Important Resuscitation Trials (and Aus-ROC)

Professor Judith Finn
Prehospital, Resuscitation and Emergency Care Research Unit (PRECRU)

Australian Resuscitation Outcomes Consortium

www.ausroc.org.au

- Centre of Research Excellence (CRE), funded by the National Health & Medical Research Council (NHMRC) for 5 years (2012-2017).
- *Initially* collaborative venture between Investigators from three Australian Universities: **Monash University (Vic); UWA/Curtin University (WA); and Flinders University (SA)** AND three State Ambulance Services: **Ambulance Victoria; St John Ambulance Service (WA) and the South Australian Ambulance Service**.
- National & International collaborators

Aus-ROC specific aims

Aus-ROC
Australian Resuscitation Outcomes Consortium

- undertake large multi-centre clinical trials (*initially)* across three jurisdictions.
- establish an Australia / NZ OHCA 'epistry' (epidemiologic registry) to monitor and report on the population-based effects of changes in pre-hospital resuscitation policy and practice.
- examine system-based strategies to improve the efficiency and effectiveness of pre-hospital emergency care for OHCA in urban and rural environments.
- build capacity in pre-hospital emergency care research across Australia through graduate research and post-doctoral training.

Aus-ROC
Australian Resuscitation Outcomes Consortium

Aus-ROC PhD Students

Dr Kylie Dyson
Paramedic exposure to cardiac arrest and patient survival: does practice make perfect?

MONASH University

Dr Susie Cartledge
Targeting high-risk cardiac patients and their family members for basic life support training.

MONASH University

Dr Milena Talikowska
The relationship between the quality of cardiopulmonary resuscitation (CPR) performed by paramedics and survival outcomes from out-of-hospital cardiac arrest (OHCA)

Curtin University

Ms Nicole McKenzie
Post-resuscitation care following out-of-hospital cardiac arrest: identification of in-hospital prognostic determinants.

Curtin University

Dr Amy Seymour-Walsh
Examining resuscitation skill education as a component of paramedics' practice development.

Flinders UNIVERSITY

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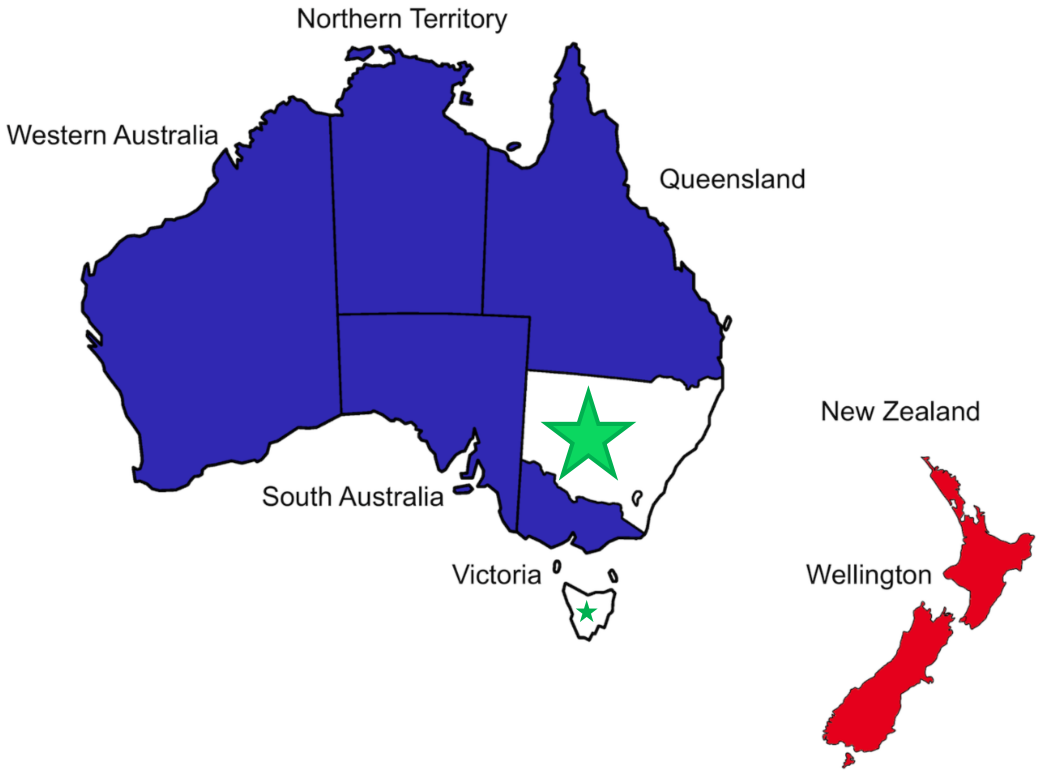
Aus-ROC Australian and New Zealand OHCA Epistry - 2015

★ NSW and Tas recently joined



Capture population: 19.5 million

Ambulance Victoria

Queensland Ambulance Service

SA Ambulance Service

St John

St John Ambulance Australia

St John

St John

Wellington Free Ambulance
kia ora te tangata

Aus-ROC Australian and New Zealand OHCA Epistry - 2015

Aus-ROC
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Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Regional variation in the characteristics, incidence and outcomes of out-of-hospital cardiac arrest in Australia and New Zealand: Results from the Aus-ROC Epistry☆

Ben Beck[a,*], Janet Bray[a,b,c], Peter Cameron[a,c], Karen Smith[a,d,e], Tony Walker[d], Hugh Grantham[b,f,g], Cindy Hein[f,g], Melanie Thorrowgood[g], Anthony Smith[h], Madoka Inoue[b], Tony Smith[i], Bridget Dicker[i,j], Andy Swain[j,k], Emma Bosley[l,m], Katherine Pemberton[l], Michael McKay[n], Malcolm Johnston-Leek[n], Gavin D. Perkins[o], Graham Nichol[p], Judith Finn[a,b,h], on behalf of the Aus-ROC Steering Committee

Beck B *et al. Regional variation in the characteristics, incidence and outcomes of out-of-hospital cardiac arrest in Australia and New Zealand: Results from the Aus-ROC Epistry.* ***Resuscitation. 2018;126:49-57***.

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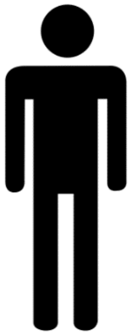
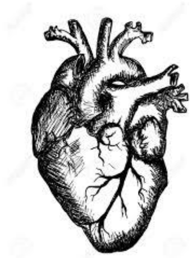
Aus-ROC Australian and New Zealand OHCA Epistry - 2015

19,722 OHCAs
Incidence of 102.5 per 100,000 pop
Aus = Estimated 24,373 per year

66% male
Median age: 66 years (IQR: 50-80 years)



75% occurred in the home



74% ‘presumed cardiac’ cause

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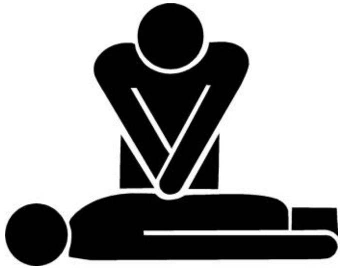
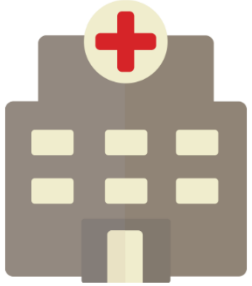
Aus-ROC Australian and New Zealand Epistry OHCA - 2015



48% of cases received attempted resuscitation by paramedics (n=9,245)



28% had ROSC on arrival at hospital

12% (Range 9%-17%) survived to discharge / 30 days
(5 Ambulance Services reporting these outcomes)

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Australian Resuscitation Outcomes Consortium

Aus-ROC Australian and New Zealand Epistry OHCA – 2015

Survival varies in different sub-groups (and across different regions)

"Utstein comparator group"
Bystander-witnessed + Shockable rhythm (VF/VT)

31% (Range 29%-40%) survived to discharge / 30 days

Aus-ROC specific aims

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- examine system-based strategies to improve the efficiency and effectiveness of pre-hospital emergency care for OHCA in urban and rural environments.
- build capacity in pre-hospital emergency care research across Australia through graduate research and post-doctoral training.

ORIGINAL RESEARCH ARTICLE

Induction of Therapeutic Hypothermia During Out-of-Hospital Cardiac Arrest Using a Rapid Infusion of Cold Saline

The RINSE Trial (Rapid Infusion of Cold Normal Saline)

Aus-ROC
Australian Resuscitation Outcomes Consortium

In adults with OHCA, induction of mild therapeutic hypothermia using a rapid infusion of large-volume, intravenous cold saline during CPR may decrease the rate of ROSC in patients with an initial shockable rhythm and produced no trend towards improved outcomes at hospital discharge.

Circulation. 2016;134:797–805

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association. Learn and Live.

ORIGINAL RESEARCH ARTICLE

Induction of Therapeutic Hypothermia During Out-of-Hospital Cardiac Arrest Using a Rapid Infusion of Cold Saline

The RINSE Trial (Rapid Infusion of Cold Normal Saline)

BACKGROUND: Patients successfully resuscitated by paramedics from out-of-hospital cardiac arrest often have severe neurologic injury. Laboratory and observational clinical reports have suggested that induction of therapeutic hypothermia during cardiopulmonary resuscitation (CPR) may improve neurologic outcomes. One technique for induction of mild therapeutic hypothermia during CPR is a rapid infusion of large-volume cold crystalloid fluid.

METHODS: In this multicenter, randomized, controlled trial we assigned adults with out-of-hospital cardiac arrest undergoing CPR to either a rapid intravenous infusion of up to 2 L of cold saline or standard care. The primary outcome measure was survival at hospital discharge; secondary end points included return of a spontaneous circulation. The trial was closed early (at 48% recruitment target) due to changes in temperature management at major receiving hospitals.

RESULTS: A total of 1198 patients were assigned to either therapeutic hypothermia during CPR (618 patients) or standard prehospital care (580 patients). Patients allocated to therapeutic hypothermia received a mean (SD) of 1193 (647) mL cold saline. For patients with an initial shockable cardiac rhythm, there was a decrease in the rate of return of a spontaneous circulation in patients who received cold saline compared with standard care (41.2% compared with 50.6%, P=0.03). Overall 10.2% of patients allocated to therapeutic hypothermia during CPR were alive at hospital discharge compared with 11.4% who received standard care (P=0.71).

CONCLUSIONS: In adults with out-of-hospital cardiac arrest, induction of mild therapeutic hypothermia using a rapid infusion of large-volume, intravenous cold saline during CPR may decrease the rate of return of a spontaneous circulation in patients with an initial shockable rhythm and produced no trend toward improved outcomes at hospital discharge.

CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov. Unique identifier: NCT01173393.

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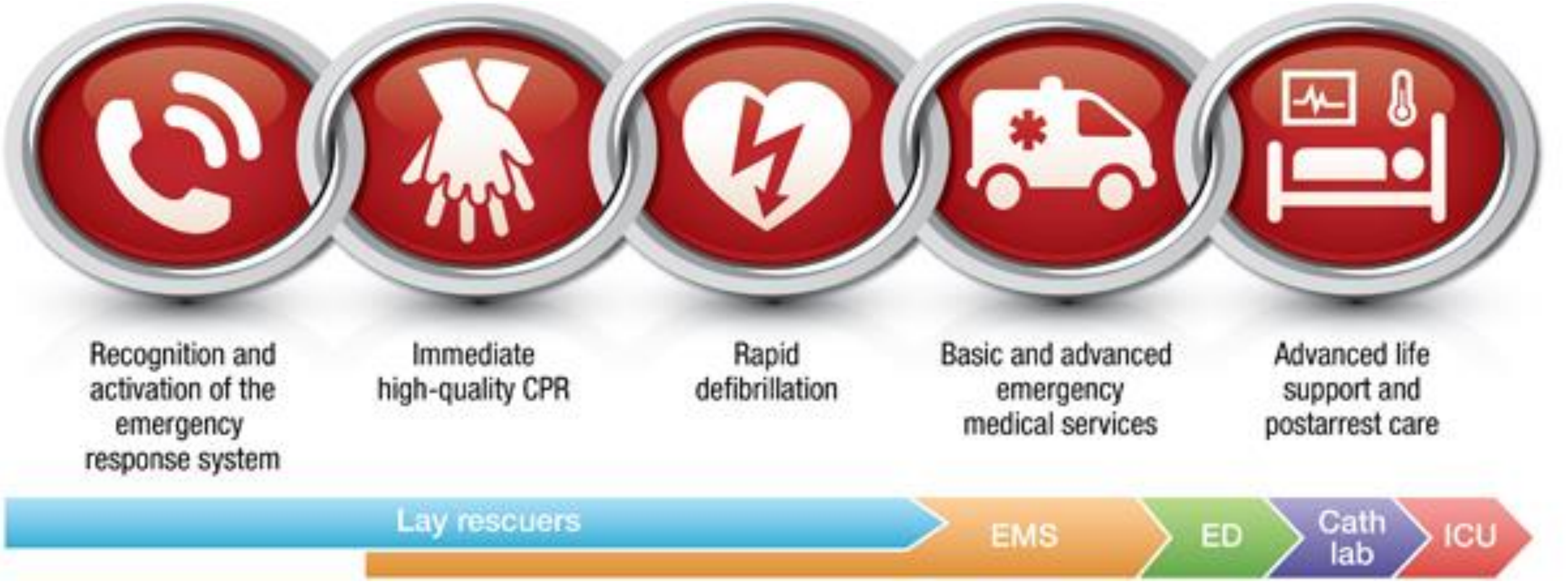
Sources of Funding, see page 804

Key Words: cardiac arrest ■ cardiopulmonary resuscitation ■ clinical trial ■ emergency medical services ■ therapeutic hypothermia



AHA OHCA Chain of Survival

1. Recognition of cardiac arrest and activation of the emergency response system
2. Early cardiopulmonary resuscitation (CPR) with an emphasis on chest compressions
3. Rapid defibrillation
4. Basic and advanced emergency medical services (EMS)
5. Advanced life support and post-cardiac arrest care (Hospital)

ILCOR: The Scientific Knowledge Gaps and Clinical Research Priorities for CPR and ECC

Resuscitation 127 (2018) 132–146

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ILCOR Consensus Statement

ILCOR Scientific Knowledge Gaps and Clinical Research Priorities for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: A Consensus Statement☆

Monica E. Kleinman, Gavin D. Perkins, Farhan Bhanji, John E. Billi, Janet E. Bray, Clifton W. Callaway, Allan de Caen, Judith C. Finn, Mary Fran Hazinski, Swee Han Lim, Ian Maconochie, Peter Morley, Vinay Nadkarni, Robert W. Neumar, Nikolaos Nikolaou, Jerry P. Nolan, Amelia Reis, Alfredo F. Sierra, Eunice M. Singletary, Jasmeet Soar, David Stanton, Andrew Travers, Michelle Welsford, David Zideman

Circulation

ILCOR CONSENSUS STATEMENT

ILCOR Scientific Knowledge Gaps and Clinical Research Priorities for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

A Consensus Statement

ABSTRACT: Despite significant advances in the field of resuscitation science, important knowledge gaps persist. Current guidelines for resuscitation are based on the International Liaison Committee on Resuscitation 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations, which includes treatment recommendations supported by the available evidence. The writing group developed this consensus statement with the goal of focusing future research by addressing the knowledge gaps identified during and after the 2015 International

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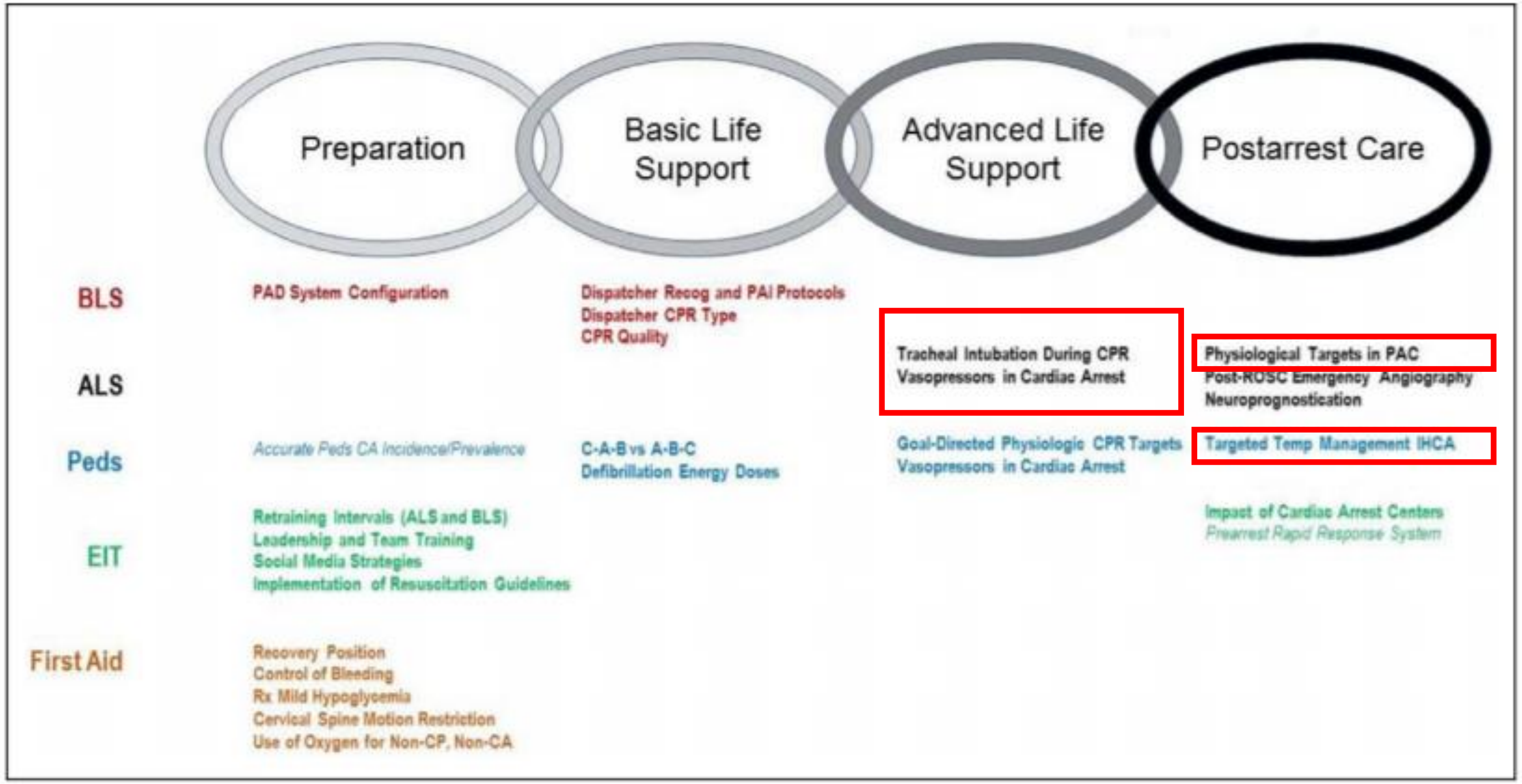


Figure. Universal chain of survival: knowledge gaps map.

Kleinman et al, *Resuscitation 2018 127:132-146* & *Circulation 2018;137:e691–e782*

Airways –big year!

JAMA | Original Investigation

Effect of Bag-Mask Ventilation vs Endotracheal Intubation During Cardiopulmonary Resuscitation on Neurological Outcome After Out-of-Hospital Cardiorespiratory Arrest

A Randomized Clinical Trial

JAMA | Original Investigation

Effect of a Strategy of Initial Laryngeal Tube Insertion vs Endotracheal Intubation on 72-Hour Survival in Adults With Out-of-Hospital Cardiac Arrest

A Randomized Clinical Trial

JAMA | Original Investigation

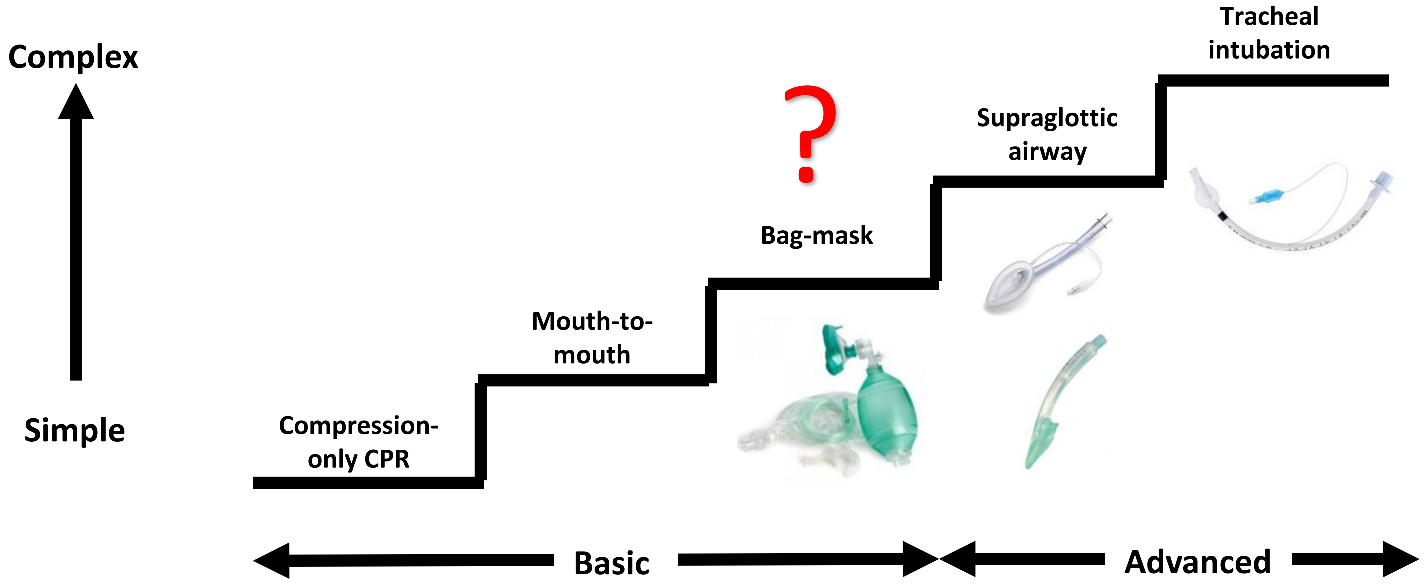
Effect of a Strategy of a Supraglottic Airway Device vs Tracheal Intubation During Out-of-Hospital Cardiac Arrest on Functional Outcome

The AIRWAYS-2 Randomized Clinical Trial

GAP: Type and duration of training required for performing advanced airway management during CPR

J. Bray slide

AIRWAYS



J. Bray slide

RCT: BMV vs ETT

Research

JAMA | Original Investigation

Effect of Bag-Mask Ventilation vs Endotracheal Intubation During Cardiopulmonary Resuscitation on Neurological Outcome After Out-of-Hospital Cardiorespiratory Arrest

A Randomized Clinical Trial

- RCT 2043 OHCA patients in France and Belgium **physician-based EMS** between 2015-2017
- Assess *non-inferiority* of Bag-Mask Ventilation (BMV) vs ETT **<u>airway management strategy</u>**

Jabre JAMA 2018;319:779-787

- **Primary outcome: survival with neurological function at day 28 (CPC)**
- Secondary outcomes:
  - ROSC
  - survival to hospital
  - survival at 28 days
  - ETI and BMV difficulty or failure

J. Bray slide

Table 2. Secondary Outcomes in Patients Included in the Study

Outcome	No. of Patients (%) BMV Group	ETI Group	Proportion Difference, BMV(%) − ETI(%) (95% CI)	P Value[a]
Intention-to-Treat Population	n = 1018	n = 1022		
Survival at 28 d	55 (5.4)	54 (5.3)	0.1 (−1.8 to 2.1)	.90
CPCs[b]				
1, Good cerebral performance	35 (3.4)	37 (3.6)		.68
2, Moderate cerebral disability	9 (0.9)	6 (0.6)		
3, Severe cerebral disability	4 (0.4)	7 (0.7)		
4, Coma or vegetative state	7 (0.7)	4 (0.4)		
5, Death	963 (94.6)	968 (94.7)		
Survival to hospital admission	294 (28.9)	333 (32.6)	−3.7 (−7.7 to 0.3)	.07
Return of spontaneous circulation	348 (34.2)	397 (38.9)	−4.7 (−8.8 to −0.5)	.03
Per-Protocol Analysis	n = 995	n = 943		
Survival at 28 d	54 (5.4)	51 (5.4)	0.1 (−10 to 9.7)	.99
CPCs[b]				
1, Good cerebral performance	35 (3.5)	34 (3.5)		.76
2, Moderate cerebral disability	8 (0.8)	6 (0.6)		
3, Severe cerebral disability	4 (0.4)	7 (0.7)		
4, Coma or vegetative state	7 (0.7)	4 (0.4)		
5, Death	941 (94.6)	892 (94.6)		
Survival to hospital admission	289 (29.1)	312 (33.1)	−4.0 (−7.6 to 0.6)	.055
Return of spontaneous circulation	342 (34.4)	377 (30.0)	−5.6 (−9.9 to −1.3)	.01

Intubated patients

- *“Equivalent”* good functional outcome: 4.2% vs 4.3% (NS)
- Survival 28 days: 5.3% vs. 5.4%
- Higher rates of ROSC: 38.9% vs 34.2%
- Less regurgitation 7.5% vs 15.2%

Limitations:

- Sample size estimation ?underpowered to show noninferioirity
- Inpatient management not collected

Jabre JAMA 2018;319:779-787

J. Bray slide

Wang JAMA 2018;320:769-778

RCT: Laryngeal Tube vs ETT

JAMA | Original Investigation

Effect of a Strategy of Initial Laryngeal Tube Insertion vs Endotracheal Intubation on 72-Hour Survival in Adults With Out-of-Hospital Cardiac Arrest

A Randomized Clinical Trial

Henry E. Wang, MD, MS; Robert H. Schmicker, MS; Mohamud R. Daya, MD, MS; Shannon W. Stephens, EMT-P; Ahamed H. Idris, MD; Jestin N. Carlson, MD, MS; M. Riccardo Colella, DO, MPH; Heather Herren, MPH, RN; Matthew Hansen, MD, MCR; Neal J. Richmond, MD; Juan Carlos J. Puyana, BA; Tom P. Aufderheide, MD, MS; Randal E. Gray, MEd, NREMT-P; Pamela C. Gray, NREMT-P; Mike Verkest, AAS, EMT-P; Pamela C. Owens; Ashley M. Brienza, BS; Kenneth J. Sternig, MS-EHS, BSN, NRP; Susanne J. May, PhD; George R. Sopko, MD, MPH; Myron L. Weisfeldt, MD; Graham Nichol, MD, MPH

- Multicenter **pragmatic cluster-crossover** (3-5 months); n= 3,004 OHCA pts
- **27 paramedic EMS** agencies (13 clusters) from the Resuscitation Outcomes Consortium 2015-2017
- **Strategies of LT and ETI** under existing clinical protocols and educational practices (no additional training or quality improvement monitoring)

- **Primary outcome was survival at 72 hours**
- Secondary outcome
  - ROSC
  - survival to hospital discharge
  - favourable neurological status at hospital discharge (mRS)
  - key adverse events

Modified J. Bray slide

Table 2. Outcomes of Patients Included in the Primary and Secondary Analyses

Characteristic	Laryngeal Tube (n = 1505) No. (%)	Endotracheal Intubation (n = 1499) No. (%)	Difference, % (95% CI)[a]	P Value
Primary Outcome				
Survival to 72 h (intention-to-treat population)	275 (18.3)	230/1495 (15.4)	2.9 (0.2 to 5.6)	.04
Secondary Outcomes				
Return of spontaneous circulation on emergency department arrival	420 (27.9)	365 (24.3)	3.6 (0.3 to 6.8)	.03
Survival to hospital discharge	163/1504 (10.8)	121/1495 (8.1)	2.7 (0.6 to 4.8)	.01
Favorable neurologic status at discharge (Modified Rankin Scale score ≤3)	107/1500 (7.1)	75/1495 (5.0)	2.1 (0.3 to 3.8)	.02
Modified Rankin Scale score	n = 1500	n = 1495		
0-No symptoms	17 (1.1)	14 (0.9)		
1-No significant disability	32 (2.1)	29 (1.9)		
2-Slight disability	22 (1.5)	12 (0.8)		
3-Moderate disability	36 (2.4)	20 (1.3)		
4-Moderately severe disability	26 (1.7)	24 (1.6)		
5-Severe disability	26 (1.7)	22 (1.5)		
6-Dead	1341 (89.4)	1374 (91.9)		

Intubated patients

- Lower survival to 72-hours:
  - **15.4% vs 18.3%**
- Lower rates of ROSC:
  - **24.3% vs 27.9%**
- Lower survival to hospital discharge:
  - **8.1% vs 10.8%**
- Lower good functional outcome:
  - **4.9% vs 7.1%**
- Lower rates of initial success:
  - **51.6% vs 90.3%**
-

Limitations:

- Sample size (funding)
- Inpatient management not collected
- Not blinded

Wang JAMA 2018;320(8):769-778

Modified *J. Bray slide*

RCT: SGA vs ETT

JAMA | Original Investigation

Effect of a Strategy of a Supraglottic Airway Device vs Tracheal Intubation During Out-of-Hospital Cardiac Arrest on Functional Outcome

The AIRWAYS-2 Randomized Clinical Trial

Jonathan R. Benger, MD; Kim Kirby, MRes; Sarah Black, DClinRes; Stephen J. Brett, MD; Madeleine Clout, BSc; Michelle J. Lazaroo, MSc; Jerry P. Nolan, MBChB; Barnaby C. Reeves, DPhil; Maria Robinson, MOst; Lauren J. Scott, MSc; Helena Smartt, PhD; Adrian South, BSc (Hons); Elizabeth A. Stokes, DPhil; Jodi Taylor, PhD; Matthew Thomas, MBChB; Sarah Voss, PhD; Sarah Wordsworth, PhD; Chris A. Rogers, PhD

- Cluster (paramedic) RCT 9296 patients from 4 UK **paramedic** EMS in England between 2015 and 2017

- **Two strategies of advanced airway management** with a supraglottic airway device (*i-gel*) compared with tracheal intubation

Primary outcome

- **MRS (0-3) at hospital discharge or 30 days**

Secondary outcome

- Ventilation success
- Regurgitation and aspiration

Benger 2018, JAMA;320(8):779-791

Modified Rankin Scale

Score	Definition
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	Dead

Table 2. Primary Outcome, Survival Status, and Main Secondary Outcomes

	No. of Patients/Total No. (%)[a]	
	Tracheal Intubation (n = 4410)	Supraglottic Airway Device (n = 4886)
Primary Outcome: Modified Rankin Scale Score at Hospital Discharge or 30 d		
0-3 range (good outcome)	300/4407 (6.8)	311/4882 (6.4)
0 (no symptoms)	124/4407 (2.8)	117/4882 (2.4)
1	48/4407 (1.1)	41/4882 (0.8)
2	50/4407 (1.1)	58/4882 (1.2)
3	78/4407 (1.8)	95/4882 (1.9)
4-6 range (poor outcome to death)	4107/4407 (93.2)	4571/4882 (93.6)
4	46/4407 (1.0)	45/4882 (0.9)
5	27/4407 (0.6)	39/4882 (0.8)
6 (died)	4034/4407 (91.5)	4487/4882 (91.9)
Secondary Outcomes		
Survival status		
Died at scene	2488/4407 (56.5)	2623/4882 (53.7)
Died prior to ICU admission	1058/4407 (24.0)	1226/4882 (25.1)
Died prior to ICU discharge	369/4407 (8.4)	503/4882 (10.3)
Died prior to hospital discharge	120/4407 (2.7)	138/4882 (2.8)
Survived to 30 d or hospital discharge	372/4407 (8.4)	392/4882 (8.0)

Intubated patients

- Equivalent mRS 0-3: **6.8% vs 6.4%**
- Equivalent survival to hospital discharge/30d: **8.4% vs 8.0%**
- Lower rates of successful placement: **79.0% vs 87.4%**

Limitations:

- Crossover between groups
- Inpatient management not collected

Benger 2018, JAMA;320(8):779-791

J. Bray slide

Editorial: Andersen LW, Granfeldt A. Pragmatic Airway Management in Out-of-Hospital Cardiac Arrest. **JAMA. 2018;320(8):761-3**.

- Study design
- Physician-staffed vs Paramedic-staffed EMS
- ETI initial success rate
- ?ETI Exposure

EDITORIAL

Pragmatic Airway Management in Out-of-Hospital Cardiac Arrest

Lars W. Andersen, MD, MPH, PhD; Asger Granfeldt, MD, PhD, DMSc

Out-of-hospital cardiac arrest is associated with high mortality, with only approximately 11% of patients surviving to hospital discharge.[1] There is a need for robust evidence to guide interventions. One of these interventions is airway management, for which contemporary strategies include bag-valve-mask ventilation, endotracheal intubation, or various types of supraglottic airway devices.[2] Supraglottic airway devices are inserted blindly and placed in the hypopharynx such that airflow is provided above the glottis. The precise design and placement depend on the type of supraglottic airway. Although each of these 3 airway strategies have theoretical advantages and disadvantages, there is little evidence to recommend one approach over the other.[2,3]

Related articles pages 769 and 779

Endotracheal intubation has traditionally been regarded as the preferred technique for airway management during cardiac arrest, but has been associated with a number of potential detrimental effects such as prolonged interruptions in chest compressions and unrecognized esophageal intubation.[4,5] Within the last decade, a number of observational studies have investigated the relationship between airway management techniques and outcomes in out-of-hospital cardiac arrest.[6] However, interpretation of these studies is difficult not only due to confounding, but also due to a lack of consideration of the timing of the intervention, such that patients with more prolonged cardiac arrests have a higher chance of receiving advanced airway management.[7] Randomized trials have therefore been long awaited.

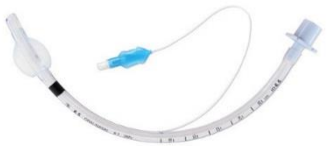
In this issue of *JAMA*, 2 such trials are reported. Wang et al[8] report the results of a pragmatic cluster-crossover randomized trial (N = 3004) conducted in the United States comparing a strategy of laryngeal tube (a type of supraglottic airway) insertion with a strategy of endotracheal intubation. The investigators found that the laryngeal tube strategy was associated with a clinical and statistically significant increase in 72-hour survival (18.3% vs 15.4%; absolute difference, 2.9% [95% CI, 0.2%-5.6%]). Secondary outcomes, such as survival to hospital discharge (10.8% vs 8.1%) and a favorable neurological status (defined as a modified Rankin Scale score ≤3) at hospital discharge (7.1% vs 5.0%), also favored the laryngeal tube strategy.

In the other trial, Benger et al[9] report the results of a pragmatic cluster randomized trial (N = 9296) conducted in the United Kingdom comparing an airway management strategy using a different type of supraglottic airway with a strategy of endotracheal intubation. In contrast to the findings of Wang et al,[8] Benger et al[9] found no significant difference in the primary outcome of a favorable neurological outcome at 30 days (defined as a modified Rankin Scale score ≤3), which occurred in 6.4% of patients in the supraglottic airway group and 6.8% in the endotracheal intubation group (absolute risk difference, −0.6% [95% CI, −1.6% to 0.4%]).

Both trials have many important strengths including the large sample sizes, inclusion of multiple emergency medical services (EMS) units, and the comparison of commonly used airway management strategies. These strengths are particularly important given the complexity of conducting research in acute conditions in the out-of-hospital setting. However, to understand why these results differ and how they might influence guidelines and clinical practice, a more detailed consideration of the trials and the settings is necessary.

For most EMS personnel, out-of-hospital cardiac arrest is encountered relatively infrequently, limiting their exposure to patients with cardiac arrest and related interventions such as advanced airway management.[10] Endotracheal intubation is a skill that needs practice to acquire and maintain.[11] In the trial by Wang et al,[8] the initial endotracheal intubation success rate was low at 51% (compared with a 91% success rate for paramedics reported in a previous meta-analysis[12] and 69% reported in the trial by Benger et al[9]). Additionally, in the trial by Wang et al,[8] 33% of patients in the endotracheal intubation group were intubated or reintubated after arrival in the emergency department. Rates of endotracheal intubation or reintubation at hospital admission were not reported in the trial by Benger et al.[9] Whether a higher intubation success rate would have altered the results in either trial remains speculative, but previous studies have found that failed airway attempts are associated with worse outcomes.[13] As such, it seems pertinent to limit generalizability of the trial findings to similar settings, ie, in settings in which endotracheal intubation success rates are low, simpler and easier techniques, such as a supraglottic airway, might be preferable.

This raises the question of whether an even simpler technique, bag-valve-mask ventilation, would have similar or better outcomes compared with a supraglottic airway. In a recent trial, Jabre et al[14] failed to establish noninferiority of bag-valve-mask ventilation compared with endotracheal intubation although the proportions of patients with a favorable neurological outcome (defined as cerebral performance category 1 or 2) at 28 days were remarkably similar (4.3% vs 4.2%). Comparison of this trial with the current trials reported by Wang et al[8] and Benger et al[9] is difficult because the airway was managed by experienced physicians with a



“But I am good at intubation –these results don’t apply to me.”

Study	Initial ETT success	Overall success
Jaber 2018	87%	
Wang 2018	51%	92%
Benger 2018	69%	
Dyson 2017 (EMS)	78%	95%
Kim 2018 (ED)	68%	-

How many of you are thinking this?

Paramedic Intubation Experience Is Associated With Successful Tube Placement but Not Cardiac Arrest Survival

Kylie Dyson, BHlthSc*; Janet E. Bray, PhD; Karen Smith, PhD; Stephen Bernard, MBBS MD; Lahn Straney, PhD; Resmi Nair, PhD; Judith Finn, PhD

- **ETI 0.5%** of emergency responses
- Average **3 per year** (range 1 to 17)
- Paediatric intubation (0)

Dyson Annals of Emerg Med 2017;70:382-390

Modified *J. Bray slide*

"Intubation is a time consuming, cognitively demanding complex skill."

"One of the risks of additional techniques in OHCA is that they detract from the things that really work."

Jonathan Benger
(Resus Room Podcast)

Kim (ED) - time to successful ETI: mean **63 sec**

Kim Resuscitation 2018;18:30829-3

Modified *J. Bray slide*

BMJ Open Respiratory Research

To intubate or not: ventilation is the question. A manikin-based observational study

Fatimata Seydou Sall,[1,2] Alban De Luca,[1,2] Lionel Pazart,[1] Aurore Pugin,[1] Gilles Capellier,[2,3] Abdo Khoury[1,2]

- **145 healthcare providers manually ventilate a manikin as a 75 kg adult patient in respiratory arrest**

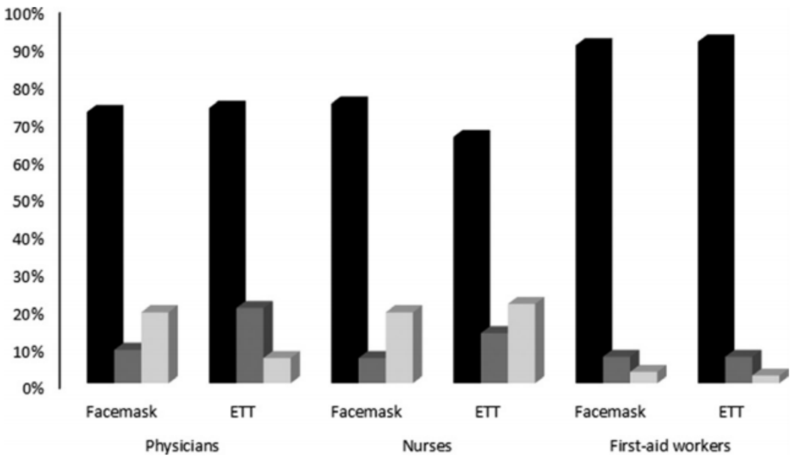


Figure 1 Percentage of hyperventilation (black), adequate ventilation (grey) and hypoventilation (light grey) for professional categories (n=280 tests for each ventilation technique). ETT, endotracheal tube.

Table 3 Ventilation performance analysis during the 5 min ventilation tests (n=280 tests for each ventilation technique)

Ventilation performance	Facemask (mean (%))	ETT (mean (%))
Adequate ventilation	21 (7.5)	37 (13.21)
Hypoventilation	37 (13.21)	27 (9.64)
Hyperventilation	222 (79.29)	216 (77.14)

ETT, endotracheal tube.

- **All healthcare professionals hyperventilated whatever the interface used (>70%).**

- Minimal improvement when ventilating through an ETT (13.2% vs 7.5%)

Sall BMJ Open Respiratory Research 2018;5:e000261

OXYGEN

- Hyperoxia
- O2 titration

Modified *J. Bray slide*

AVOID Study

Air Versus Oxygen In ST-elevation MyocarDial Infarction

Dr Dion Stub MBBS PhD FRACP
Baker IDI Heart & Diabetes Institute, Melbourne Australia
St Paul's Hospital Vancouver, Canada

On behalf of Karen Smith, Stephen Bernard, Ziad Nehme, Michael Stephenson, Janet E. Bray, Peter Cameron, Bill Barger, Andris H. Ellims, Andrew J. Taylor, Ian T. Meredith, David M. Kaye for the AVOID Investigators.

Conclusion

Supplemental oxygen therapy in patients with STEMI but without hypoxia increased myocardial injury, recurrent myocardial infarction and major cardiac arrhythmia, and was associated with larger myocardial infarct size assessed at six months.

Stub D, et al. Air Versus Oxygen in ST-Segment-Elevation Myocardial Infarction. Circulation. 2015;131(24):2143-50.

Contents lists available at ScienceDirect
Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation

Review

Association between intra- and post-arrest hyperoxia on mortality in adults with cardiac arrest: A systematic review and meta-analysis

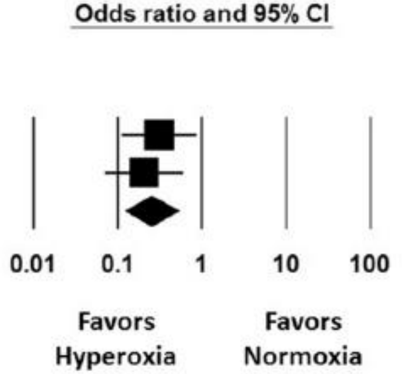
Jignesh K. Patel[a,*], Abdo Kataya[a], Puja B. Parikh[b]

- SR & meta-analysis of intra- and post-arrest hyperoxia
- 40,573 IHCA & OHCA adults
- Meta-analysis of 10 observational studies (2010 - 2017)

Post-arrest hyperoxia associated with higher mortality
[OR 1.34, 95% CI 1.08–1.67, p=0.008]

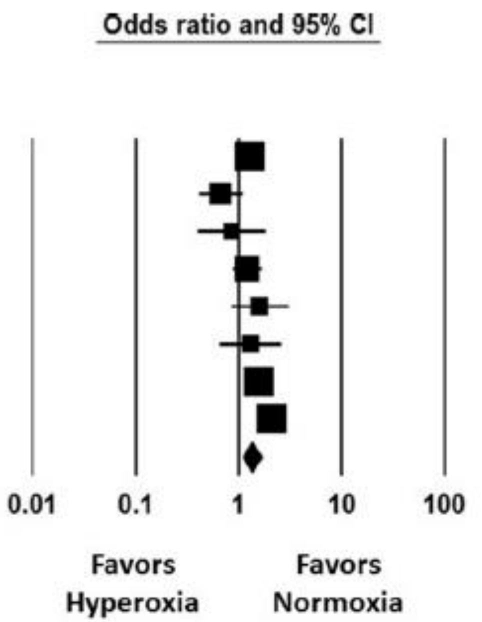
Intra-arrest hyperoxia associated with lower mortality
[OR=0.25, 95% CI 0.12–0.53, p < 0.001]

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Patel et al (2016)	0.310	0.112	0.858	0.024
Spindelboeck et al (2013)	0.205	0.072	0.587	0.003
	0.254	0.122	0.527	0.000



Heterogeneity: $I^2 = 0.00$

Study name	Odds ratio	Lower limit	Upper limit	p-Value
Wang et al (2017)	1.277	1.139	1.432	0.000
Johnson et al (2017)	0.670	0.413	1.087	0.105
Von Auenmueller et al (2017)	0.850	0.397	1.818	0.675
Helmerhorst et al (2015)	1.212	0.866	1.695	0.262
Oh et al (2014)	1.599	0.832	3.075	0.159
Ihle et al (2013)	1.302	0.654	2.594	0.453
Bellomo et al (2011)	1.571	1.362	1.812	0.000
Kilgannon et al (2010)	2.074	1.757	2.448	0.000
	1.340	1.078	1.666	0.008



Heterogeneity: $I^2 = 17.3$

Patel Resuscitation 2018;127:83-88

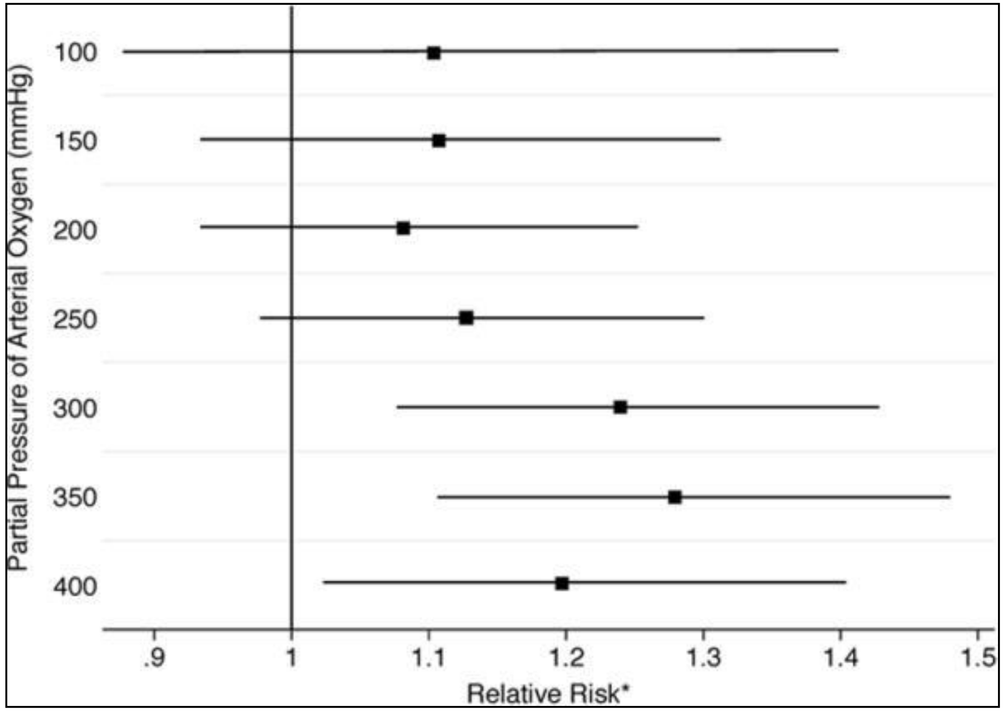
Circulation

ORIGINAL RESEARCH ARTICLE

Association Between Early Hyperoxia Exposure After Resuscitation From Cardiac Arrest and Neurological Disability

Prospective Multicenter Protocol-Directed Cohort Study

- 6 hospitals across the United States
- Adult comatosed non-traumatic cardiac arrest after ROSC 2013-2017
- ABG 1±2 and 6±2 hours (Hyperoxia PaO2 >300mmhg)
- Primary outcome was poor neurological function (mRS 4-6) at hospital discharge



- 38% hyperoxic exposure
- **Early hyperoxia associated with death & poor neurological** function at hospital discharge (relative risk:1.42:95%CI:1.09-1.87)
- **PaO2 >300 mmHg is associated with poor neurological function**

Roberts 2018, Circulation, 137(20); 2114-24

Oxygen titration

EXACT

Resuscitation 128 (2018) 211–215

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Oxygen titration after resuscitation from out-of-hospital cardiac arrest: A multi-centre, randomised controlled pilot study (the EXACT pilot trial)

Check for updates

Janet E. Bray[a,b,c,*], Cindy Hein[d,e], Karen Smith[a,f,g], Michael Stephenson[a,f,g], Hugh Grantham[d,e], Judith Finn[a,b,h], Dion Stub[a,c,f], Peter Cameron[a,c], Stephen Bernard[a,c,f], on behalf of the EXACT Investigators

[a] *Department of Epidemiology and Preventive Medicine, Monash University*
[b] *Prehospital, Resuscitation and Emergency Care Research Unit, Curtin University*
[c] *Alfred Hospital*
[d] *SA Ambulance Service*
[e] *Flinders University*
[f] *Ambulance Victoria*
[g] *Department of Community Emergency Health and Paramedic Practice, Monash University*
[h] *St John Ambulance Western Australia*

ARTICLE INFO   ABSTRACT

Bray Resuscitation 2018;128:211-215

Aus-ROC
Australian Resuscitation Outcomes Consortium

- **Phase 2 RCT (Melbourne & Adelaide) 2015-2017 – test feasibility of oxygen titration prehospital**
- Adult, presumed cardiac OHCA with ROSC and airway, O2 sat >94%
  (O2 flow 10L/min vs 2-4L/min into bag)
- Primary outcome was a **SpO2 ≥94% at ED**
- **Stopped early** –mechanical ventilators

Table 4
Comparison of outcomes by study group.

N (%)	2–4L/min (n = 37)	≥10 L/min (n = 24)
SpO2 at ED ≥94%	33 (90)	24 (100)
SpO2 at ED ≥90%	37 (100)	25 (100)
Re-arrest prehospital	0 (0)	1 (4)
Survived to hospital discharge	19 (51)	13 (54)

SpO2: oxygen saturation; ED: emergency department.

Reduction of Oxygen After Cardiac Arrest: The EXACT Study

__NHMRC funded__ multi-centre RCT to test the effectiveness of titrated oxygen (90-94%) vs 'usual care' on survival to hospital discharge after OHCA

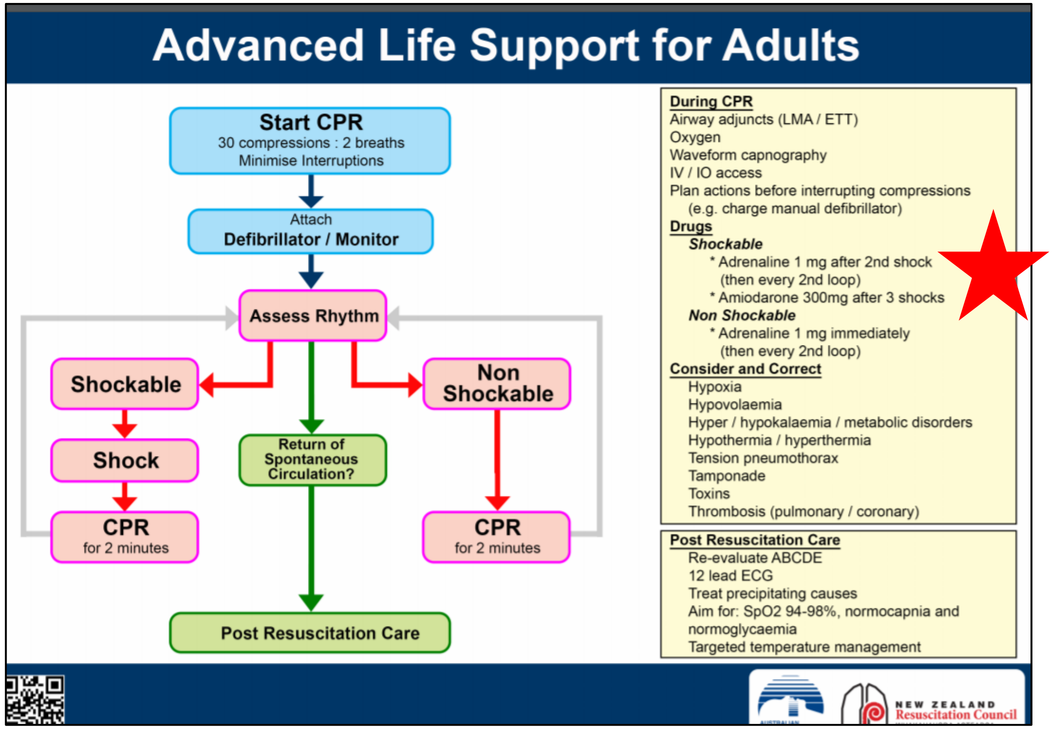
Drugs in cardiac arrest?

AUSTRALIAN RESUSCITATION COUNCIL

NEW ZEALAND Resuscitation Council WHAKAHAUORA AOTEAROA

ANZCOR Guideline 11.5 – Medications in Adult Cardiac Arrest

Summary



Guideline

While the listed drugs have theoretical benefits in selected situations, no medication has been shown to improve long-term survival in humans after cardiac arrest. Priorities are defibrillation, oxygenation and ventilation together with external cardiac compression.

Adrenaline (*aka* epinephrine)

Resuscitation 82 (2011) 1138–1143

Contents lists available at ScienceDirect

Resuscitation

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

ELSEVIER

Clinical paper

Effect of adrenaline on survival in out-of-hospital cardiac arrest: A randomised double-blind placebo-controlled trial☆

Ian G. Jacobs[a,c,*], Judith C. Finn[a,c], George A. Jelinek[b], Harry F. Oxer[c], Peter L. Thompson[d,e]

[a] Discipline of Emergency Medicine (M516), University of Western Australia, 35 Stirling Highway, Crawley, 6009 Western Australia, Australia
[b] Department of Medicine, University of Melbourne (St Vincents Hospital), Victoria Parade, Fitzroy, 3065 Melbourne, Australia
[c] St John Ambulance (Western Australia), PO Box 183, Belmont 6984, Western Australia, Australia
[d] School of Medicine and Population Health, University of Western Australia, Western Australia, Australia
[e] Sir Charles Gairdner Hospital, Hospital Avenue, Nedlands, 6009 Western Australia, Australia

Table 2
Outcomes for patients receiving placebo versus adrenaline.

Outcome	Placebo ($n = 262$), n (%)	Adrenaline ($n = 272$), n (%)	OR (95% CI)	p-Value
ROSC achieved pre-hospital	22 (8.4%)	64 (23.5%)	3.4 (2.0–5.6)	<0.001
Admitted to hospital	34 (13.0%)	69 (25.4%)	2.3 (1.4–3.6)	<0.001
Survived to hospital discharge	5 (1.9%)	11 (4.0%)	2.2 (0.7–6.3)	0.15
CPC 1 or 2	5 (100%)	9 (81.8%)	n/a	0.31

Jacobs et al, Resuscitation 2011, 82(9), 1138-43

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med. July 18 2018.

Outcome	Epinephrine	Placebo	Odds Ratio (95% CI)†	
			Unadjusted	Adjusted
Primary outcome				
Survival at 30 days — no./total no. (%)‡	130/4012 (3.2)	94/3995 (2.4)	1.39 (1.06–1.82)	1.47 (1.09–1.97)

Table 3. Primary and Secondary Outcomes.*

Outcome	Epinephrine	Placebo	Odds Ratio (95% CI)†	
			Unadjusted	Adjusted
Primary outcome				
Survival at 30 days — no./total no. (%)‡	130/4012 (3.2)	94/3995 (2.4)	1.39 (1.06–1.82)	1.47 (1.09–1.97)
Secondary outcomes				
Survival until hospital admission — no./total no. (%)§	947/3973 (23.8)	319/3982 (8.0)	3.59 (3.14–4.12)	3.83 (3.30–4.43)
Median length of stay in ICU (IQR) — days				
Patients who survived	7.5 (3.0–15.0)	7.0 (3.5–12.5)	NA	NA
Patients who died¶	2.0 (1.0–5.0)	3.0 (1.0–5.0)	NA	NA
Median length of hospital stay (IQR)				
Patients who survived	21.0 (10.0–41.0)	20.0 (9.0–38.0)	NA	NA
Patients who died‖	0	0	NA	NA
Survival until hospital discharge — no./total no. (%)	128/4009 (3.2)	91/3995 (2.3)	1.41 (1.08–1.86)	1.48 (1.10–2.00)
Favorable neurologic outcome at hospital discharge — no./total no. (%)	87/4007 (2.2)	74/3994 (1.9)	1.18 (0.86–1.61)	1.19 (0.85–1.68)
Survival at 3 mo — no./total no. (%)	121/4009 (3.0)	86/3991 (2.2)	1.41 (1.07–1.87)	1.47 (1.08–2.00)
Favorable neurologic outcome at 3 mo — no./total no. (%)	82/3986 (2.1)	63/3979 (1.6)	1.31 (0.94–1.82)	1.39 (0.97–2.01)

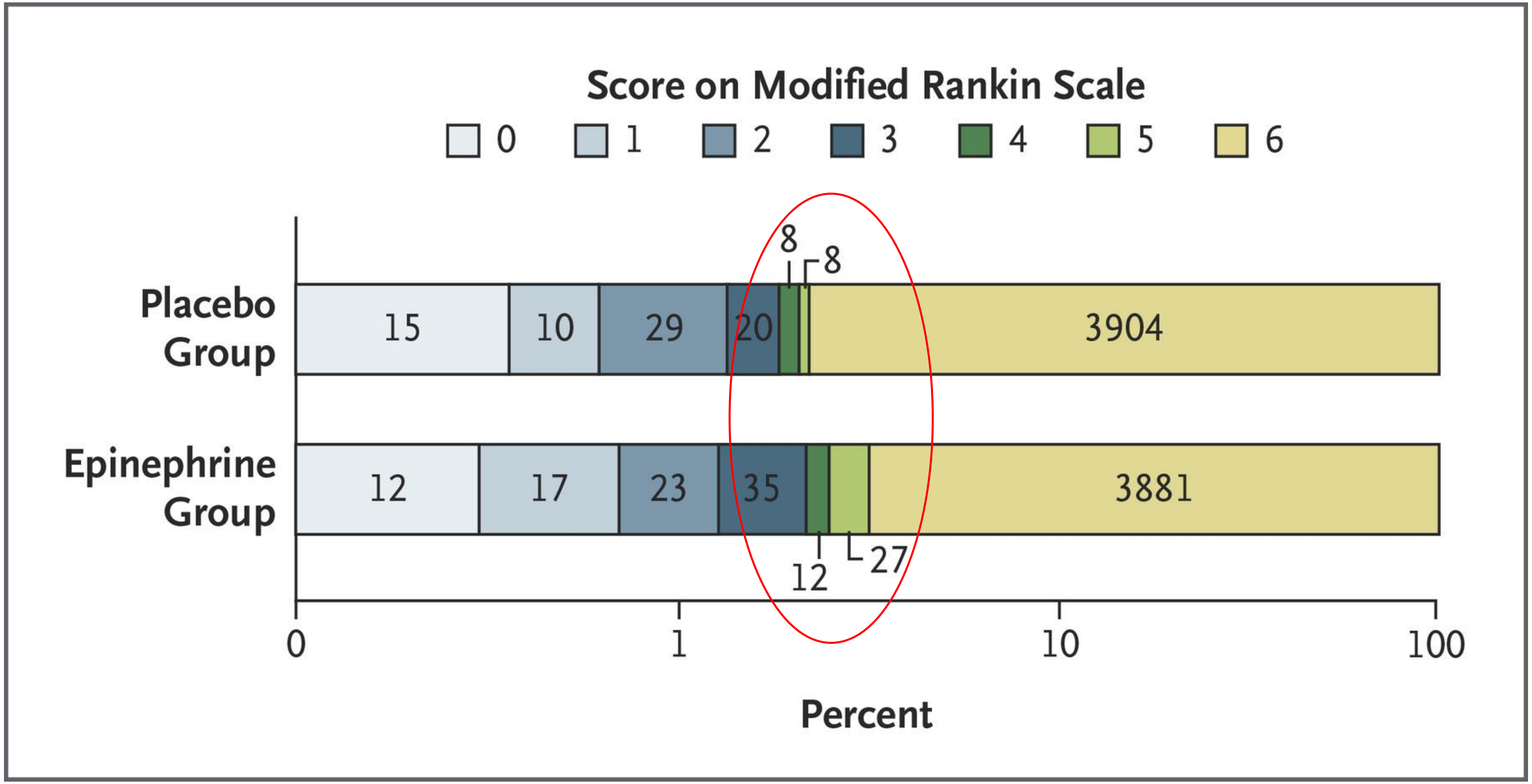


Figure 2. Survival with a Favorable Neurologic Outcome at Hospital Discharge.

Severe neurologic impairment (a score of 4 or 5) was more frequent in the epinephrine group than in the placebo group (39 of 126 patients [31.0%] vs. 16 of 90 patients [17.8%])

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

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

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med. July 18 2018.

CONCLUSIONS

In adults with OHCA, the use of epinephrine resulted in a significantly higher rate of 30-day survival than the use of placebo, but there was no significant between-group difference in the rate of a favorable neurologic outcome because more survivors had severe neurologic impairment in the epinephrine group.

Original Article

Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest

Peter J. Kudenchuk, M.D., Siobhan P. Brown, Ph.D., Mohamud Daya, M.D., Thomas Rea, M.D., M.P.H., Graham Nichol, M.D., M.P.H., Laurie J. Morrison, M.D., Brian Leroux, Ph.D., Christian Vaillancourt, M.D., Lynn Wittwer, M.D., Clifton W. Callaway, M.D., Ph.D., James Christenson, M.D., Debra Egan, M.Sc., M.P.H., Joseph P. Ornato, M.D., Myron L. Weisfeldt, M.D., Ian G. Stiell, M.D., Ahamed H. Idris, M.D., Tom P. Aufderheide, M.D., James V. Dunford, M.D., M. Riccardo Colella, D.O., M.P.H., Gary M. Vilke, M.D., Ashley M. Brienza, B.S., Patrice Desvigne-Nickens, M.D., Pamela C. Gray, NREMT-P, Randal Gray, M.Ed., NREMT-P, Norman Seals, B.S., Ron Straight, M.Ed., Paul Dorian, M.D., for the Resuscitation Outcomes Consortium Investigators

N Engl J Med
Volume 374(18):1711-1722
May 5, 2016

The NEW ENGLAND JOURNAL of MEDICINE

Outcomes According to Trial Group in the Per-Protocol Population.

Table 3. Outcomes According to Trial Group in the Per-Protocol Population.*

Outcome	Amiodarone (N=974)	Lidocaine (N=993)	Placebo (N=1059)	Amiodarone vs. Placebo: Difference (95% CI), *percentage points*	Amiodarone vs. Placebo: P Value	Lidocaine vs. Placebo: Difference (95% CI), *percentage points*	Lidocaine vs. Placebo: P Value	Amiodarone vs. Lidocaine: Difference (95% CI), *percentage points*	Amiodarone vs. Lidocaine: P Value
Primary outcome: survival to discharge — no./total no. (%)†	237/970 (24.4)	233/985 (23.7)	222/1056 (21.0)	3.2 (−0.4 to 7.0)	0.08	2.6 (−1.0 to 6.3)	0.16	0.7 (−3.2 to 4.7)	0.70
Secondary outcome: modified Rankin score ≤3 — no./total no. (%)‡	182/967 (18.8)	172/984 (17.5)	175/1055 (16.6)	2.2 (−1.1 to 5.6)	0.19	0.9 (−2.4 to 4.2)	0.59	1.3 (−2.1 to 4.8)	0.44
Mechanistic (exploratory) outcomes									
Return of spontaneous circulation at ED arrival — no./total no. (%)	350/974 (35.9)	396/992 (39.9)	366/1059 (34.6)	1.4 (−2.8 to 5.5)	0.52	5.4 (1.2 to 9.5)	0.01	−4.0 (−8.3 to 0.3)	0.07
Admitted to hospital — no. (%)	445 (45.7)	467 (47.0)	420 (39.7)	6.0 (1.7 to 10.3)	0.01	7.4 (3.1 to 11.6)	<0.001	−1.3 (−5.7 to 3.1)	0.55
Modified Rankin score in all patients‡	5.0±1.9	5.1±1.8	5.2±1.8	−0.14 (−0.30 to 0.02)	0.09	−0.06 (−0.22 to 0.10)	0.45	−0.08 (−0.24 to 0.08)	0.34
Modified Rankin score in survivors‡	2.0±2.7	2.2±2.7	2.0±2.6						
Distribution of modified Rankin scores — no./total no. (%)‡									
0	60/966 (6.2)	49/981 (5.0)	55/1053 (5.2)						
1	47/966 (4.9)	37/981 (3.8)	39/1053 (3.7)						
2	41/966 (4.2)	46/981 (4.7)	40/1053 (3.8)						
3	34/966 (3.5)	37/981 (3.8)	41/1053 (3.9)						
4	31/966 (3.2)	36/981 (3.7)	27/1053 (2.6)						
5	21/966 (2.2)	24/981 (2.4)	18/1053 (1.7)						
6	732/966 (75.8)	752/981 (76.7)	833/1053 (79.1)						

* CI denotes confidence interval, and ED emergency department.
† The difference and 95% CI were adjusted for sequential monitoring.
‡ Scores on the modified Rankin scale range from 0 (no symptoms) to 6 (death). A score of 3 or less indicates the ability to conduct daily activities independently or with minimal assistance.

Outcomes According to Trial Group in the Per-Protocol Population.

Table 3. Outcomes According to Trial Group in the Per-Protocol Population.*

Outcome	Amiodarone (N=974)	Lidocaine (N=993)	Placebo (N=1059)	Amiodarone vs. Placebo		Lidocaine vs. Placebo		Amiodarone vs. Lidocaine	
				Difference (95% CI)	P Value	Difference (95% CI)	P Value	Difference (95% CI)	P Value
				percentage points		*percentage points*		*percentage points*	
Primary outcome: survival to discharge — no./total no. (%)†	237/970 (24.4)	233/985 (23.7)	222/1056 (21.0)	3.2 (−0.4 to 7.0)	0.08	2.6 (−1.0 to 6.3)	0.16	0.7 (−3.2 to 4.7)	0.70

There were no significant between-group differences in survival to hospital discharge (STHD).

Kudenchuk PJ et al. N Engl J Med 2016;374:1711-1722

The NEW ENGLAND JOURNAL of MEDICINE

The NEW ENGLAND JOURNAL of MEDICINE
374(18):1711-1722

Table S2. Survival to Discharge in A Priori Subgroups in the Per-Protocol Population

	Amiodarone	Lidocaine	Placebo	Amiodarone vs Placebo Difference (95% CI) P	Lidocaine vs Placebo Difference (95% CI) P	Amiodarone vs Lidocaine Difference (95% CI) P	P for Interaction
Witnessed status							0.05
EMS witnessed, n (%) [N=57;43;54]	22 (38.6%)	10 (23.3%)	9 (16.7%)	21.9% (5.8%, 38.0%) P=0.01	6.6% (-9.5%, 22.7%) P=0.42	15.3% (-2.6%, 33.2%) P=0.09	
Bystander witnessed, n (%) [N=618;632;684]	171 (27.7%)	176 (27.8%)	155 (22.7%)	5.0% (0.3%, 9.7%) P=0.04	5.2% (0.5%, 9.9%) P=0.03	-0.1% (-5.1%, 4.9%) P=0.97	
Unwitnessed, n (%) [N=271;282;286]	41 (15.1%)	45 (16.0%)	48 (16.8%)	-1.7% (-7.8%, 4.4%) P=0.58	-0.8 (-6.9%, 5.3%) P=0.80	-0.9% (-6.9%, 5.1%) P=0.77	
Bystander CPR							0.15
Yes, n (%) [553;546;593]	161 (29.1%)	144 (26.4%)	149 (25.1%)	4.0% (-1.2%, 9.1%)	1.2% (-3.8%, 6.3%)	2.7% (-2.6%, 8.0%)	

STHD was also higher among amiodarone recipients (38.6%) than placebo recipients (16.7%) with **EMS-witnessed arrest**

In the 1,934 patients with **bystander-witnessed arrest**, STHD was higher with amiodarone (27.7%) or lidocaine (27.8%) than with placebo (22.7%).

In Press..ILCOR update

This summary addresses the role of antiarrhythmic drugs in adults and children

Treatment Recommendation

"We suggest the use of amiodarone or lidocaine in adults with shock refractory VF/pVT (weak recommendation, low-quality evidence).

We suggest against the routine use of magnesium in adults with shock-refractory VF/pVT (weak recommendation, very low-quality evidence)."

ARTICLE IN PRESS

Resuscitation xxx (xxxx) xxx–xxx

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ILCOR Summary Statement

2018 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations Summary

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ABSTRACT

The International Liaison Committee on Resuscitation has initiated a continuous review of new, peer-reviewed, published cardiopulmonary resuscitation science. This is the second annual summary of International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations that includes the most recent cardiopulmonary resuscitation science reviewed by the International Liaison Committee on Resuscitation. This summary addresses the role of antiarrhythmic drugs in adults and children and includes the Advanced Life Support Task Force and Pediatric Task Force consensus statements, which summarize the most recent published evidence and an assessment of the quality of the evidence based on Grading of Recommendations, Assessment, Development, and Evaluation criteria. The statements include consensus treatment recommendations approved by members of the relevant task forces. Insights into the deliberations of each task force are provided in the Values and Preferences and Task Force Insights sections. Finally, the task force members have listed the top knowledge gaps for further research.

This is the second in a series of annual International Liaison Committee on Resuscitation (ILCOR) International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations (CoSTR) summary publications that summarize the ILCOR task force analyses of published resuscitation evidence. The review this year addresses the use of antiarrhythmic drugs for the management of adult and pediatric cardiac arrest and the period immediately after return of spontaneous circula-

A total of 8 CoSTRs are now available online, and they have been viewed by ≈11 000 visitors.

This summary statement contains the final wording of the CoSTR as approved by the task forces and by the ILCOR member councils. This statement differs in several respects from the website draft CoSTRs: The language used to describe the evidence is not restricted to standard Grading of Recommendations, Assessment, Development, and Evaluation terminology, making it more transparent to a wider audi-

Original Article

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

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N Engl J Med
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The NEW ENGLAND JOURNAL of MEDICINE

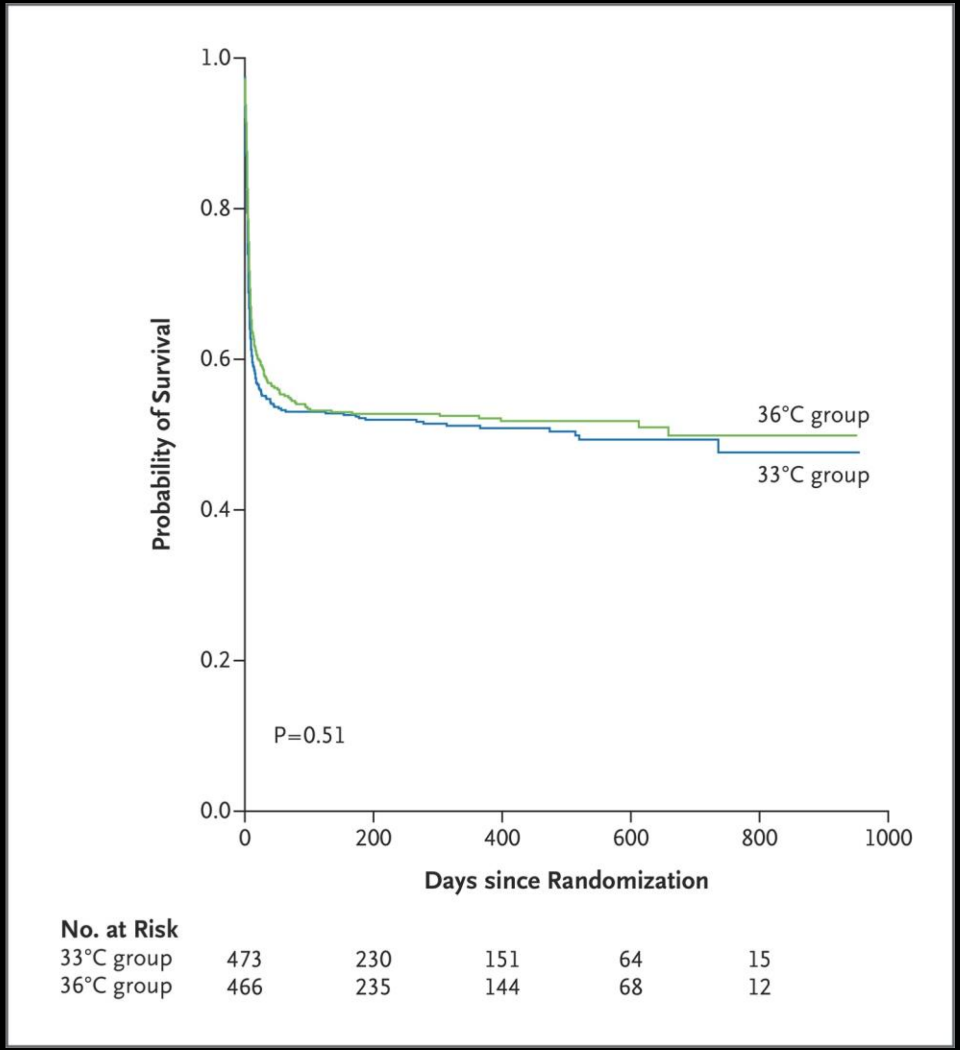
Probability of Survival through the End of the Trial

DESIGN

- In this trial, 950 OHCA pts with ROSC were randomly assigned to targeted temperature management at either 33°C or 36°C.

RESULTS

- There was no significant difference between the two groups in survival or neurologic outcome.



Nielsen N et al. N Engl J Med 2013;369:2197-2206

CONCLUSION

In unconscious survivors of OHCA of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C.

The NEW ENGLAND JOURNAL of MEDICINE

Changes in Temperature Management of Cardiac Arrest Patients Following Publication of the Target Temperature Management Trial

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- **To evaluate knowledge translation after publication of the TTM 33C versus 36C after OHCA**

- Retrospective cohort study 2005-2016 from The Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS-CORE) adult patient database

- Temporal trends n=11,068 adults from 140 hospitals admitted to ICU after OHCA:
  - pre-TTM n=4,450
  - post-TTM n=5,184

Primary outcomes

- **Lowest temperature in the first 24 hours in ICU**

- **Primary clinical outcome variable of interest was in-hospital mortality**

- Secondary outcomes included proportion of patients with fever in the first 24 hours in ICU

Salter, Crit Care Med, 2018, 46(11): 1722-1730

J. Bray slide

Lowest temp first 24-hours of ICU

In-hospital mortality

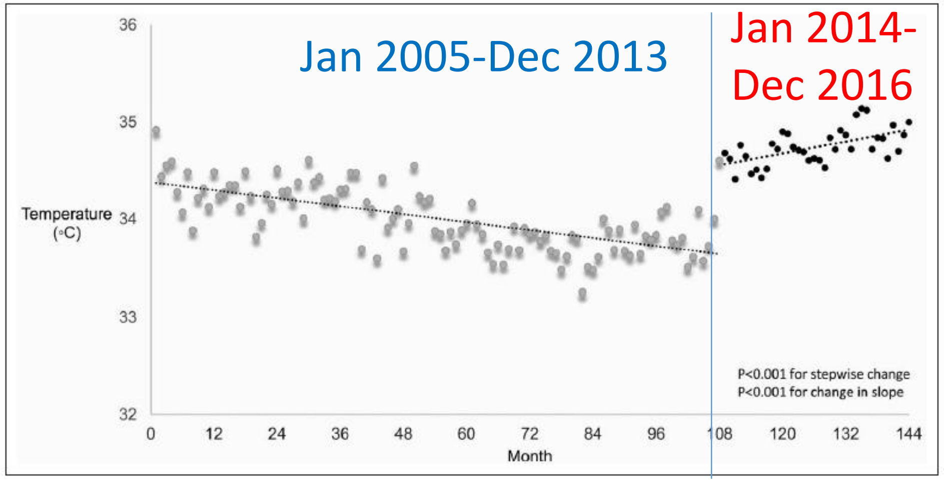


Figure 2. Lowest body temperature in the first 24 hr in the ICU by month. *Data points* represent the average lowest body temperature in the first 24 hr in the ICU for eligible patients by month. The *gray dots* are for the months from January 2005 until December 2013 inclusive; the *black dots* are for the months from January 2014 until December 2016 inclusive. The targeted temperature management study was published online on November 17, 2013, and was published in print on December 5, 2013.

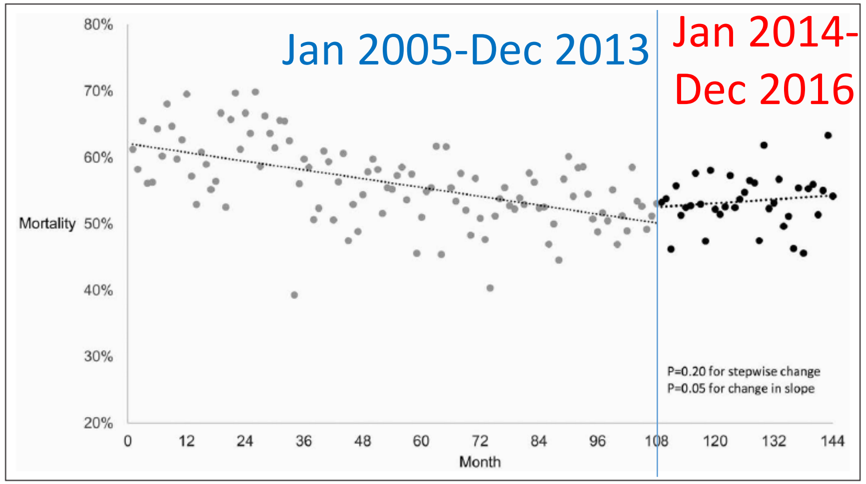


Figure 3. Inhospital mortality by month. The *gray dots* are for the months from January 2005 until December 2013 inclusive; the *black dots* are for the months from January 2014 until December 2016 inclusive. The targeted temperature management study was published online on November 17, 2013, and was published in print on December 5, 2013.

Temp	Pre-TTM	Post-TTm
32-34C	⬆ 46%	25%
35.5-36.5C	17%	⬆ 27%
>37C	37%	⬆ 53%
>38	12.8%	⬆ 16.5%

- Widespread change in practice
- Survey **80% changed** practice ERC poster
- Increase in fever in 36C group not found in TTM trial
- Mortality trending up!

Salter, Crit Care Med, 2018, 46(11): 1722-1730

Based on *J. Bray slide*

Future trials…

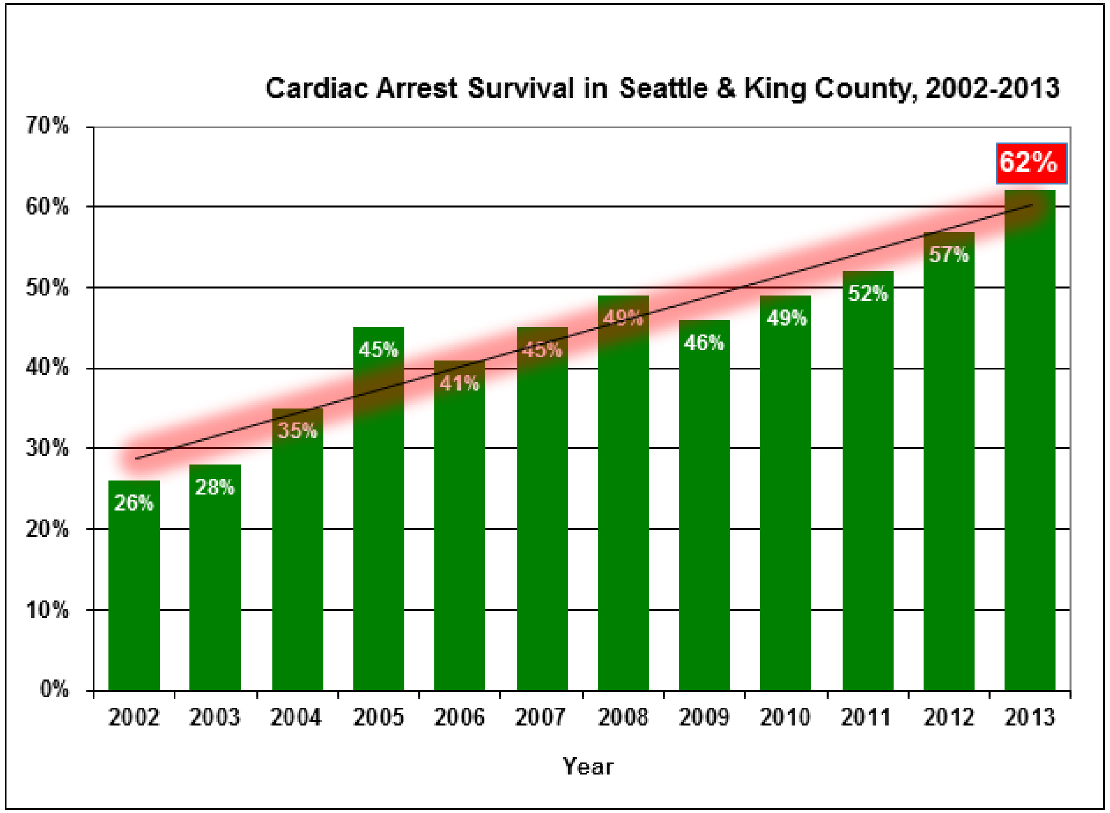
Table 1 Ongoing or planned resuscitation studies listed on clinical trials registries

	Topic	Studies	Primary outcome and study status
ECMO	Extracorporeal CPR	Prospective study of E-CPR versus standard advanced life support for selected OHCAs unresponsive to initial resuscitation (NCT011511666)	Survival with good neurological outcome Recruiting
		Prospective study of E-CPR versus standard advanced life support for selected OHCAs unresponsive to initial resuscitation (NCT01605409)	ROSC Recruiting
O2/CO2	Oxygenation and carbon dioxide targets after ROSC	RCT of oxygen titrated to 90–94% versus 98–100% as soon as possible after ROSC and continued until ICU admission (EXACT phase 3 trial)	Survival to hospital discharge Not yet recruiting
		RCT comparing targeted therapeutic mild hypercapnia ($PaCO_2$ 50–55 mmHg) with targeted normocapnia ($PaCO_2$ 35–45 mmHg) (TAME study)	Neurological outcome at 6 months (GOSE) Not yet recruiting
TTM2	Targeted temperature management and pharmacological neuroprotection	Mild induced hypothermia (33 °C) versus fever control (≤37.8 °C) only (TTM-2, NCT02908308)	Mortality at 6 months Not yet recruiting
		Targeted temperature management after non-shockable cardiac arrest: 32.5–33.5 °C versus 36.5–37.5 °C (NSE-HYPERION study, NCT02722473)	NSE values day 1 to day 3 Recruiting
		Targeted temperature management after cardiac arrest: 33 °C for 24 versus 48 h (TTH48 study, NCT01689077)	Neurological outcome at 6 months (CPC) Finished recruiting
Early angio	Early coronary angiography after ROSC	Feasibility study—cardiac arrest survivors without ST-elevation randomised to acute coronary angiography versus routine care (DISCO study, NCT02309151)	Feasibility for multiple outcomes Recruiting
		Feasibility study—cardiac arrest survivors without ST-elevation randomised to acute coronary angiography versus standard care (PEARL study, NCT02387398)	Safety and feasibility Recruiting
		Cardiac arrest survivors without ST-elevation randomised to transfer to a cardiac arrest centre and urgent coronary catheterisation versus transfer to a district general hospital (ARREST trial, ISRCTN96585404)	All-cause mortality at 30 days Recruiting
		Emergency versus delayed coronary angiogram in survivors of OHCA with no obvious non-cardiac cause of arrest (EMERGE trial—NCT02876458)	Survival with no or minimal neurological sequel at 180 days Recruiting

OHCA out-of-hospital cardiac arrest, *ROSC* return of spontaneous circulation, *E-CPR* extracorporeal cardiopulmonary resuscitation, *GOSE* Glasgow outcome scale extended, *NSE* neuron-specific enolase, *CPC* cerebral performance category

J. Bray slide

King County (Seattle) has world's highest survival rate for OHCA

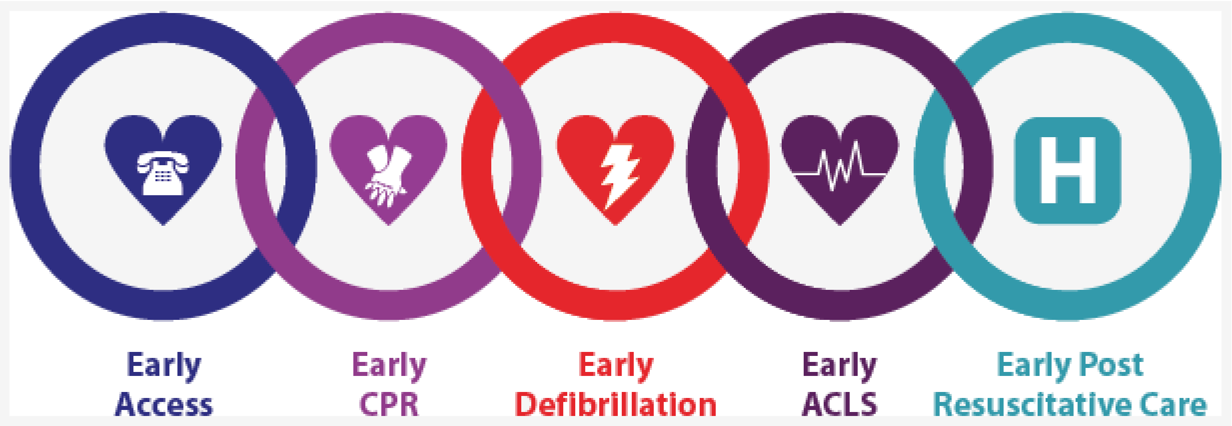


Survival to hospital D/C for bystander-witnessed OHCA of presumed cardiac cause in VF/VT: 2002-2013

http://www.sca-aware.org/sca-news/king-county-wa-has-worlds-highest-survival-rate-for-cardiac-arrest

So why does Seattle/King County have the best OHCA survival rates in the world?

"We like to say that **it takes a system to save a cardiac arrest victim**, and it's proven true again and again with every new survivor," said Dr Mickey Eisenberg, King County Emergency Medical Services Medical Director.



http://www.sca-aware.org/sca-news/king-county-wa-has-worlds-highest-survival-rate-for-cardiac-arrest

Thank you for your attention

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