



# The ACLS 2015 Guidelines: Discussion and Debate

Michael J. Cawley, PharmD., RRT, CPFT, FCCM

Suprat Saely Wilson, PharmD., BCPS

Philippe Mentler, PharmD., BCPS

# Disclosure

The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:

- **Philippe Mentler** - Vizient: Employee

# Learning Objectives

- Evaluate differences in Advanced Cardiac Life Support (ACLS) treatment, comparing the 2010 and 2015 American Heart Association (AHA) ACLS guidelines.
- Develop a pharmacotherapeutic plan for ACLS using the 2015 AHA guidelines.
- Justify the use of therapeutic hypothermic strategies post cardiac arrest.



Michael J. Cawley, PharmD., RRT, CPFT, FCCM  
Vice-Chair and Professor of Clinical Pharmacy  
Philadelphia College of Pharmacy  
University of the Sciences  
Philadelphia, PA

# Pre and Post Question

How do you rate your understanding of the new 2015 American Heart Association (AHA) guideline update for cardiopulmonary resuscitation and emergency cardiovascular care?

- A Excellent
- B Good
- C Fair
- D Poor

# Pre and Post Question

Most of the 2015 guidelines update recommendations are supported by the lowest level of evidence [(LOE C-LD - limited data) or LOE C-EO – expert opinion)?

A TRUE

B FALSE

# Resuscitative Demographics

- Ischemic heart disease is the leading cause of death in the world <sup>1</sup>
- Cardiovascular disease is responsible for 1 of every 3 deaths in US <sup>2</sup>
- Approximately 326,200 out-of-hospital cardiac arrests (OHCAs) assessed by EMS providers <sup>2</sup>
- Approximately 209,000 treated in hospital cardiac arrests (IHCAs) <sup>2</sup>
- Incidence of patients with OHCA in whom resuscitation was attempted is higher in North America (58 per 100,000 population) compared to other continents (35 Europe, 32 Asia and 44 Australia) <sup>3</sup>

1. Lozano R et al. *Lancet* 2012; 380:2095-2128

2. Mozaffarian D et al. *Circulation* 2015; 131:e29-e322.

3. Berdowski J et al. *Resuscitation* 2010;81:1479-1487

# Resuscitative History

- 2015 marks 49 years from first CPR guidelines published in 1966
- Ad Hoc Committee on CPR by National Academy of Sciences
- Periodic revisions have been published by American Heart Association (AHA): 1974, 1980, 1986, 1992, 2000, 2005, 2010 and now 2015
- AHA partners with International Liaison Committee on Resuscitation (ILCOR) in evidence review process
- Future guidelines will utilize a Web-based format

# 2015 AHA Guidelines Update for CPR and Emergency Cardiac Care (ECC)

- 2012 ILCOR formed 7 task forces (BLS, ACLS, ACS, pediatric BLS, ALS, neonatal resuscitation and EIT)
- Methodological approach for evidence evaluation – Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group
- Written summaries of evidence for each outcome were developed
- In 2012-2015, 250 evidence reviewers from 139 countries completed 169 systematic reviews addressing resuscitation
- On-line platform known as Scientific Evaluation and Evidence Review System (SEERS) to guide task forces and for public comments and suggestions.

# AHA Classification System for Evidence

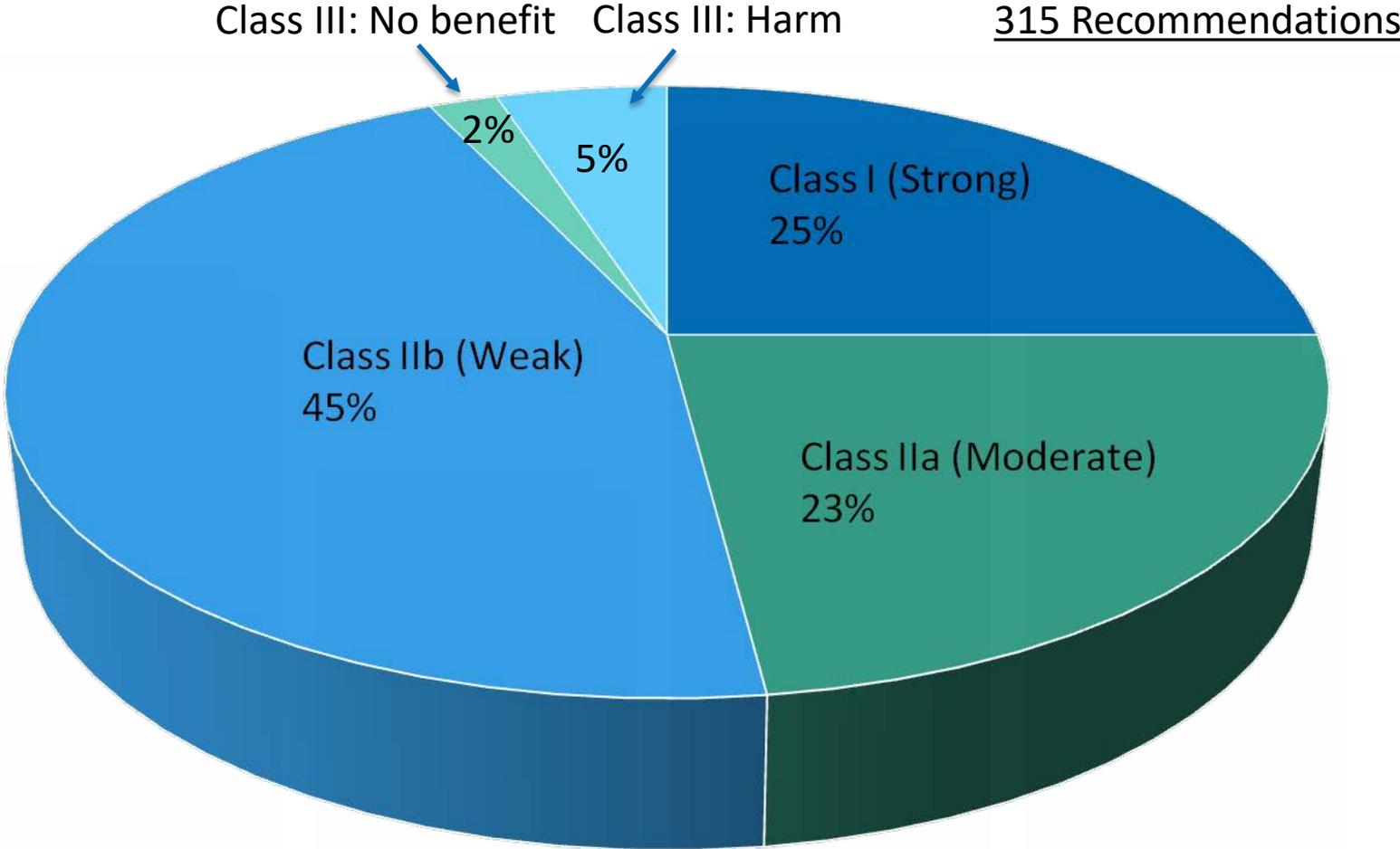
## Class (Strength) of Recommendation

- Class I: (Strong)
- Class IIa: (Moderate)
- Class IIb: (Weak)
- Class III: No benefit (Moderate)
- Class III: Harm (Strong)

## Level (Quality) of Evidence

- Level A (High-quality)
- Level B-R (Randomized)
- Level B-NR (Nonrandomized)
- Level C-LD (Limited data)
- Level C-EO (Expert opinion)

# Distribution of Classes of Recommendations

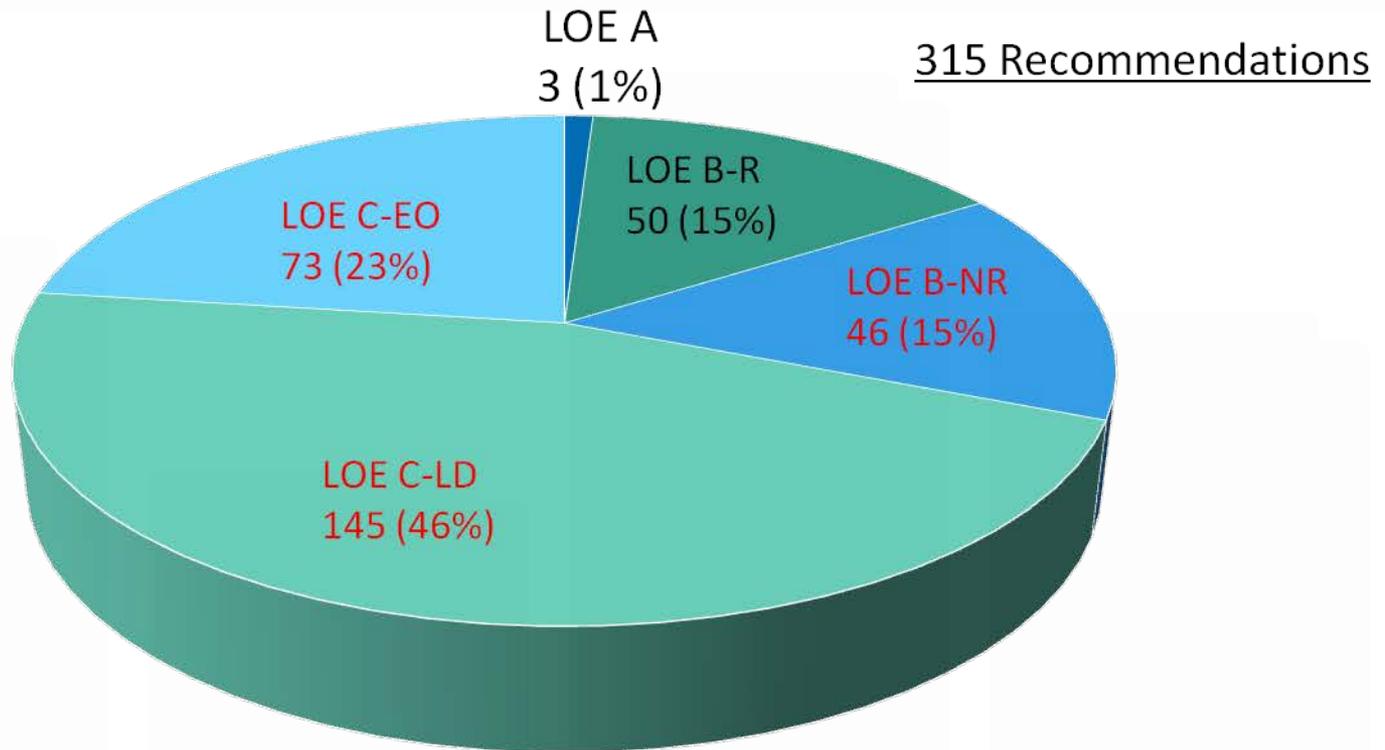


■ Class I   ■ Class IIa   ■ Class IIb   ■ Class III:No benefit   ■ Class III:Harm

Modified - Neumar RW et al. *Circulation* 2015;132[suppl 2]:S215-S367



# Level of Evidence (LOE)



- LOE A (high quality)
- LOE B-R (randomized)
- LOE B-NR (nonrandomized)
- LOE C-LD (limited data)
- LOE C-EO (expert opinion)

84% of results are based upon non-randomized, limited data or expert opinion  
Results demonstrate knowledge gap in resuscitative science

Modified - Neumar RW et al. *Circulation* 2015;132[suppl 2]:S215-S367

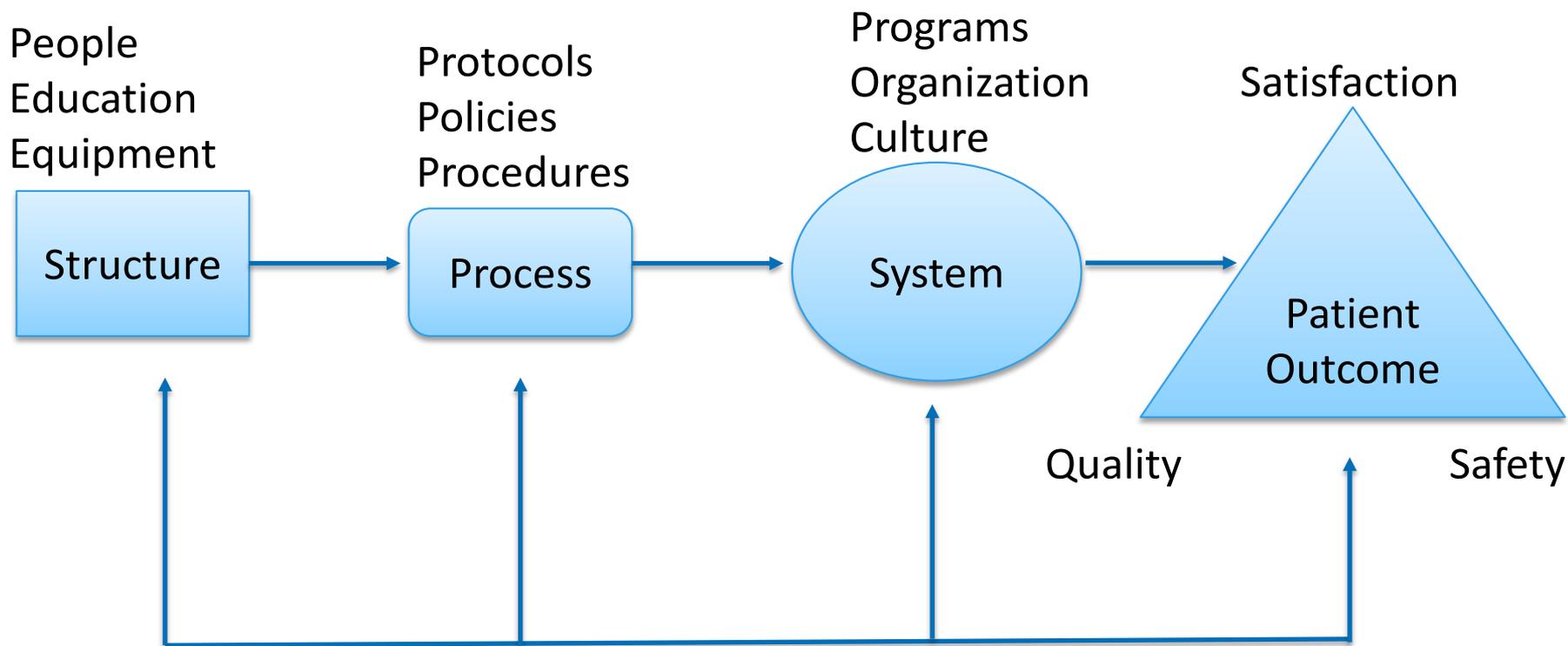
# Ethical Issues

- New resuscitative strategies (extracorporeal CPR) have made decisions to discontinue cardiac arrest more difficult
- Targeted temperature management (TTM) and challenges in predicting neurological outcomes
- Accuracy of particular tests during TTM
- Implications around organ transplant in an emergency setting
- Discussions with children and adolescents using language appropriate for their level of development
- Physician Orders for Life-Sustaining Treatment (POLST) form to identify patients who wish to have specific limits on interventions at the end of life

# Systems of Care and Continuous Quality Improvement

- Replaces the “CPR Overview” part of the 2010 guidelines
- Stakeholders with a common framework to assemble an integrated resuscitation system (taxonomy or systems of care)
- Out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) chains of survival
- Use of social media to summon rescuers
- Early warning sign systems, rapid response teams and medical emergency team systems
- Continuous quality improvement for resuscitation programs
- Regionalization approach to out of hospital cardiac arrest care may be considered

# Systems of Care



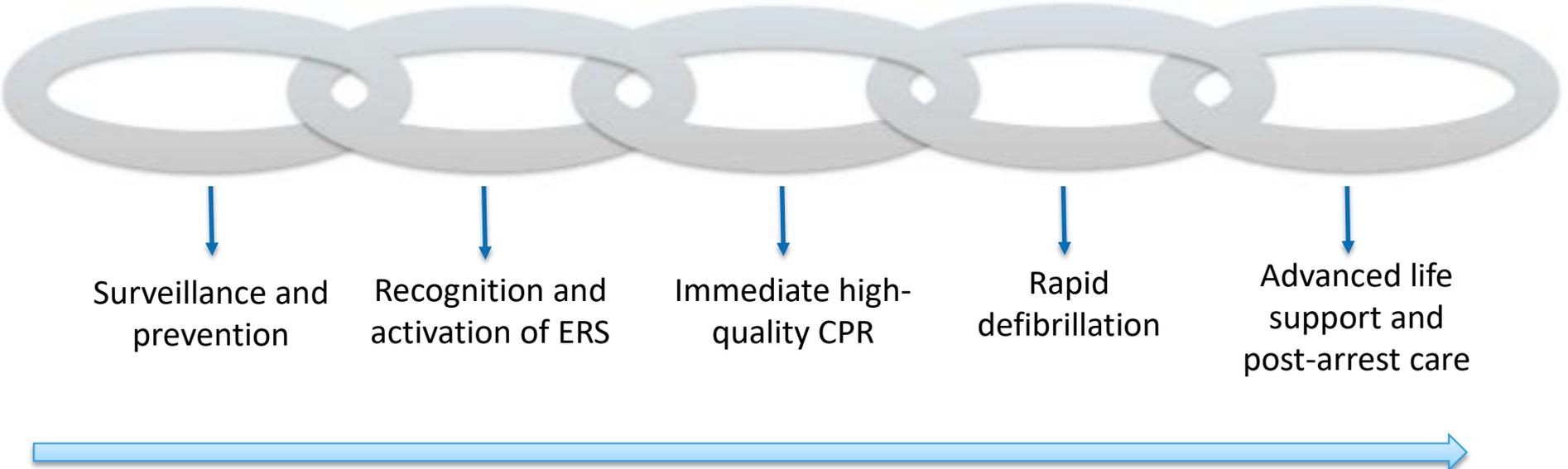
*Continuous Quality Improvement*

Integration, Collaboration, Measurement, Benchmarking, Feedback

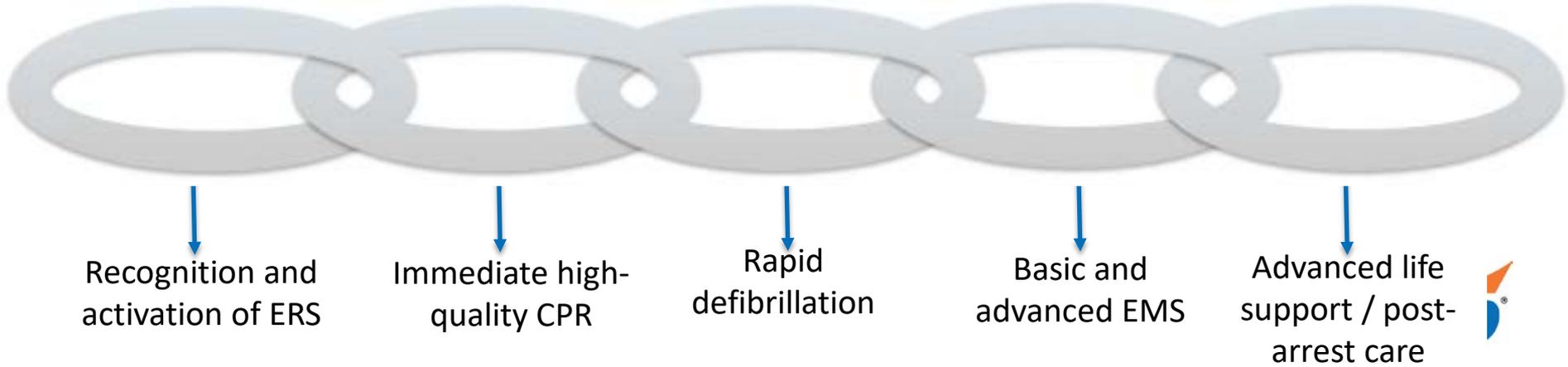
Modified - Neumar RW et al. *Circulation* 2015;132[suppl 2]:S215-S367

# Chains of Survival

## In-hospital Cardiac Arrest (IHCA)



## Out-of-hospital Cardiac Arrest (OHCA)



# Patient Case

Jim is a 64 year-old male who is attending his granddaughter's birthday party. While having a conversation with his brother-in-law (Tom), Jim begins to experience nausea, SOB and chest pain. He immediately collapses and falls to the ground.

Tom notices that Jim is unresponsive and not breathing. He is not trained in performing CPR and is not sure what to do.

# Question

Based on the 2015 guidelines what should be the **FIRST** intervention for Jim at this time?

- A Wait for friend to call 911
- B Perform compression-only CPR
- C Initiate ventilations every 6-8 seconds
- D Initiate social media technology to summon a rescuer

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Not trained in CPR, the bystander should provide **compression-only CPR and “push hard and fast”** (Class IIa, LOE B)
- Trained lay rescuer can perform rescue breaths, compressions and breaths at a ratio of 30 compressions to 2 breaths (Class I, LOE B)

## New (2015)

- Not trained in CPR, the bystander should **provide compression-only CPR** (Class I, LOE C-LD)
- Trained lay rescuer can perform rescue breaths, compressions and breaths at a ratio of 30 compressions to 2 breaths (Class I, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Dispatchers ask about a victims responsiveness and attempt to distinguish victims with agonal respirations (Class I, LOE B)

## New (2015)

- Dispatchers ask about victims responsiveness and quality of breathing (normal vs abnormal) (Class I, LOE C-LD)
- Dispatchers should be educated to identify unresponsiveness and abnormal/agonal respirations across a broad range of clinical presentations (Class I, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- HCP should check for response while looking at patient to determine if breathing is absent or not normal

## New (2015)

- HCP must call for nearby help upon finding victim unresponsive, but practical for HCP to continue to assess breathing and pulse before activating ERS

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Question

Which of the following would be the **MOST** optimum technique for Jim to perform compression-only CPR ?

- A Chest compression up to 120/minute
- B Chest compression up to 100/minute
- C Chest compressions should be “hard and fast”
- D Rescuer may pause compressions up to or greater than 10 seconds

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Lay person and HCP to perform chest compressions at a rate of at least 100/min (Class IIa, LOE B)

## New (2015)

- Rescuers to perform chest compressions at a rate of 100 to 120/min (Class IIa, LOE C-LD)
- Minimal pauses in compressions (< 10 sec)
- Also applies to BLS for healthcare providers

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Question

Which of the following would be the **MOST** optimum quality markers for Jim to perform compression-only CPR ?

- A Chest compression depth up to 1 inch
- B Chest compression depth at least 2 inches
- C Chest compressions depth at least 2 inches and not greater than 2.4 inches
- D Chest compression rate is more important than the depth of compressions

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- The adult sternum should be depressed at least 2 in or (5 cm) (Class IIa, LOE B)

## New (2015)

- During manual CPR, perform chest compressions to a depth of 2 in (5 cm) for average adult (Class I, LOE C-LD)
- Avoid excessive chest compression depths greater than 2.4 in (6 cm) (Class I, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Rescuers should allow complete recoil of chest after each compression (Class IIa, LOE B)

## New (2015)

- It is reasonable for rescuers to avoid leaning on the chest between compressions (Class IIa, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Not discussed

## New (2015)

- Known or suspected opioid overdose to administer intramuscular or intranasal naloxone.  
(Class IIa, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Advanced airway ventilation give 1 breath every 6 to 8 seconds resulting in delivery of 8 to 10 bpm (Class IIa, LOE B)

## New (2015)

- Provider to deliver 1 breath every 6 seconds (10 bpm) while chest compressions are performed (Class IIb, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- Not discussed

## New (2015)

- It may be reasonable for communities to incorporate social media technology that summon rescuers (Class IIb, LOE B-R)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Adult Basic Life Support (BLS) and CPR Quality

## OLD (2010)

- CPR and use of AED by 1<sup>st</sup> responders were recommended to increase survival for OHCA (Class IIa, LOE C)
- Establishment of AED programs in public locations where high likelihood of witnessed cardiac arrest

## New (2015)

- It is recommended that PAD programs for patients with OHCA be implemented in public locations where high likelihood of witnessed cardiac arrest (Class I, LOE C-LD)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://www.sca-aware.org/sites/default/files/comparison\\_chart\\_2015\\_aha\\_guidelines\\_for\\_cpr\\_and\\_ecc.pdf](http://www.sca-aware.org/sites/default/files/comparison_chart_2015_aha_guidelines_for_cpr_and_ecc.pdf)

Accessed August 2016.

# Alternative Techniques and Ancillary Devices for CPR

- Routine use of impedance threshold devices as an adjunct to CPR is not recommended
- Evidence does not demonstrate a benefit with the use of mechanical piston devices for chest compressions
- Extracorporeal techniques may be considered an alternative to conventional CPR for select patients

# Key Takeaways

- More ethical questions are becoming more evident based upon advances in resuscitative science
- Systems of care and continuous quality improvement lays the framework for future efforts to improve these systems of care
- Chest compression recommendations including rate (100-120 minute) and depth of 2 inches are emphasized
- Ventilations - 1 breath every 6 seconds (10 breaths/min) is recommended during airway resuscitation
- Naloxone is recommended for administration for suspected opioid overdose
- Alternative techniques and ancillary devices for CPR have demonstrated mixed results



Suprat Saely Wilson, PharmD., BCPS

Pharmacy Coordinator – Emergency Medicine Services

PGY-2 Emergency Medicine Pharmacy Residency Program Director

Detroit Receiving Hospital and University Health Center

Detroit, MI

# Patient Case

Jim is brought to your hospital resuscitation bay. CPR is ongoing. He still has no pulse. On the monitor, the rhythm is



# Question

Based on the 2015 guidelines what medication should be given to Jim at this time?

- A Epinephrine
- B Vasopressin
- C Both epinephrine and vasopressin

# Vasopressin

## OLD (2010)

Vasopressin 40 units IV/IO may replace either the first or second dose of epinephrine (Class IIb, LOE A)

## NEW (2015)

Vasopressin offers no advantage as a substitute for standard-dose epinephrine (Class IIb, LOE B-R)

# Pre and Post Question

Why was vasopressin removed from the ACLS algorithm?

- A** Because evidence showed that vasopressin has worse outcome (i.e. ROSC) than epinephrine
- B** Because vasopressin is expensive
- C** Because vasopressin requires refrigeration for storage
- D** Because vasopressin complicates the algorithm yet it has no benefit when compared to epinephrine

# Vasopressin vs. Epinephrine

- RCT comparing epinephrine 1 mg Q 5-10 min, max 4 doses (n=118) vs vasopressin 40 units Q 5-10 min, max 4 doses (n=137) in the ED after OHCA
- No benefit with the use of vasopressin for
  - ROSC (vaso 28.7% vs. epi 26.6%)
  - 24-h survival (vaso 16.9% vs. epi 20.3%)
  - Survival to discharge (vaso 5.6% vs. epi 3.8%)

# Vasopressin + Epinephrine Combination vs. Epinephrine Alone

## OLD (2010)

Vasopressin 40 units IV/IO may replace either the first or second dose of epinephrine (Class IIb, LOE A)

## NEW (2015)

Vasopressin in combination with epinephrine offers no advantage as a substitute for standard-dose epinephrine (Class IIb, LOE B-R)

Neumar RW, et al. *Circulation* 2010;122:S729-S767

Link MS, et al. *Circulation*. 2015;132:S444-S464

# Vasopressin + Epinephrine Combination vs. Epinephrine Alone

Study	Methods, N	Interventions	Outcomes
Linder, 1997	RCT, N=40	Vaso x1 + epi vs. epi alone	Hospital admission: VE > E
Wenzel, 2004	RCT N=1219	Vaso x 1-2 dose + epi vs. epi alone	Hospital admission: VE = E ROSC: VE = E Hospital discharge: VE = E
Callaway, 2006	RCT N=325	Vaso x1 + epi vs. epi alone	Hospital admission: VE = E ROSC: VE = E
Gueugniaud, 2008	RCT N=2894	Vaso x 1-2 dose + epi vs. epi alone	Hospital admission: VE = E ROSC: VE = E Hospital discharge: VE = E Good neuro recovery: VE = E
Ducros, 2011	RCT, n=48	Vaso + Epi ± Nitro 300mcg vs. Epi alone	ROSC: VE = E
Ong, 2012	RCT N=727	Vaso x1 + epi vs. epi alone	Hospital admission: VE > E ROSC: VE = E Hospital discharge: VE = E Good neuro recovery: VE = E

# Vasopressin + Epinephrine Combination vs. Epinephrine Alone

- Meta-analyses of outcomes showed no benefit with the use of combination epinephrine/vasopressin for
  - Survival to hospital discharge with CPC score of 1 or 2 (n = 2402)
  - Survival for hospital discharge (n=2438)
  - Survival for hospital admission (n=2438)
  - Rate of ROSC

# Poll

Does your hospital still have vasopressin in the crash cart?

A Yes

B No

# Vasopressin Summary

- No advantage over epinephrine
- Removed from ACLS guidelines to simplify algorithms
- Epinephrine is the vasopressor of choice

# Question

Based on the 2015 guidelines, what dose of epinephrine should be given to Jim at this time?

- A 0.2 mg/kg every 3-5 minutes
- B 1 mg every 3-5 minutes
- C 1 mg every 5-10 minutes
- D 5 mg every 3-5 minutes

# Standard-Dose Epinephrine

## OLD (2010)

It is **reasonable to consider** administering a 1-mg dose of IV/IO epinephrine every 3-5 minutes during adult cardiac arrest (Class IIb, LOE A)

## NEW (2015)

Standard-dose epinephrine (1 mg every 3-5 minutes) **may be reasonable** for patients in cardiac arrest (Class IIb, LOE B-R)

Neumar RW, et al. *Circulation* 2010;122:S729-S767

Link MS, et al. *Circulation*. 2015;132:S444-S464

# Standard-Dose Epinephrine

- RCT comparing standard-dose epinephrine (n=272) vs placebo (n=262) showed<sup>1</sup>
  - No benefit with epinephrine in survival to discharge with good neurologic outcome
  - Improved survival to hospital admission and ROSC with use of epinephrine
- 2 observational trials have conflicting results
  - Epinephrine improved ROSC, but decreased survival and good functional outcomes [n=417,188]<sup>2</sup>
  - Epinephrine did not improved any clinical outcome (i.e. ROSC, hospital admission, discharge or neurologic recovery) [n=644]<sup>3</sup>

1. Jacobs IG, et al. *Resuscitation* 2011;82:1138– 1143

2. Hagihara A, et al. *JAMA*. 2012;307(11):1161-1168

3. Machida M, et al. *J Card* 2012;60: 503–507

# Standard-Dose Epinephrine vs. High-Dose Epinephrine

## OLD (2010)

High-dose epinephrine was not recommended except in special circumstances, such as for BB, CCB overdose, or when titrated to real-time physiologically monitored parameters

## NEW (2015)

High-dose epinephrine is not recommended for routine use in cardiac arrest (Class III: No Benefit, LOE B-R)

Neumar RW, et al. *Circulation* 2010;122;S729-S767

Link MS, et al. *Circulation*. 2015;132:S444-S464

# Standard-Dose Epinephrine vs. High-Dose Epinephrine

Author	Design	Dose	Hospital Discharge
Gueugniaud, 1998	RCT N=3327	1 mg vs 5 mg	ROSC: HD > SD Hospital admission: HD = SD Hospital discharge: HD = SD Neurological status: HD = SD
Choux, 1995	RCT N=536	1 mg vs 5 mg (up to 15 doses)	ROSC: HD = SD Hospital admission: HD = SD
Stiell, 1992	RCT N=650	1 mg vs 7 mg (up to 5 doses)	Hospital discharge: HD = SD CPC 1 or 2: HD = SD
Brown, 1992	RCT N=1280	0.02 mg/kg vs 0.2 mg/kg	ROSC: HD = SD Hospital admission: HD = SD
Callaham, 1992	RCT N=816	1 mg vs 15 mg	ROSC: HD > SD Hospital admission: HD > SD Hospital discharge: HD = SD
Sherman, 1997	RCT N=140	0.01 mg/kg vs. 0.1 mg/kg up to 4 doses	ROSC: HD = SD

# Standard-Dose Epinephrine vs. High-Dose Epinephrine

- Meta-analyses of outcomes showed no benefit for high-dose epinephrine over standard-dose epinephrine for
  - Survival to discharge with good neurologic recovery (CPC score) [n=1920]
  - Survival to discharge [n=2859]
  - Survival to hospital admission [n=2882]
- Improved ROSC with high-dose epinephrine [n=3130]

# Question

Based on the 2015 guidelines, when should you give epinephrine to Jim (assuming that he is in the current rhythm mentioned previously)?

- A** Wait until at least 1 minute of chest compression
- B** During the next pulse check
- C** As soon as possible
- D** After Jim is intubated

# Timing of Epinephrine

## OLD (2010)

Not specifically discussed

## NEW (2015)

It may be reasonable to administer epinephrine **as soon as feasible** after the onset of cardiac arrest due to an initial non-shockable rhythm (Class IIb, LOE C-LD)

# Timing of Epinephrine

- Early administration of epinephrine in non-shockable rhythms was associated with increased ROSC, survival to hospital discharge, neurologically intact survival (1-3 min > 4-6 min > 7-9 min > >9 min) in IHCA (n=25,905)
- 3 studies showed improved survival to hospital discharge with early epinephrine administration in non-shockable rhythms in OHCA (early is < 9 to 10 min)

# Epinephrine Summary

- Use **standard dose** of epinephrine (1 mg Q 3 – 5 min)
- **High-dose epinephrine** not recommended
- If you can't shock, **give epinephrine ASAP**

# Post-Cardiac Arrest Lidocaine

## OLD (2010)

Not specifically discussed

## NEW (2015)

There is **inadequate evidence to support the routine use of lidocaine after cardiac arrest.** However, the initiation or continuation of lidocaine may be considered immediately after ROSC from cardiac arrest due to VF/pVT (Class IIb, LOE C-LD)

# Post-Cardiac Arrest Lidocaine

- Retrospective cohort study of patients resuscitated from OHCA VF/pVT arrest (n=1721)
- Multivariate analysis: prophylactic administration of lidocaine associated with lower rate of recurrent VF/pVT and higher rate of hospital admission and survival to hospital discharge
- Propensity score-adjusted analysis: no difference in rates of hospital admission or survival to hospital discharge

# Post-Cardiac Arrest $\beta$ -Blockers

## OLD (2010)

Not specifically discussed

## NEW (2015)

There is **inadequate evidence to support the routine use of a  $\beta$ -blocker after cardiac arrest.**

However, the initiation or continuation of an oral or IV  $\beta$ -blocker may be considered early after hospitalization from cardiac arrest due to VF/pVT. (Class IIb, LOE C-LD)

# Post-Cardiac Arrest $\beta$ -Blockers

- Retrospective study of patients resuscitated from OHCA VF/pVT arrest (n=98)
- Multiple logistic regression analysis: use of oral or IV  $\beta$ -blockers (metoprolol or bisoprolol) during the first 72 h of post-resuscitation care was associated with survival (mortality 44% vs. 79%)

# Extracorporeal CPR

## OLD (2010)

Not specifically discussed

## NEW (2015)

ECPR **may be considered among select cardiac arrest patients** who have not responded to initial conventional CPR, in settings where it can be rapidly implemented. (Class IIb, LOE C-LD)

# Thrombolysis

## OLD (2010)

In patients with cardiac arrest due to presumed or known PE, it is reasonable to administer fibrinolytics.

Survival has been described with percutaneous mechanical thrombectomy or surgical embolectomy with or without prior treatment with fibrinolysis.

## NEW (2015)

In patients with confirmed PE as the precipitant of cardiac arrest, thrombolysis, surgical embolectomy, and mechanical embolectomy are reasonable emergency treatment options. (Class IIa, LOE C-LD)

Thrombolysis may be considered when cardiac arrest is suspected to be caused by PE

# Question

If you have to give thrombolysis during cardiac arrest from PE, what dose of alteplase would you give?

- A 100 mg over 15 minutes
- B 50 mg bolus
- C 15 mg bolus, 50 mg over 30 minutes, 35 mg over 60 minutes
- D 100 mg bolus

# Intralipid Emulsion

## OLD (2010)

Prompt consultation with a medical toxicologist, anesthesiologist, or other specialist with up-to-date knowledge is strongly recommended for local anesthetic toxicity (Class IIb, LOE C) and when managing treatment-refractory hypotension from  $\beta$ -blocker overdose

## NEW (2015)

It may be reasonable to administer ILE, concomitant with standard resuscitative care, to patients with local anesthetic systemic toxicity and particularly to patients who have premonitory neurotoxicity or cardiac arrest due to bupivacaine toxicity. (Class IIb, LOE C-EO) It may be reasonable to administer ILE to patients with other forms of drug toxicity who are failing standard resuscitative measures. (Class IIb, LOE C-EO)

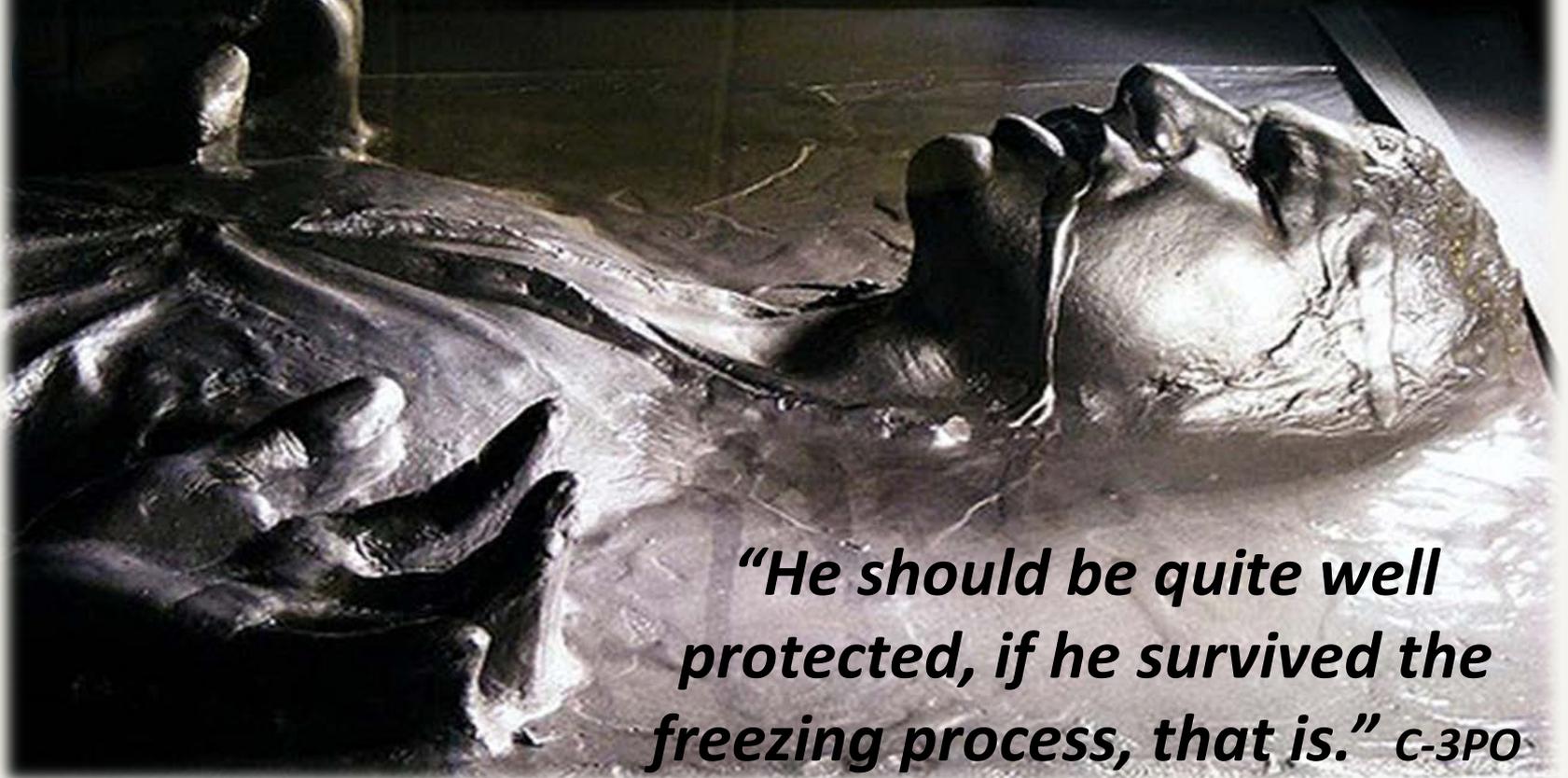
# Key Takeaways

- Vasopressin is out!
- Use standard dose of epinephrine (1 mg Q 3-5 min)
- If you can't shock, give epinephrine ASAP
- Post cardiac arrest lidocaine and  $\beta$ -blockers may be considered
- ECMO is a possible alternative
- Lyse when PE is confirmed or suspected
- Consider intralipid in local anesthetic toxicity or other overdose situations



Philippe Mentler, PharmD., BCPS  
Executive Pharmacy Director  
Pharmacy Advisory Services  
Vizient Inc

# ***Targeted Temperature Management***



***“He should be quite well protected, if he survived the freezing process, that is.” C-3PO***

# Patient Case Continued

After several rounds of effective BLS/ACLS care, Jim develops a pulse. Total duration of resuscitation was 32 minutes from witnessed arrest. Jim's glasgow coma score is 4 (intubated, no sedation/paralytics)

- Current Vitals:
  - HR: 123 BPM
  - BP: 120/70
  - RR: On ventilator, pressure-controlled, RR 18
  - Temp: 36.2 Celsius
- Initial PMHx, Medications, Physical Exam non-contributory
- Initial point of care labs Chem-7, H/H, Coags are WNL

# Pre and Post Question

Based on the 2015 guidelines what is the ideal Targeted Temperature Management (TTM) to achieve in this patient?

- A Targeted temp is contraindicated in Jim
- B 32° - 34° Celsius
- C Maintain afebrile state ( $\leq 38^\circ$  Celsius)
- D 32°- 36° Celsius

# ACLS TTM Recommendations

“We recommend that comatose adult patients with ROSC after...

## OLD (2010)

- VF cardiac arrest
  - (Class I, LOE B)
- Pulseless electric activity or asystole
  - (Class IIb, LOE B)

## NEW (2015)

- VF cardiac arrest
  - (Class I, LOE B-R)
- Pulseless electric activity or asystole
  - Class I, LOE C-EO

...have targeted temperature management”

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://circ.ahajournals.org/content/132/18\\_suppl\\_2/S465](http://circ.ahajournals.org/content/132/18_suppl_2/S465)

Accessed August 2016.

# TTM Landmark Trials

Study	Methods, N	Interventions	Outcomes
HACA, 2002	9-center (EU), RCT, partly blinded, N=275	Temp Control 32-34 C vs normothermic for 24 hours	Favorable neuro outcome at 6 months in 32-34 C group (55% vs 39%, p=0.009)
Bernard, 2002	4-center (AUS), RCT N=77	Temp goal of 33 Celsius vs normothermic for 12 hours	Favorable outcome in 33 C group (49% vs 36%, p=0.046)

- Focused on Vfib patients. Multiple exclusions
- Numerically greater pneumonia, sepsis, bleeding
- Statistically lower HR and higher SVR

# TTM in ROSC from non-shockable rhythm?

- Why Not?
- Schenone et al: Meta-analysis of expanded indications
  - Included 11 studies with 1,381 patients
    - 3 RCT, 8 Cohort
    - 48.4% had a non-shockable rhythm
  - Decreased mortality (OR 0.51, 95%CI [0.41–0.64])
  - Improved the odds good neuro outcome (OR 2.48, 95%CI [1.91–3.22])

# ACLS TTM Recommendations

## OLD (2010)

- Iced isotonic fluid can be [rapidly] infused to initiate core cooling (Class not defined)

## NEW (2015)

- Recommend against routine pre-hospital rapid infusion of cold intravenous fluids (Class III: No Benefit, LOE A)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://circ.ahajournals.org/content/132/18\\_suppl\\_2/S465](http://circ.ahajournals.org/content/132/18_suppl_2/S465)

Accessed August 2016.

# Question

Are you using cold fluids as part of induction of hypothermia pre-hospital?

A Yes

B No

Are you using cold fluids as part of induction of hypothermia in-hospital?

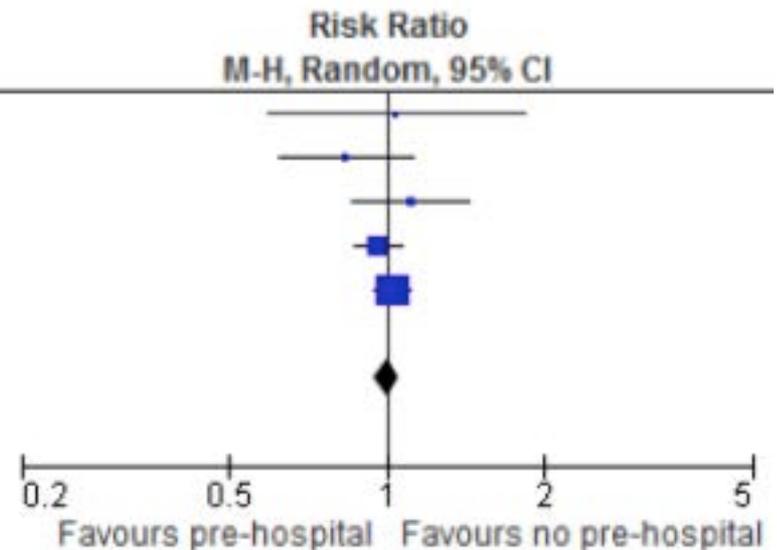
A Yes

B No

# Pre-hospital Rapid Induction of TTM?

- Forest Plot – Neurologic Outcome

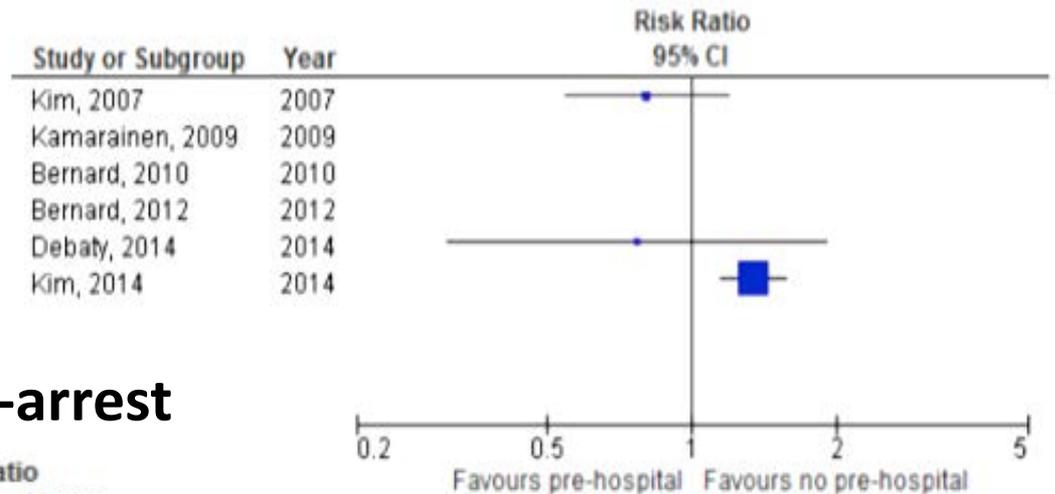
Study or Subgroup	Total	Weight	Risk Ratio		Year
			M-H, Random, 95% CI		
Kamarainen, 2009	18	1.1%	1.04	[0.59, 1.83]	2009
Castren, 2010	42	3.9%	0.84	[0.62, 1.12]	2010
Bernard, 2010	116	5.1%	1.11	[0.86, 1.43]	2010
Bernard, 2012	81	30.8%	0.96	[0.87, 1.07]	2012
Kim, 2014	671	59.2%	1.03	[0.95, 1.11]	2014
	<b>928</b>	<b>100.0%</b>	<b>1.00</b>	<b>[0.95, 1.06]</b>	



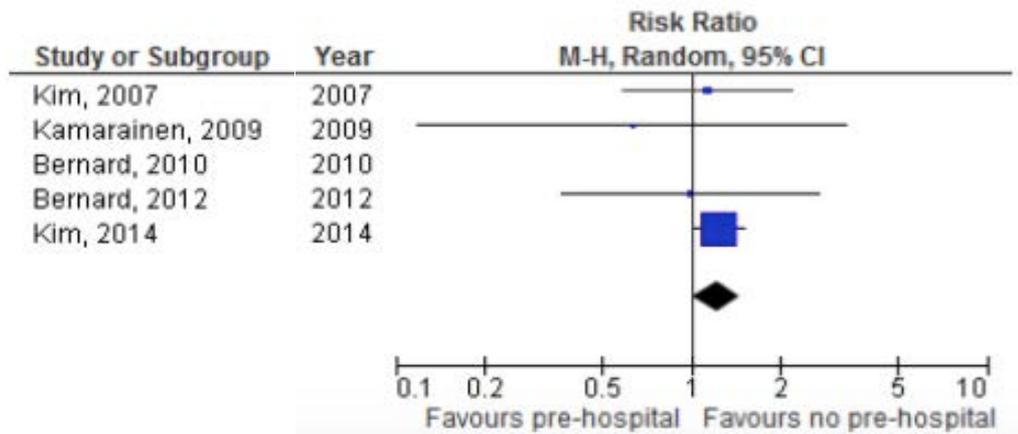
Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 3.31, df = 4 (P = 0.51); I<sup>2</sup> = 0%  
 Test for overall effect: Z = 0.06 (P = 0.95)

# Pre-Hospital Rapid Induction of TTM?

- Forest Plot – Pulmonary Edema



- Forest Plot – Outcome: Re-arrest



# Pre-Hospital Rapid Induction of TTM?

- Pre-hospital cold fluid trials fraught with weakness
  - Patients not consistently cooled after admission
    - Bernard 2010, Bernard 2012, Kim 2007, Kim 2014
  - Target temperature not always reached in intervention group
    - Bernard 2010, Bernard 2012
  - Mean Temp and Target Temp was set at 34° C
    - Bernard 2010, Bernard 2012, Castren, Debaty

# When do you use cold IV fluids?

- In-hospital TTM induction
- In the right patients
  - Without signs/symptoms cardiogenic shock??
- Looking to decrease time to target
  - No supporting evidence in humans
- 1-2 Liters (~30ml/kg) over 30-60 minutes
  - +/- insulated tubing/bag

# Question

What is the current Targeted Temperature that your Hospital uses?

- A Maintain afebrile
- B 32° - 34° C
- C Target 36° C
- D 32° - 36° C

# ACLS TTM Recommendations

“We recommend...”

## OLD (2010)

- Should be cooled to 32°C to 34°C (Class I, LOE B)

## NEW (2015)

- Maintain a constant temperature between 32°C and 36°C (Class I, LOE B-R)

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care.

[http://circ.ahajournals.org/content/132/18\\_suppl\\_2/S465](http://circ.ahajournals.org/content/132/18_suppl_2/S465)

Accessed August 2016.

# Original TTM Landmark Trials

Study	Methods, N	Intervention	Outcomes
HACA, 2002	MC (EU), RCT, N=275	Temp Control 32-34° C for 24 hours	Favorable neuro outcome at 6 months (55% vs 39%)
Bernard, 2002	MC (AUS), RCT N=77	Temp goal of 33° C for 12 hours	Favorable outcome (49% vs 36%)

# TTM: The argument for 36° C

- Targeted temperature of 32-34° C is not without risk



*Seinfeld*, Episode 85, "The Hamptons". NBC

# TTM: The argument for 36° C

- Targeted temperature of 32-34° C is not without risk
  - Fluctuating electrolyte and glucose abnormalities
  - Fluid abnormalities
  - Bradycardia
  - Shivering
  - Infection risk
  - Dysrhythmias, particularly with overcooling
  - Bleeding abnormalities

# TTM: The argument for 36° C

- Targeted temperatures of 32-34 C is resource intense
  - Managing adverse events
  - Induction and Maintenance of targeted temperature
    - Special cooling devices
      - A** Blankets/Pads   **B** Ice packs
      - C** Helmets   **D** Endovascular devices
    - Special temp monitoring devices
      - A** Tympanic   **B** Bladder
      - C** Rectal   **D** Intravascular
  - Careful controlled re-warming
    - 0.25°/hr or over 12+ hours

# The TTM Trial: 33° C vs 36° C

- Randomized, Controlled, Multicenter (EU and AUS)
- Included: Adults, any-rhythm cardiac arrest, 20-240 min post ROSC and GCS<8
- Assigned to either 33°C or 36°C
  - Induction with cold fluids, ice packs, surface or endovascular devices
- Rewarming starting at 28 hours after randomization
  - $\leq 0.5^{\circ}\text{C}$  per hour
- Temp maintained  $<37.5^{\circ}\text{C}$  for 72 hours post arrest

# The TTM Trial: 33° C vs 36° C

- Results: Notable characteristics

	33° C	36° C
N	473	466
% Patients with Shockable	79	81
Median Time to ROSC (min)	25	25
First measured temp	35.2° C	35.3° C

# The TTM Trial: 33° C vs 36° C

## ■ Results: Efficacy

	33°C	36°C	<i>p</i>
N	473	466	
Death through end of Trial (primary outcome)	50%	48%	0.51
Cerebral Performance Category (CPC) 3-5 at ~180 days (ie. bad)	54%	52%	0.78
Modified Rankin 4-6 at ~180 days (ie. bad)	52%	52%	0.87

# The TTM Trial: 33° C vs 36° C

## ■ Results: Safety

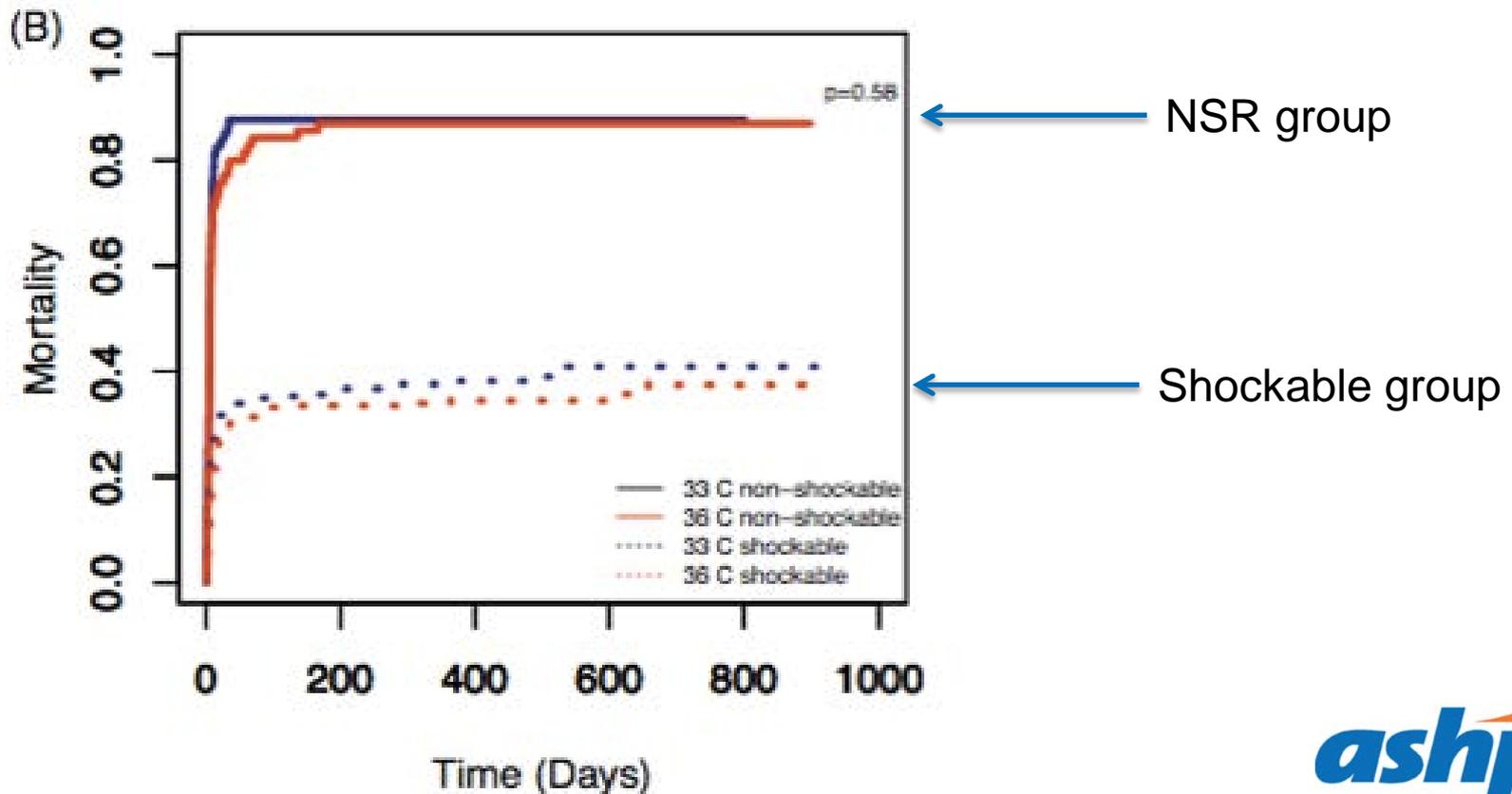
	33° C	36° C	<i>p</i>
Shivering	30%	34%	0.2
Hypokalemia	19%	13%	0.018
Pneumonia	52%	46%	0.089
Uncontrolled Bleeding	2.2%	1.3%	0.45

## ■ Conclusion

- There is no difference between 33° and 36° C as targeted temperature for post-arrest management

# The TTM Trial Criticisms

- Inclusion of non-shockable rhythms (NSR)
  - TTM Sub-study in NSR cases (178 of 950), no difference



# The TTM Trial Criticisms

- Inclusion of non-shockable rhythms (NSR)
  - TTM Sub-study in NSR cases (178 of 950), no difference
- Delayed cooling (8 hours to reach goal after randomization)
  - HACA (2002): Median time to goal was 8 hours
  - Registries offer conflicting results on timing
- Rewarming rate was too rapid (0.5°C per hour)
  - Rapid rewarming can have negative impact
  - Best rate not clearly defined. Duration and Fever prevention may be more important

# Question

What is the current Rewarming rate at your Hospital?

- A Over 12 hours ( $\sim 0.25^\circ/\text{hr}$ )
- B  $0.5^\circ \text{ C/hr}$
- C Over 24 hours
- D Range  $0.25^\circ\text{-}0.5^\circ \text{ C/hr}$

# Hypothermia Impact on Medications

- Therapeutic hypothermia impacts drug metabolism, particularly P450 system
  - Midazolam: 11-44%  $\square$  clearance at 33°C
  - Propofol: reduced clearance
  - Dexmedetomidine: reduced clearance
  - Fentanyl: reduced clearance, even after rewarming
  - Morphine: reduced clearance
  - Vecuronium: reduced clearance
  - Rocuronium: reduced clearance
  - Phenytoin: reduced clearance, even after rewarming
  - P2Y12 receptor inhibitors: decreased response

# Key Takeaways

- Stronger recommendations for Targeted Temperature Management (TTM) of non-shockable rhythms
- Cold fluids are not recommended for out of hospital induction of TTM
- Goal duration of TTM should be at least 24 hours
  - Active fever prevention may be important too
- Goal temperature is now 32°C to 36°C

# Pre and Post Question

How do you rate your understanding of the new 2015 American Heart Association (AHA) guideline update for cardiopulmonary resuscitation and emergency cardiovascular care?

- A Excellent
- B Good
- C Fair
- D Poor

# Pre and Post Question

Most of the 2015 Guidelines Update recommendations are supported by the lowest level of evidence [(LOE C-LD - limited data) or LOE C-EO – expert opinion)?

A TRUE

B FALSE

# Pre and Post Question

Why was vasopressin removed from the ACLS algorithm?

- A** Because evidence showed that vasopressin has worse outcome (i.e. ROSC) than epinephrine
- B** Because vasopressin is expensive
- C** Because vasopressin requires refrigeration for storage
- D** Because vasopressin complicates the algorithm yet it has no benefit when compared to epinephrine

# Pre and Post Question

Based on the 2015 guidelines what is the ideal Targeted Temperature Management (TTM) to achieve in this patient?

- A** Targeted temp is contraindicated in Jim
- B** 32° - 34° Celsius
- C** Maintain afebrile state ( $\leq 38^\circ$  Celsius)
- D** 32°- 36° Celsius



**Thank you!!**

Michael J. Cawley, PharmD., RRT, CPFT, FCCM

Suprat Saely Wilson, PharmD., BCPS

Philippe Mentler, PharmD., BCPS