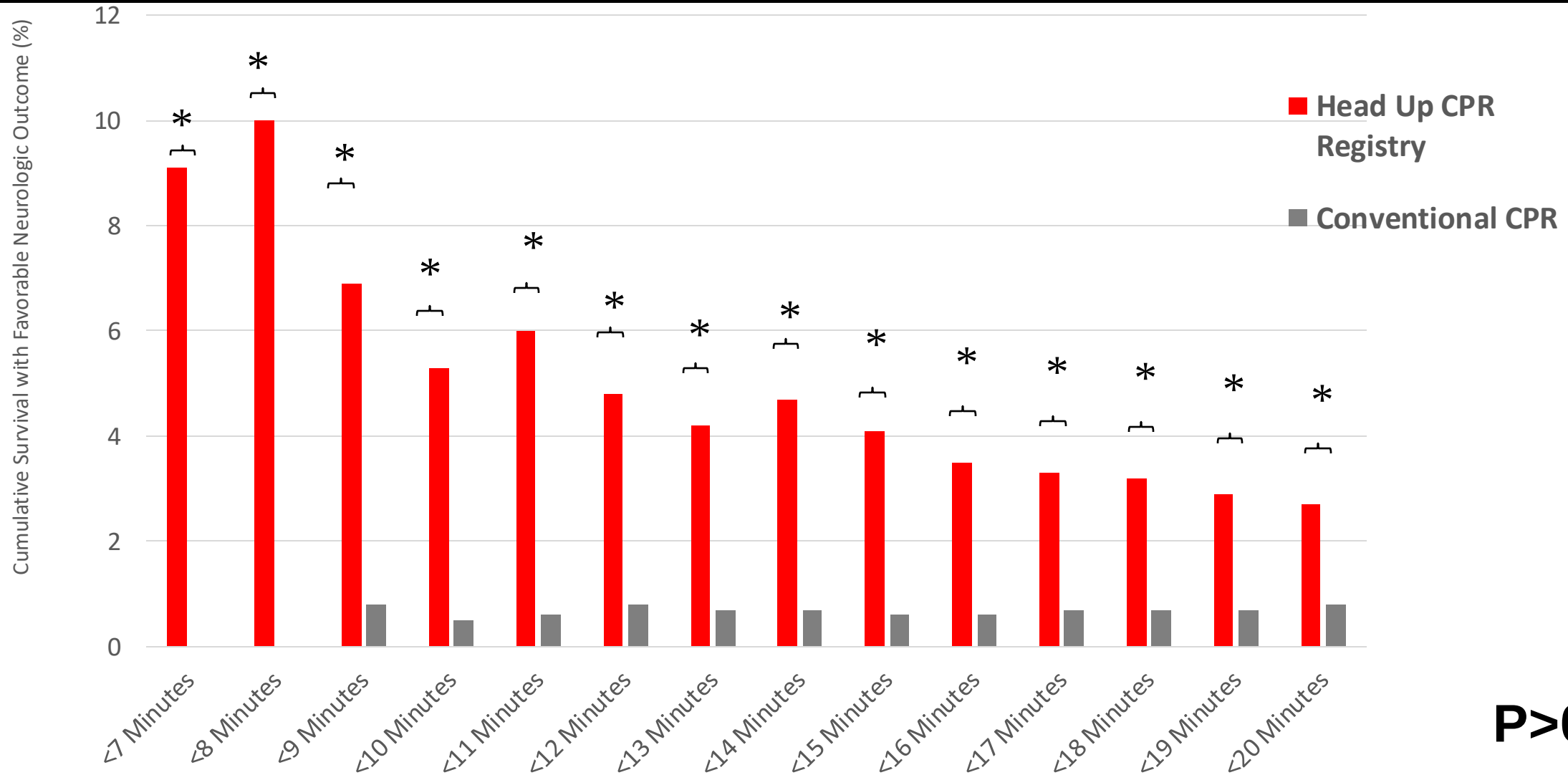
Pepe, Paul[1]; Moore, Johanna[2]; Labarère, José[3]; Lick, Charles[4]; Scheppke, Kenneth[5]; Antevy, Peter[6]; Coyle, Charles[7]; Quinn, Ryan[8]; Holley, Joseph[9]; Hutchison, Edwin (Mack)[10]; Adams, Paul[11]; Crowe, Remle[12]; Duval, Sue[2]; Debaty, Guillaume[3]; Lurie, Keith[13]

% Survival with Good Neurological Outcome

According to Time Elapsed from 9-1-1 Call to Time of Head-Up Bundle Application

(Compared to Propensity Matched Conventional CPR Cohort)

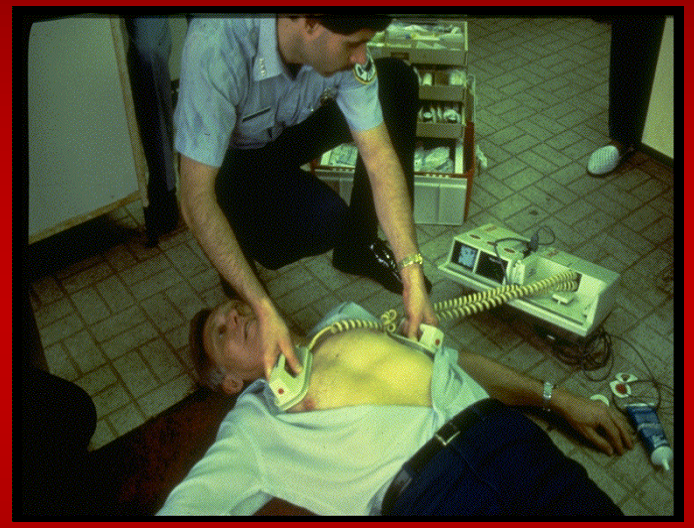
Non-Shockable



P>0.05

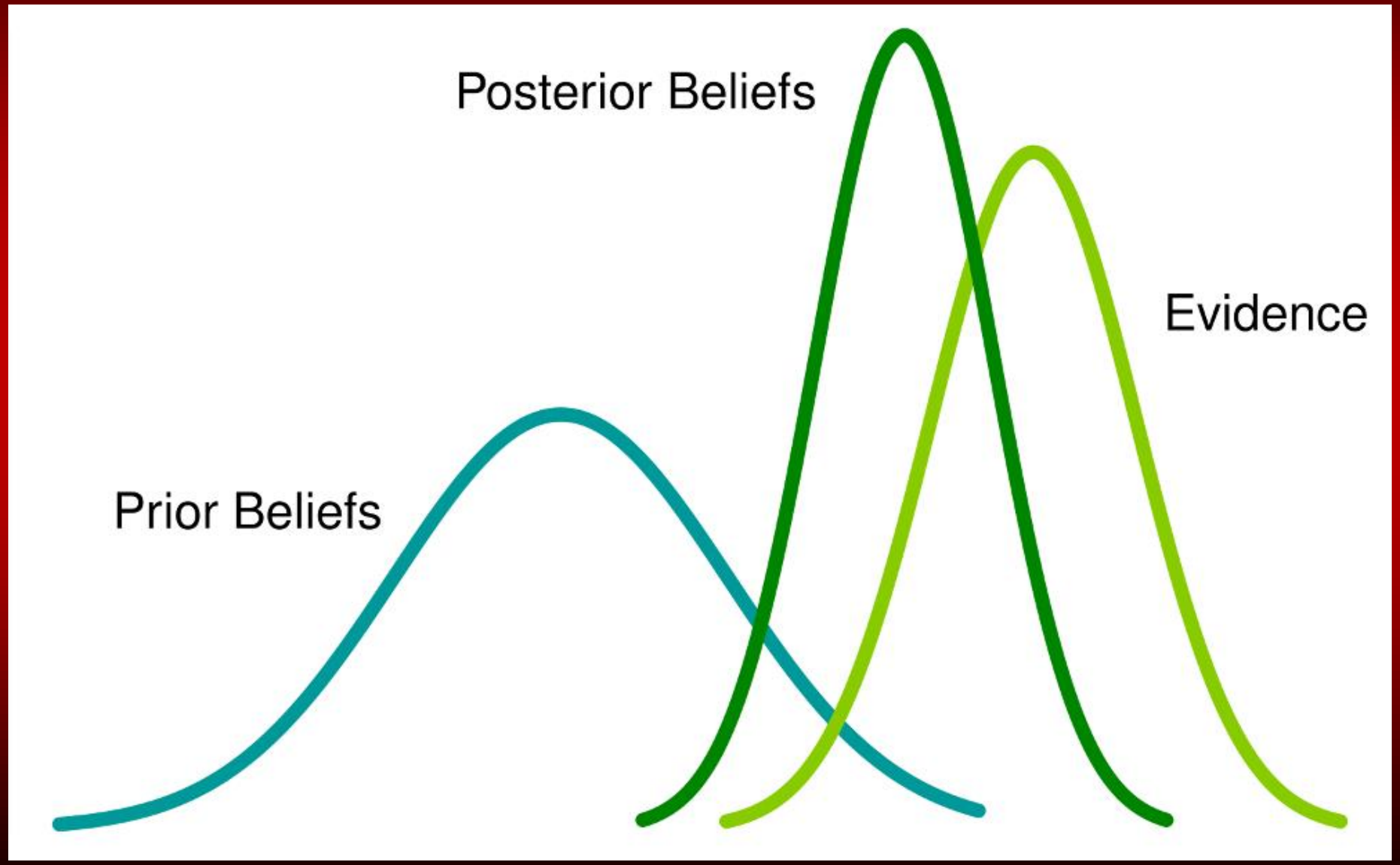
NPCPR is Really ….
a Basic Life Support Function

Propensity-Matched Controls

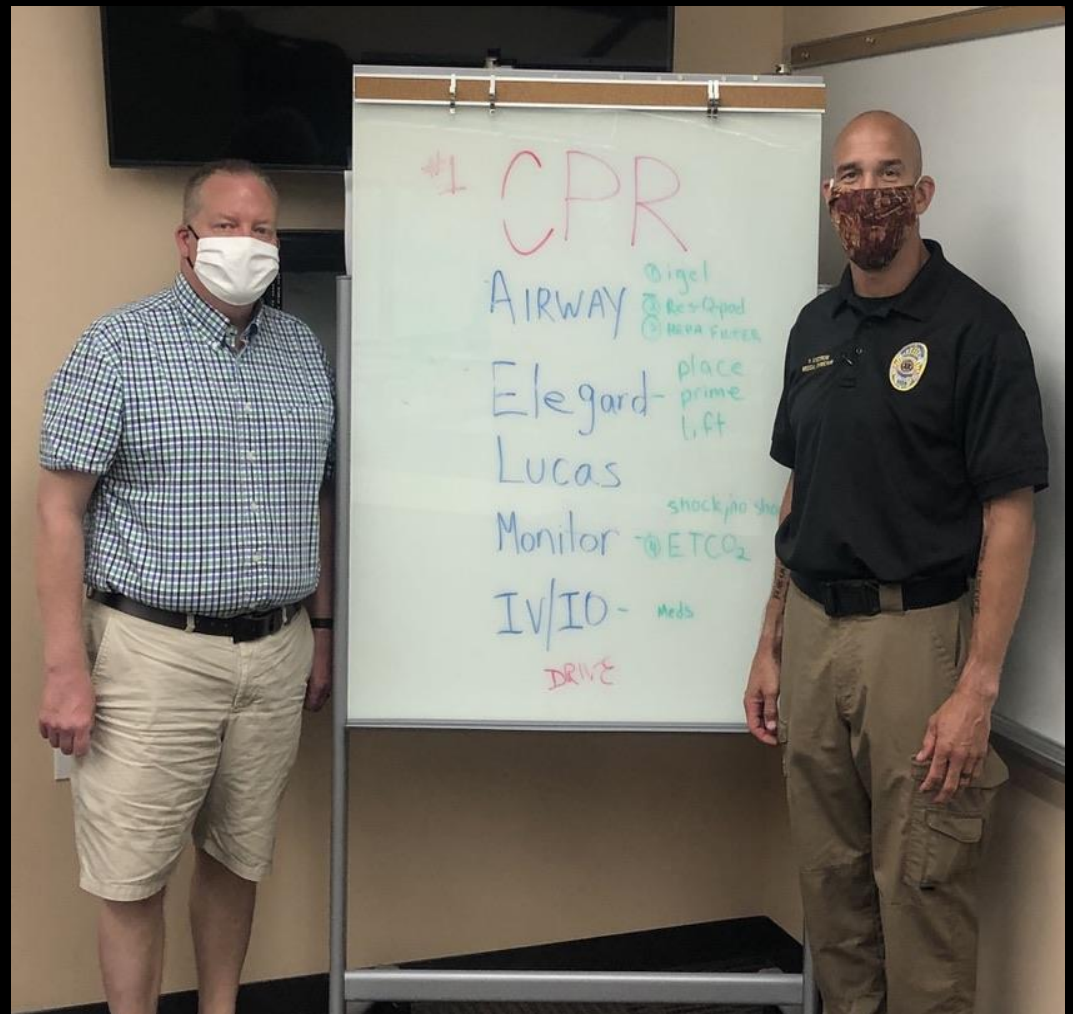


…What Is It and Does It Work ?

For example -- **Bayesian Statistics**



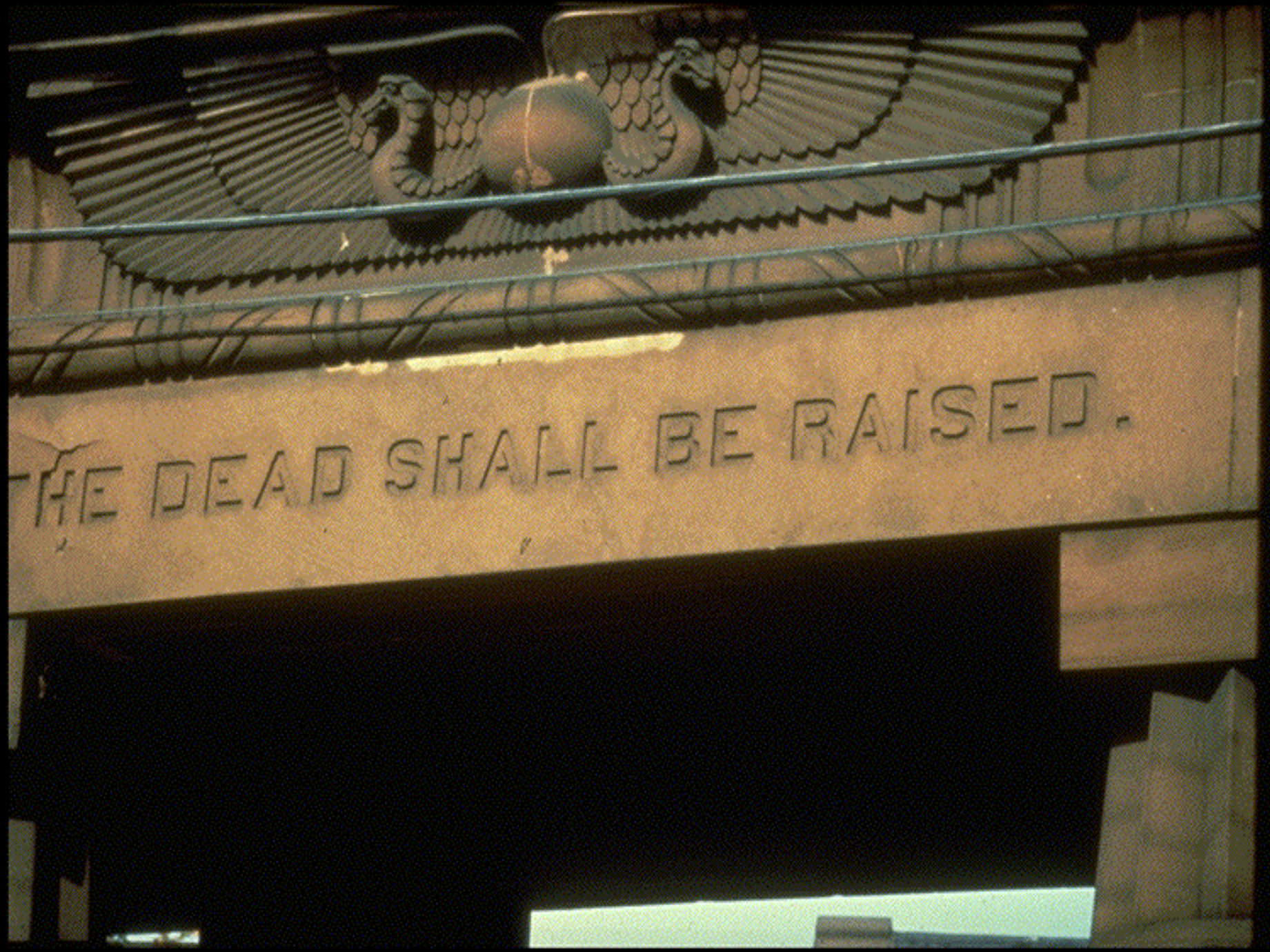
Many Patients Awake While in VF and Remember Exactly What Had Happened



If You're Gonna Run a Study …

… "Alternate Clinical Life Style"

“In Conclusion…”


THE DEAD SHALL BE RAISED.


You mean you're still
ALIVE !?

We'll Make Life Better for Future Generations ….

I'm Paul Pepe …

… *and I approved*

this Message

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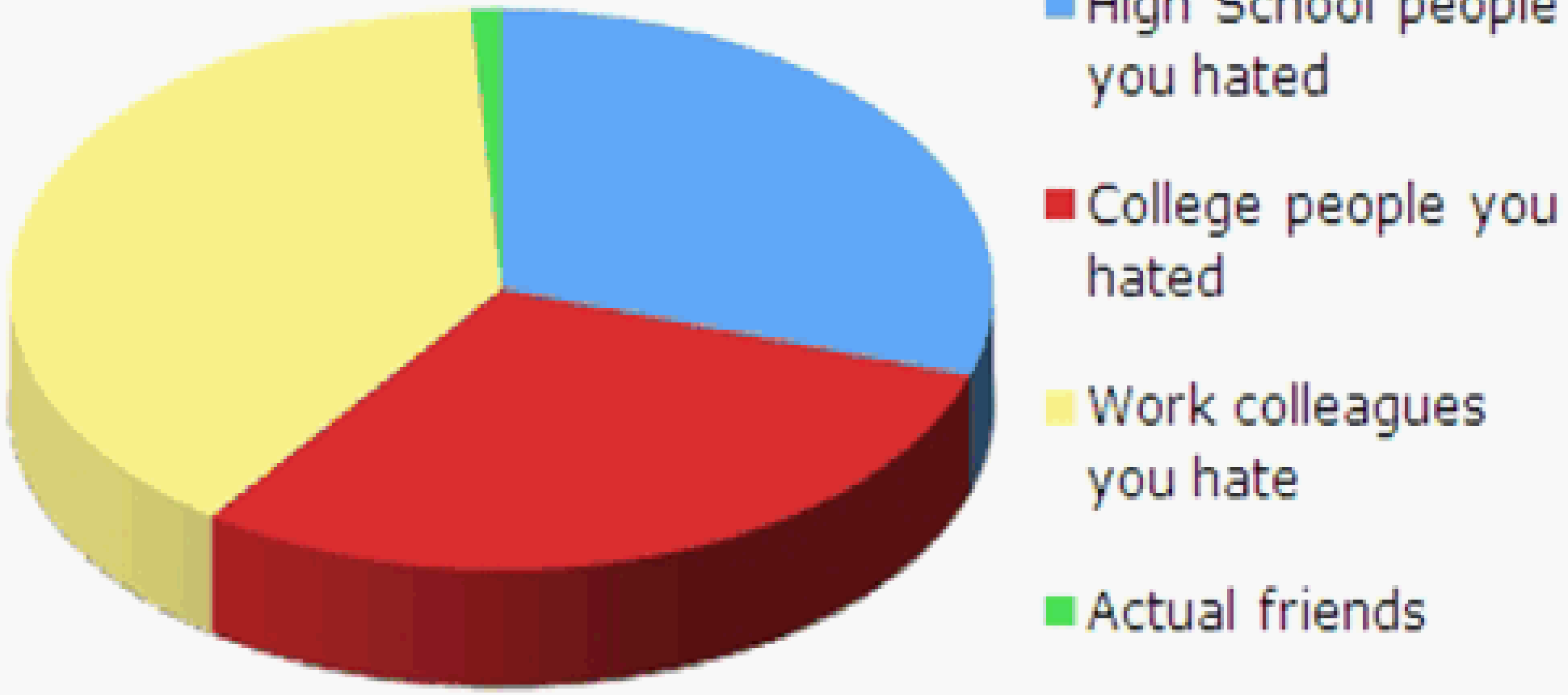
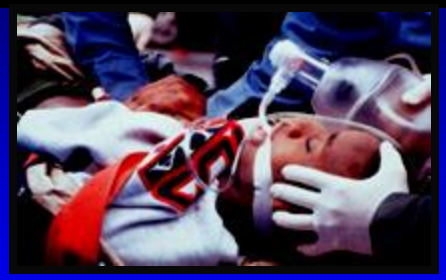
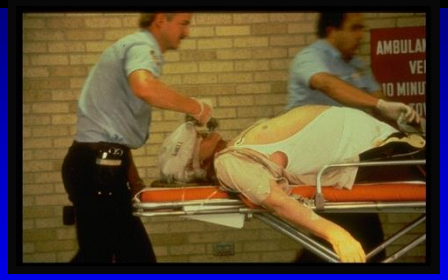


Scoop & Run vs. Stay & Play



CANCER:

Surgery vs. Chemo vs. Radiation

(vs. mRNA) ?