AGENDA

ICEMA
MEDICAL ADVISORY COMMITTEE

December 18, 2014

1300

Purpose: Information Sharing

Meeting Facilitator: Todd Sallenbach

Timekeeper: Danielle Ogaz

Record Keeper: Danielle Ogaz

AGENDA ITEM		PERSON(S)	DISCUSSION/ACTION	TIME
I.	Welcome/Introductions	Todd Sallenbach		1300 - 1301
II.	Approval of Minutes	All	Discussion	1301 - 1303
III.	Discussion/Action Items			1303 - 1330
	A. Standing EMS System Updates			
	1. Review of Action Items 2. Trauma Program 3. STEMI Program: STEMI Data 4. Stroke Program: Stroke Data 5. STEMI/Stroke Center Regulations 6. CQI Report Update 7. SAC Update 8. Literature Review • Recent Trends in Survival from Out-of-Hospital Cardiac Arrest in the United States • Out-of-hospital cardiac arrest: manual or mechanical CPR? • Outcomes After Out-of-Hospital Cardiac Arrest Treated by Basic vs Advanced Life Support • Mechanical versus manual chest compression for out-of-hospital cardiac arrest (PARAMEDIC): a pragmatic, cluster randomized controlled trial	1. Todd Sallenbach 2. Chris Yoshida-McMath 3. Chris Yoshida-McMath 4. Chris Yoshida-McMath 5. Reza Vaezazizi 6. Todd Sallenbach 7. Todd Sallenbach 8. Reza Vaezazizi	1. Discussion/Action 2. Discussion 3. Discussion 4. Discussion 5. Discussion 6. Discussion 7. Discussion 8. Discussion	

	B. EMS Trends			1330 - 1345
	1. TXA Study Update 2. Paramedicine Step I Research Update 3. Art of Resuscitation	1.Reza Vaezazizi/Michael Neeki 2. Michael Neeki 3. Reza Vaezazizi	1. Discussion 2. Discussion 3. Discussion	
	C. ARMC Strike	Ron Holk	Discussion	1345 - 1400
	D. Procainamide	Kevin Parkes	Discussion	1400 - 1415
	E. Membership Review	Ron Holk	Discussion	1415 - 1420
	F. 2015 Meeting Dates	Reza Vaezazizi	Discussion	1420 - 1430
V.	Public Comment	All	Discussion	1430 - 1440
VI.	Round Table/Announcements	All	Discussion	1440 - 1450
VII.	Future Agenda Items	All	Discussion	1450 - 1455
VIII.	Next Meeting Date: February 26, 2015	All	Discussion	1455 - 1456
IX.	Adjournment	Todd Sallenbach	Action	1456 -1500

MINUTES

MEDICAL ADVISORY COMMITTEE

October 23, 2014

1300 to 1500

AGENDA ITEM		DISCUSSION/FOLLOW UP	RESPONSIBLE PERSON(S)
I.	WELCOME/INTRODUCTIONS	Meeting called to order at 1312.	Todd Sallenbach
II.	APPROVAL OF MINUTES	The June 26, 2014, minutes were approved. Motion to approve. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
III.	DISCUSSION ITEMS		
	A. Standing EMS System Updates		
	1. Review of Action Items	Nothing to report.	Todd Sallenbach
	2. Trauma Program	Nothing to report.	Chris Yoshida-McMath
	3. STEMI Program: STEMI Data	Nothing to report.	Chris Yoshida-McMath
	4. Stroke Program: Stroke Data	Nothing to report.	Chris Yoshida-McMath
	5. STEMI/Stroke Center Regulations	Nothing to report.	Reza Vaezazizi
	6. CQI Report Update	Nothing to report.	Todd Sallenbach
	7. SAC Update	SAC has not had a quorum for the past three (3) meetings.	Todd Sallenbach
	8. Literature Review		Reza Vaezazizi
	• Dextrose 10% in the Treatment of Out-of-Hospital Hypoglycemia	Synopsis of article presented by Dr. Vaezazizi. Full article distributed with agenda packet.	
	• Effect of Out-of Hospital Noninvasive Positive-Pressure Support Ventilation in Adult Patients With Severe Respiratory Distress: A Systematic Review and Meta-analysis	Synopsis of article presented by Dr. Vaezazizi. Full article distributed with agenda packet.	

	• "No Diversion": A Qualitative Study of Emergency Medicine Leaders in Boston, MA, and the Effects of a Statewide Diversion Ban Policy	Synopsis of article presented by Dr. Vaezazizi. Full article distributed with agenda packet.	
	• Two Cheers for Regulation	Synopsis of article presented by Dr. Vaezazizi. Full article distributed with agenda packet.	
	B. EMS Trends		
	1. TXA Study Update	Pending final approval by the State, the goal is to have the first paramedic dose of TXA administered in the beginning part of 2015. Pending final approval this will be the first study in North America with paramedics administering TXA.	Reza Vaezazizi/ Michael Neeki
	2. Paramedicine Step I Research Update	Required changes were sent to IRB. Goal is to begin in November 2014, with Rialto Fire Department.	Michael Neeki
	3. Art of Resuscitation	SCEPTICAL link on website for CE credit available if administered by EMS Coordinator. In process of developing parameters for pilot program.	Reza Vaezazizi
	C. Active Shooter	BC Rojer and Firefighter Lichtman from Rancho Cucamonga FD gave a presentation on RCFD's active shooter program.	Ron Holk
	D. Continuous Quality Improvement		
	1. ICEMA CQI Plan Review - MAC/SAC Task Force	Motion for ICEMA to reach out to constituents for participation on task force. Motion to endorse MSC: Joe Powell/Leslie Parham APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	Ron Holk
	E. Procainamide	Tabled.	Kevin Parkes
	F. Membership Review	Attendance tracking was distributed in agenda packet.	Todd Sallenbach
	G. Protocol Survey Results	The results from the protocol survey were reviewed. Motion to endorse condensed protocols. MSC: Michael Neeki/Debbie Bervel APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin,	Ron Holk

		Todd Sallenbach, Andrea Thorp, Joanna Yang	
	H. Protocol Review		All
	1. 7010 - BLS/LALS/ALS Standard Drug & Equipment List	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	2. 7020 - EMS Aircraft Standard Drug & Equipment List	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	3. 7040 - Medication Standard Orders	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang Motion to establish transition period December 1, 2014 - June 1, 2014 from D50 to D10. MSC: Michael Neeki/Debbie Bervel APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang Motion to endorse transition period from Morphine to Fentanyl December 1, 2014 - June 1, 2014, determine pediatric dose, and dose for burn patient. Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	

	4. 8020 - Critical Care Interfacility Transport	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	5. 9130 (DRAFT) - Procedures for EMS Monitoring of Multiple Patients (San Bernardino County Only)	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	6. 6070 - Cardiovascular ST Elevation Myocardial Infarction Receiving Center Criteria and Destination Policy	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	7. 6100 - Neurovascular Stroke Receiving Center and Destination Policy	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	8. 8120 - Continuation of Care (San Bernardino County Only)	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	9. 11110 - Stroke Treatment - Adult	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss, Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
	10. 15020 - Trauma - Pediatric (Less than 15 years of age)	Motion to endorse. MSC: Michael Neeki/Joy Peters APPROVED Ayes: Debbie Bervel, Jeff Grange, Susie Moss,	

		Michael Neeki, Leslie Parham, Joy Peters, Joe Powell, Aaron Rubin, Todd Sallenbach, Andrea Thorp, Joanna Yang	
IV.	PUBLIC COMMENT	None	All
V.	ROUND TABLE/ ANNOUNCEMENTS	None	All
VI.	FUTURE AGENDA ITEMS	None	Danielle Ogaz
VII.	NEXT MEETING:	December 18, 2014	
VIII.	ADJOURNMENT	The meeting adjourned at 1505.	Todd Sallenbach

Attendees:

NAME	MAC POSITION	EMS AGENCY STAFF	POSITION
☐ VACANT ☒ Jeff Grange - LLUMC	Trauma Hospital Physicians (2)	☒ Reza Vaezazizi, MD	Medical Director
☐ Phong Nyugen - RDCH ☒ Todd Sallenbach - HDMC (Chair)	Non-Trauma Base Physician s (2)	☐ Tom Lynch	EMS Administrator
☒ Aaron Rubin - Kaiser	Non-Base Hospital Physician	☐ Denice Wicker-Stiles	Assist. Administrator
☒ Michael Neeki - Rialto FD	Public Transport Medical Director	☐ George Stone	Program Coordinator
☐ Sam Chua - AMR	Private Transport Medical Director	☒ Ron Holk	EMS Nurse Specialist
☒ Debbie Bervel - SB City FD	Fire Department Medical Director	☒ Chris Yoshida-McMath	EMS Nurse Specialist
☒ Joy Peters - ARMC	EMS Nurses	☒ Danielle Ogaz	EMS Specialist
☒ Joe Powell - Rialto FD	EMS Officers		
☐ Leslie Parham	Public Transport Medical Rep (Paramedic/RN)		
☒ Susie Moss	Private Transport Medical Rep (Paramedic/RN)		
☐ Lance Brown	Specialty Center Medical Director		
☒ Joanna Yang - LLUMC	Specialty Center Coordinator		
☐ Troy Pennington	Private Air Transport Medical Director		
☐ Stephen Patterson - Sheriff's Air Rescue	Public Air Transport Medical Director		
☐ Micheal Guirguis - SB Comm Center	PSAP Medical Director		
☐ Andrew Stevens	Inyo County Representative		
☐ Rosemary Sachs	Mono County Representative		
☐ Kevin Parkes	SAC Liaison		
☒ Andrea Thorp	Pediatric Critical Care Physician		

GUESTS	AGENCY
Carly Crews	SBCFD
Patti Eickholt	SACH
Lisa Higuchi	AMR
Christopher Linke	AMR
Sara Morning	Redlands Hospital
Leigh Overton	SBCOFD
Brian Parham	Big Bear FD
Leslie Parham	SBCOFD

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Recent Trends in Survival from Out-of-Hospital Cardiac Arrest in the United States

Paul S. Chan, Bryan McNally, Fengming Tang and Arthur Kellermann

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Recent Trends in Survival From Out-of-Hospital Cardiac Arrest in the United States

Paul S. Chan, MD, MSc; Bryan McNally, MD, MPH; Fengming Tang, BS; Arthur Kellermann, MD, MPH; for the CARES Surveillance Group

Background—Despite intensive efforts over many years, the United States has made limited progress in improving rates of survival from out-of-hospital cardiac arrest. Recently, national organizations, such as the American Heart Association, have focused on promoting bystander cardiopulmonary resuscitation, use of automated external defibrillators, and other performance improvement efforts.

Methods and Results—Using the Cardiac Arrest Registry to Enhance Survival (CARES), a prospective clinical registry, we identified 70 027 U.S. patients who experienced an out-of-hospital cardiac arrest between October 2005 and December 2012. Using multilevel Poisson regression, we examined temporal trends in risk-adjusted survival. After adjusting for patient and cardiac arrest characteristics, risk-adjusted rates of out-of-hospital cardiac arrest survival increased from 5.7% in the reference period of 2005 to 2006 to 7.2% in 2008 (adjusted risk ratio, 1.27; 95% confidence interval, 1.12–1.43; $P<0.001$). Survival improved more modestly to 8.3% in 2012 (adjusted risk ratio, 1.47; 95% confidence interval, 1.26–1.70; $P<0.001$). This improvement in survival occurred in both shockable and nonshockable arrest rhythms (P for interaction=0.22) and was also accompanied by better neurological outcomes among survivors (P for trend=0.01). Improved survival was attributable to both higher rates of prehospital survival, where risk-adjusted rates increased from 14.3% in 2005 to 2006 to 20.8% in 2012 (P for trend<0.001), and in-hospital survival (P for trend=0.015). Rates of bystander cardiopulmonary resuscitation and automated external defibrillator use modestly increased during the study period and partly accounted for prehospital survival trends.

Conclusions—Data drawn from a large subset of U.S communities suggest that rates of survival from out-of-hospital cardiac arrest have improved among sites participating in a performance improvement registry. **(*Circulation*. 2014;130:00-00.)**

Key Words: cardiac arrest ■ survival ■ trends

Despite intensive efforts over 3 decades, the United States has made little progress in improving the overall rate of survival from out-of-hospital cardiac arrest, with survival rates remaining relatively unchanged at 7.6%.[1] However, in recent years, advances in resuscitation science have generated promising findings. In randomized, clinical trials, early use of therapeutic hypothermia[2,3] and automated external defibrillators (AEDs)[4,5] were found to improve survival and neurological outcomes in selected populations. National efforts have focused on delivery of higher-quality cardiopulmonary resuscitation.

Editorial see p 1844
Clinical Perspective on p 7

Although there is ample reason to believe that adoption of these practices and other performance improvement activities should lead to higher rates of out-of-hospital cardiac arrest survival in the United States, this has not been consistently demonstrated. If quality improvement efforts are making a difference, it should be possible to document improved survival at the community level. Isolated studies in the United States have generated encouraging findings,[6,7] but these may not be generalizable to the nation at large.

Accordingly, we analyzed contemporary trends in rates of survival to hospital discharge for out-of-hospital cardiac arrest from 2005 to 2012 in a large and geographically diverse set of U.S. communities—those that participate in the Cardiac Arrest Registry to Enhance Survival (CARES), which was established to improve prehospital care at the local level.[8,9] To determine which phase of resuscitation care may be influencing outcomes, we examined temporal trends in survival to hospital admission and, among those who survived to hospital admission, their likelihood of surviving to hospital discharge. Finally, to determine whether any survival trends are attributable to improving rates of bystander cardiopulmonary resuscitation (CPR) or AED use, we evaluated trends in both and their aggregate effect on out-of-hospital cardiac arrest survival.

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From Saint Luke's Mid America Heart Institute, Kansas City, MO (P.S.C., F.T.); the Department of Emergency Medicine, Emory University, and Rollins School of Public Health, Atlanta, GA (B.M.); and the Uniformed Services University of the Health Sciences, Bethesda, MD (A.K.).

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Methods

Data Source and Study Population

CARES is a large, prospective clinical registry of patients with out-of-hospital cardiac arrest in the United States. Since the system was established in 2005, it has grown, by 2012, to collect data from 248 emergency medical services (EMS) systems across 23 states, representing a catchment area of >64 million people. Established by the Centers for Disease Control and Emory University for public health surveillance and continuous quality improvement, the design of the registry has been previously described in detail.[8,9] Briefly, all patients with a confirmed out-of-hospital cardiac arrest (defined as apneic and unresponsive) of presumed cardiac cause and for whom resuscitation is attempted are identified and followed, including those with termination of resuscitation before hospital arrival. Data are collected from three sources that together define the continuum of emergency cardiac care: 911 dispatch centers, EMS agencies, and receiving hospitals. Standardized international Utstein definitions for defining clinical variables and outcomes are used to ensure uniformity.[10] A CARES analyst reviews every record for completeness and accuracy.[9]

Our analysis is based on 73 390 cases submitted to the CARES registry between October 1, 2005 and December 31, 2012 (Figure 1). We excluded 8 patients with obvious signs of death and 315 patients with a valid do-not-attempt resuscitation order, as well as 2544 events occurring in a facility with an on-site healthcare professional (eg, hospital, medical clinic), because these cases have response and treatment times that are different from other out-of-hospital cardiac arrests. We also excluded 496 events (0.7%) in which information on patient survival to hospital admission (n=409 [0.6%]) or discharge (n=87 [0.1%]) was missing. The final sample comprised 70 027 patients treated by 248 EMS agencies.

Independent Variable and Study Outcome

The independent variable was calendar year, which was evaluated as a continuous variable. The primary outcome of interest was survival to hospital discharge. Because the probability of survival from ventricular fibrillation or pulseless ventricular tachycardia is generally better than from asystole or pulseless electric activity, we analyzed temporal survival trends in the overall cohort and separately by these 2 rhythm groups. As secondary outcomes, we analyzed temporal trends in the rate of survival to hospital admission to an inpatient unit (prehospital survival) and, among those who survived to be admitted, the likelihood of survival to hospital discharge (in-hospital survival). To determine whether any recent changes in out-of-hospital cardiac arrest survival could be attributed to rising rates of bystander CPR or AED use, we examined the effect of both interventions on overall survival trends and for prehospital and in-hospital survival.

In addition to documenting survival to hospital discharge, CARES documents the degree of neurological disability from the inpatient record among survivors at discharge, measured by the cerebral performance category (CPC) score.[11] A CPC score of 1 denotes a patient with mild or no neurological disability, 2 reflects moderate neurological disability, 3 indicates severe neurological disability, and 4 is assigned to patients in a persistent coma or vegetative state. For this study, we evaluated temporal trends in discharge neurological status as an ordinal variable.

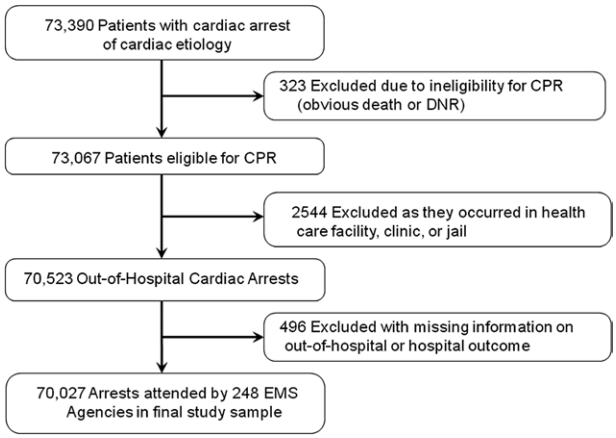

Figure 1. Definition of study cohort. CPR indicates cardiopulmonary resuscitation; DNR, do not resuscitate; and EMS, emergency medical services.

Statistical Analyses

To evaluate changes in baseline characteristics by calendar year, we used the Mantel-Haenszel test of trend for categorical variables and linear regression for continuous variables. To assess whether survival to discharge has improved over time, 3-level multilevel Poisson regression models were constructed for the overall cohort and by rhythm type, in which patients were nested within EMS agencies and EMS agencies were nested within U.S. states. In these models, random intercepts were estimated for each EMS agency and U.S. state.[12] Because survival rates for out-of-hospital cardiac arrest have been noted to differ markedly among EMS agencies,[13] the use of multilevel models ensures that our analyses reflect survival trends within EMS agency sites. Moreover, multilevel models account for the fact that different EMS agencies joined CARES at different time points. In these models, to obtain more interpretable estimates of effect, we directly estimated rate-ratios instead of odds ratios by specifying a Poisson distribution and including a robust variance estimate in our models.[14,15]

Our independent variable, calendar year, was included in the model as a continuous variable with polynomial (quadratic and cubic) terms for year, as appropriate. We defined years 2005 to 2006 as the reference period, because CARES did not begin enrollment until October 1, 2005. We multiplied the adjusted rate-ratios for each subsequent year (2007–2012) with the observed survival rate for the reference period (2005–2006) to obtain yearly risk-adjusted survival rates for the study period. These rates represent what the survival would be for each year if the patient case-mix was identical to the reference period within each EMS agency. Our models adjusted for age, sex, race/ethnicity (coded by the EMS provider as white, black, Latino, other, or unknown), initial cardiac arrest rhythm (ventricular fibrillation, pulseless ventricular tachycardia, asystole, pulseless electric activity), location of arrest (private residence, public area with likely AED availability [eg, sporting facility, airport], other public areas, and other), and whether the arrest was witnessed. To examine the robustness of our survival trend findings (because any improvement in survival trends may have been attributable to later enrolling sites with higher survival rates), we repeated the models and included only those EMS agencies that have been enrolling patients within CARES since 2005 through 2006 with an average annual case volume of ≥20 out-of-hospital cardiac arrests.

We conducted several additional analyses. To evaluate whether there were geographical variations in any temporal survival trends, we constructed 2-level models (patients nested within EMS agencies) and evaluated for an interaction between U.S. census region (Northeast, Midwest, South, and West) and time. We also assessed temporal trends in neurological disability among those surviving to hospital discharge. In these analyses, we constructed multinomial 3-level models to evaluate discharge CPC score as an ordinal variable, with time assessed as a continuous variable with polynomial terms (as described for the primary analysis).

Finally, to discern potential reasons for any improvement over time, we constructed similar 3-level logistic regression models to examine whether survival trends were attributable to increased rates of survival to hospital admission, in-hospital survival, or both. Because bystander CPR or AED use are potential mediators of any observed survival trends, we further examined whether increasing rates of bystander CPR or AED use were associated with survival trends by adding these 2 variables to the multilevel models described above and evaluated whether their inclusion attenuated year-over-year risk ratio estimates.

Besides race, data were missing in only 0.3% of cases, and the average number of missing data fields per patient was 0.003. There were no differences in baseline characteristics between those with missing data and those with complete data (results not shown). We used multiple imputation methods to impute missing values on the basis

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of all other observed data. Imputations were performed with Markov Chain Monte Carlo methods as implemented in SAS PROC MI. Five imputed data sets were generated; analyses were replicated across data sets and pooled to obtain final estimates. Patients with missing information on race were categorized as unknown as a separate dummy variable in our models. Results with and without imputation were very similar; only the former are presented. All statistical analyses were conducted using SAS Version 9.1.3 (SAS Institute, Cary, NC) and R Version 2.6.0 (Free Software Foundation, Boston, MA). All hypothesis tests were 2-sided with a significance level of 0.05. Because this study used only deidentified data, it was considered exempt research by the Mid America Heart Institute's Institutional Review Board.

Results

Patient and cardiac arrest characteristics of the study cohort are summarized in Table 1. The mean age of the study population was 64.1 years (standard deviation of 18.2 years), and 61% were men. Approximately 5 of 6 cardiac arrests occurred in a private residence, and <2% of all cardiac arrests occurred in a public area with likely access to an AED. Fewer than half of events were witnessed. More than three-quarters of patients were found in asystole or pulseless electric activity, whereas 23.6% had cardiac arrest rhythms amenable to defibrillation treatment. During the study period, there were no temporal differences in patients' sex or presenting rhythm. There were, however, modest changes in the age and racial composition of the study cohort, with an increasingly older and white population in the later years. There were also small changes in the proportion of patients whose cardiac arrest occurred at home or were witnessed.

Survival to Discharge

During the study interval, unadjusted rates of survival to hospital discharge increased from 5.7% in 2005 to 2006 to 9.8% in 2012 (Figure 2). For cardiac arrests attributable to ventricular fibrillation or pulseless ventricular tachycardia, the unadjusted rate of survival increased from 16.1% to 27.9%, whereas for cardiac arrests attributable to asystole or pulseless

Table 1. Trends in Baseline Characteristics

	Year Group			
	2005 to 2007 n = 4630	2008 to 2010 n = 26 058	2011 to 2012 n = 39 339	*P* for Trend*
Age group				0.02
<50	923 (20.1%)	4810 (18.5%)	7148 (18.2%)	
50–59	901 (19.6%)	4964 (19.1%)	7434 (18.9%)	
60–69	910 (19.8%)	5433 (20.9%)	8509 (21.7%)	
70–79	854 (18.6%)	4944 (19.0%)	7385 (18.8%)	
≥80	1010 (22.0%)	5872 (22.6%)	8786 (22.4%)	
Missing	32	35	77	
Sex				0.22
Female	1846 (39.9%)	10 066 (38.6%)	15 176 (38.6%)	
Male	2783 (60.1%)	15 980 (61.4%)	24 155 (61.4%)	
Missing	1	12	8	
Race				0.005
White	1794 (38.7%)	10 037 (38.5%)	16 513 (42.0%)	
Black	1236 (26.7%)	6986 (26.8%)	8433 (21.4%)	
Latino	238 (5.1%)	1400 (5.4%)	2314 (5.9%)	
Other	88 (1.9%)	697 (2.7%)	1036 (2.6%)	
Unknown	1274 (27.5%)	6938 (26.6%)	11 043 (28.1%)	
Location of Arrest				< 0.001
Private residence	3859 (83.3%)	21 809 (83.7%)	33 232 (84.5%)	
Public area with likely AED	80 (1.7%)	459 (1.8%)	684 (1.7%)	
Other public areas	575 (12.4%)	3064 (11.8%)	4916 (12.5%)	
Other	116 (2.5%)	726 (2.8%)	507 (1.3%)	
First documented rhythm				0.24
Asystole and PEA	3536 (76.4%)	19 965 (76.7)	30 283 (77.0)	
VF and pulseless VT	1092 (23.6%)	6081 (23.3%)	9056 (23.0%)	
Missing	2	12		
Witnessed arrest	2208 (47.7%)	12 052 (46.3%)	18 815 (47.8%)	0.01

For illustrative purposes, trends in baseline characteristics are presented as 3 time periods. AED indicates automated external defibrillator; BLS, basic life support; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; PEA, pulseless electric activity; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Temporal changes in patient characteristics were assessed, with calendar year evaluated as a continuous variable, and expressed as a *P* for trend.

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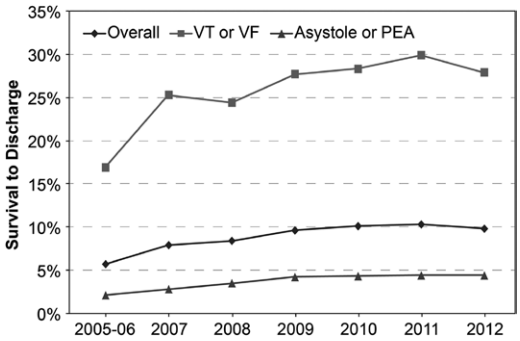

Figure 2. Unadjusted rates of survival to hospital discharge by calendar year. Observed rates for survival to discharge are displayed for the overall cohort and separately for shockable (ventricular fibrillation [VF] and pulseless ventricular tachycardia [VT]) and nonshockable (asystole and pulseless electric activity [PEA]) cardiac arrest rhythms.

Table 2. Overall Survival*

Year	Unadjusted Rate	Adjusted Rate	Adjusted Rate Ratio (95% CI)	*P* Value for Trend
2005–2006	5.7%	Reference	Reference	<0.001
2007	7.9%	6.5%	1.14 (1.06–1.22)	
2008	8.4%	7.2%	1.27 (1.12–1.43)	
2009	9.6%	7.8%	1.37 (1.18–1.59)	
2010	10.0%	8.2%	1.44 (1.22–1.69)	
2011	10.3%	8.4%	1.47 (1.25–1.73)	
2012	9.8%	8.3%	1.47 (1.26–1.70)	

Model-adjusted rates of survival to discharge were compared against the reference period, 2005 to 2006.

*Rates are adjusted for emergency medical services agency and temporal changes in age, sex, race/ethnicity, initial cardiac arrest rhythm, location of arrest, and whether the arrest was witnessed.

electric activity, the unadjusted rate of survival increased from 2.1% to 4.4%.

After adjusting for temporal trends in patient and cardiac arrest characteristics, risk-adjusted rates of survival improved markedly over the study period (*P* for trend <0.001). For instance, compared with the 5.7% survival rate in 2005 to 2006, the risk-adjusted survival rate in 2008 increased to 7.2% (adjusted risk ratio, 1.27; 95% confidence interval [CI], 1.12–1.43) and continued to increase more modestly thereafter (eg, 8.3% in 2012; adjusted risk ratio, 1.47; 95% CI, 1.26–1.70; Table 2; full model in Table I in the online-only Data Supplement). These gains were observed for both types of arrest rhythms (*P* for interaction between calendar year and rhythm type = 0.22), and yearly risk-adjusted survival rates by rhythm type are summarized in Table II in the online-only Data Supplement. The improved survival trends persisted (*P* for trend <0.001) when our analyses were restricted to only those EMS agencies which participated in CARES throughout the entire study period (Table III and Figure I in the online-only Data Supplement). Importantly, this improvement in overall rates of survival to hospital discharge was also accompanied by lower rates of neurological disability in survivors over time (*P* value of 0.01 for yearly trend, compared with discharge CPC of 1; Figure 3). Finally, there were geographical differences in overall survival trends (*P* for interaction of 0.04), with the greatest improvement in out-of-hospital cardiac arrest survival in the Northeast and little to no improvement in the Midwest (Table IV in the online-only Data Supplement).

Secondary Outcomes

Because gains in survival to hospital discharge might be attributable to better prehospital or in-hospital care, we examined temporal trends in these 2 phases of resuscitation care. Unadjusted rates of prehospital survival improved from 14.3% in 2005 to 2006 to 26.4% in 2012 (Table 3). After multivariable adjustment, prehospital survival improved by 45% from 2005 to 2012 (*P* for trend <0.001). There was also a significant, though less substantial, temporal trend for improved in-hospital survival for patients who survived to hospital admission (*P* for trend of 0.015).

To discern potential reasons for the improvement in prehospital survival, we considered several potential explanations (Table 4). Bystander CPR increased from 28.2% of cases in 2005 to 2006 to 36.3% of cases in 2012 (*P* for trend <0.001). In addition, there was a modest increase in rates of bystander AED use over the study period (*P* for trend <0.001 for all arrests and 0.048 for witnessed arrests). Further adjustment for these 2 factors in our models showed modest attenuation of the adjusted rate ratios for prehospital survival, whereas estimates for overall and in-hospital survival were not affected (Table V in the online-only Data Supplement).

Discussion

Based on data collected from a large, prospectively collected registry of cardiac arrest cases in communities across the United States, we found that overall rates of survival from out-of-hospital cardiac arrest improved dramatically between 2005 and 2012, with accompanying improved trends in both prehospital and in-hospital survival. This finding stands in stark contrast to the lack of progress in out-of-hospital cardiac arrest

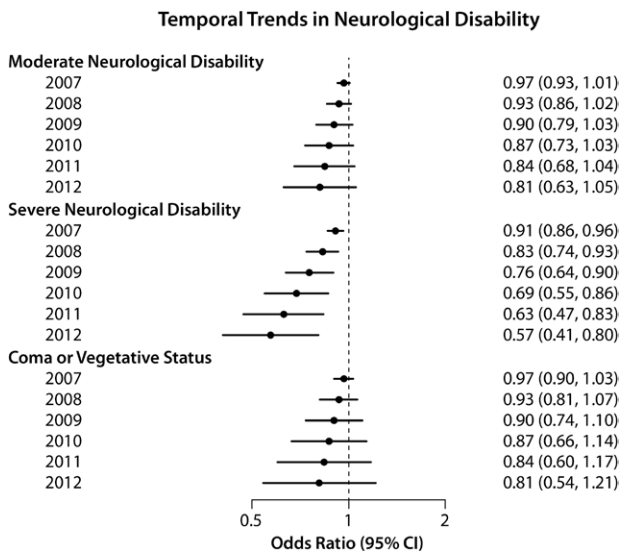

Figure 3. Trends in neurological outcomes. Compared with a discharge cerebral performance category score of 1 (little to no neurological disability), there was a significant trend (*P* for trend of 0.01) for lower rates of neurological disability over time. CI indicates confidence interval.

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Table 3. Prehospital and In-Hospital Survival*

Year	Unadjusted Rate	Adjusted Rate	Adjusted Rate Ratio (95% CI)	*P* Value for Trend
Prehospital survival				0.001
2005–2006	14.3%	Reference	Reference	
2007	22.2%	17.9%	1.25 (1.14–1.37)	
2008	26.1%	20.0%	1.40 (1.23–1.59)	
2009	27.0%	20.8%	1.45 (1.27–1.65)	
2010	27.1%	20.7%	1.45 (1.28–1.64)	
2011	26.2%	20.5%	1.43 (1.27–1.61)	
2012	26.4%	20.8%	1.45 (1.28–1.65)	
In-hospital survival				0.015
2005–2006	34.6%	Reference	Reference	
2007	35.6%	35.9%	1.02 (1.00–1.04)	
2008	32.1%	35.6%	1.04 (1.01–1.07)	
2009	35.5%	37.2%	1.06 (1.02–1.11)	
2010	36.9%	39.3%	1.08 (1.01–1.15)	
2011	39.4%	40.7%	1.10 (1.02–1.20)	
2012	37.2%	39.5%	1.12 (1.02–1.24)	

Model-adjusted rates of survival to hospital admission and in-hospital survival (among those surviving to hospital admission) are compared against the reference period, 2005 to 2006.

*Rates are adjusted for emergency medical services agency and temporal changes in age, sex, race/ethnicity, initial cardiac arrest rhythm, location of arrest, and whether the arrest was witnessed.

survival over the preceding 30 years in the United States.[1] Improved rates of survival were noted in both shockable and nonshockable cardiac arrest rhythms and were also accompanied by lower rates of neurological disability over time. Finally, bystander CPR and use of AEDs modestly increased during the study period and appeared to, in part, account for some of the observed improved trends in prehospital survival.

We are not the first to report encouraging survival trends for out-of-hospital cardiac arrest. Recent studies involving single communities or much smaller populations have also reported improved rates of survival,[6,7] but the generalizability of these findings was unknown. Non-U.S. groups have also documented favorable survival trends.[16–18] However, these studies did not account for the potentially confounding role of EMS agency, and findings in other countries may not pertain to the United States, given differences in the organization and delivery of emergency care. Our study—by far the largest conducted to date in the United States—includes data from a much larger and more diverse set of U.S. communities than previous studies and takes local characteristics into account.

Several aspects of our study warrant comment. Our use of multilevel models allowed us to control for clustering of patients within sites to estimate overall survival trends across EMS agencies. In addition, we confirmed a similar survival trend when we restricted our analyses to only those sites that began participation in CARES from its inception. These analyses ensured that our findings were not simply attributable to recruitment of higher-performing EMS systems during the later years. Moreover, we found that the improvement in survival was not at the expense of higher rates of neurological disability among survivors; in fact, we found that rates of neurological disability actually decreased over time. We also examined temporal trends in survival from out-of-hospital cardiac arrests caused by ventricular fibrillation or pulseless ventricular tachycardia—cardiac arrest rhythms less likely to be confounded by differences in patient characteristics over time—and found the same pattern of improved survival. Lastly, we observed that the improvement in out-of-hospital cardiac arrest survival was attributable to both gains in prehospital resuscitation and in-hospital survival, although the improvement in prehospital survival appeared larger.

What might explain the recent improvements in rates of out-of-hospital cardiac arrest survival? In contrast to a recent study from Denmark,[18] we found that the higher rates of bystander CPR and AED use did not appear to be the principal contributors to overall improvements in survival, perhaps owing to the fact that overall rates of bystander CPR and AED use in the United States increased only modestly during the study interval and remained relatively low. However, higher rates of bystander CPR and AED use did attenuate the adjusted rate ratios for prehospital survival trends, suggesting that these factors may have mediated, in part, some of the prehospital survival improvement. Other factors that were not measured within CARES but may have contributed to the survival trends we observed include a renewed focus on the delivery of high quality CPR (eg, appropriate depth and rate of

Table 4. Trends in Bystander CPR and AED Use

	2005–2006	2007	2008	2009	2010	2011	2012	*P* for Trend
Person performing CPR								<0.001
Bystander	28.2%	33.1%	33.8%	31.6%	31.8%	36.7%	36.3%	
First responder	35.1%	32.1%	35.0%	36.4%	38.1%	26.5%	29.3%	
EMS personnel	36.7%	34.8%	31.2%	32.0%	30.1%	36.8%	34.4%	
Bystander AED use*								
All arrests	1.9% (18/946)	2.3% (49/2173)	3.7% (138/3686)	3.5% (210/6021)	3.6% (298/8270)	4.5% (493/10 853)	4.2% (692/16 614)	<0.001
Witnessed arrests	6.5% (14/217)	5.6% (27/481)	9.2% (78/847)	9.1% (122/1340)	10.3% (183/1784)	9.5% (259/2719)	9.4% (398/4224)	0.048

Rates of both bystander CPR and lay person deployment of AEDs increased during the study period. AED indicates automated external defibrillator; CPR, cardiopulmonary resuscitation; and EMS, emergency medical services.

*By convention, for calculations of bystander AED use, we excluded from consideration patients with a witnessed arrest for whom CPR was initiated by a first responder (police, firemen) or EMS personnel, because bystanders would not be expected to deploy an AED in these circumstances.

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chest compressions), avoidance of interruptions in compressions, and elimination of stacked defibrillations and frequent pulse checks after defibrillation, but these require confirmation in future studies.

Our findings indicate that the pace of improvement in study communities has slowed in recent years, but it has not stopped. It is possible that additional progress can be achieved. For example, clinical trials have reported that compression-only (ie, hands only) CPR is as effective as conventional CPR, and is considerably easier to perform and retain.[19] If national efforts to disseminate an easier to perform and retain method of CPR lead to marked improvements in rates of bystander CPR, which parenthetically was initiated in only one-third of our study cohort, additional gains in survival may be realized.[19,20] Likewise, more consistent provision of advanced cardiac life support, including techniques that emphasize uninterrupted delivery of chest compressions and postcardiac arrest care, may produce better outcomes.[21]

Our study is limited in certain respects. CARES was designed as a public health surveillance system to make it less burdensome for communities to participate. For that reason, it only collects essential data elements.[8] Therefore, we do not have access to detailed clinical information to assess other factors (eg, comorbidities or EMS response times) that may influence survival. However, because the average age of patients with an out-of-hospital cardiac arrest increased over the study interval, it is unlikely that the survival gains we observed were attributable to lower severity of illness. Second, although we had information on rates of bystander CPR and AED use, CARES does not collect information on every aspect of resuscitation care, including the quality of CPR. Third, before 2011, information on therapeutic hypothermia was not systematically collected in CARES. Consequently, we were unable to assess trends in hypothermia use. Fourth, because CARES does not specify the catchment area of individual EMS agencies, we cannot compare local differences in cardiac arrest incidence. Fifth, although many studies have documented neurological outcomes based on the broad categories encompassed in a CPC score, interpretation of a particular neurological outcome as a CPC score of 1 or 2 may vary somewhat among sites. Therefore, this secondary outcome should be interpreted with some caution. Sixth, CARES collected information on only cardiac arrests attributable to a presumed cardiac cause during the study period. Because noncardiac arrests (eg, drowning, trauma, progressive respiratory failure, overdoses, asphyxia, primary respiratory arrests) may be associated with different outcomes, our findings of improved trends could reflect, in part, differences in classification of cardiac arrests as cardiac versus noncardiac over time. Because CARES did not collect information on noncardiac arrests we could not exclude this possibility, although there were no changes in the registry's definition of cardiac arrest during the study period. Finally, although this study encompassed communities representing nearly 25% of the U.S. population, our findings may not apply to communities that do not participate in CARES.

In conclusion, in a large, prospective, quality improvement registry, we found that rates of survival from out-of-hospital cardiac arrest in the United States have substantially improved since 2005. This improvement was attributed to both improved prehospital and in-hospital survival and was accompanied by lower rates of neurological disability over time among survivors. These findings indicate that the dismal rates of out-of-hospital cardiac arrest survival that have persisted for so long are not immutable.

Appendix

Member sites of the Cardiac Arrest Registry to Enhance Survival (CARES) Surveillance Group are depicted at https://mycares.net/cares_maps.jsp.

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Disclosures

Dr Chan has received funding support from the American Heart Association, which currently helps to fund the CARES registry. CARES was funded by the Centers for Disease Control and Prevention from 2004 to 2012. The program is now supported through private funding from the American Red Cross, the Medtronic Foundation Heart Rescue Program, the American Heart Association, Zoll Corporation, and in-kind support from Emory University. Dr McNally is supported by grant funding from CARES and serves as Executive Director of the program. None of these funding partners had a role in the study design, data analysis, or manuscript preparation and revision. The views expressed do not necessarily represent those of the Uniformed Services University of the Health Sciences or the US Department of Defense. Dr Chan had full access to all of the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. The other authors report no conflicts.

References

1. Sasson C, Rogers MA, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Circ Cardiovasc Qual Outcomes*. 2010;3:63–81.
2. Mild therapeutic hypothermia to improve the neurological outcome after cardiac arrest. *N Engl J Med*. 2002;346:549–556.
3. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002;346:557–563.
4. Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, Zalenski R, Becker LB, Schron EB, Proschan M; Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351:637–646.
5. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med*. 2000;343:1206–1209.
6. Rea TD, Crouthamel M, Eisenberg MS, Becker LJ, Lima AR. Temporal patterns in long-term survival after resuscitation from out-of-hospital cardiac arrest. *Circulation*. 2003;108:1196–1201.
7. Hinchey PR, Myers JB, Lewis R, De Maio VJ, Reyer E, Licatese D, Zalkin J, Snyder G; Capital County Research Consortium. Improved out-of-hospital cardiac arrest survival after the sequential implementation of 2005 AHA guidelines for compressions, ventilations, and induced hypothermia: the Wake County experience. *Ann Emerg Med*. 2010;56:348–357.
8. McNally B, Stokes A, Crouch A, Kellermann AL; CARES Surveillance Group. CARES: Cardiac Arrest Registry to Enhance Survival. *Ann Emerg Med*. 2009;54:674–683.e2.
9. McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, Sasson C, Crouch A, Perez AB, Merritt R, Kellermann A; Centers for Disease Control and Prevention. Out-of-hospital cardiac arrest surveillance—Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005–December 31, 2010. *MMWR Surveill Summ*. 2011;60:1–19.
10. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, Halperin H, Handley A, Herlitz J, Hickey

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R, Idris A, Kloeck W, Larkin GL, Mancini ME, Mason P, Mears G, Monsieurs K, Montgomery W, Morley P, Nichol G, Nolan J, Okada K, Perlman J, Shuster M, Steen PA, Sterz F, Tibballs J, Timerman S, Truitt T, Zideman D. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110:3385–3397.

11. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet*. 1975;1:480–484.
12. Goldstein H. *Multilevel Statistical Models*, 3rd Edition. London. Free 2nd Edition: http://www.ats.ucla.edu/stat/examples/msm_goldstein/goldstein.pdf: Arnold Publishers; 2003.
13. Eisenberg M, White RD. The unacceptable disparity in cardiac arrest survival among American communities. *Ann Emerg Med*. 2009;54:258–260.
14. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702–706.
15. Greenland S. Model-based estimation of relative risks and other epidemiological measures in studies of common outcomes and in case-control studies. *Am J Epidemiol*. 2004;160:301–305.
16. Kitamura T, Iwami T, Kawamura T, Nitta M, Nagao K, Nonogi H, Yonemoto N, Kimura T; Japanese Circulation Society Resuscitation Science Study Group. Nationwide improvements in survival from out-of-hospital cardiac arrest in Japan. *Circulation*. 2012;126:2834–2843.
17. Hollenberg J, Herlitz J, Lindqvist J, Riva G, Bohm K, Rosenqvist M, Svensson L. Improved survival after out-of-hospital cardiac arrest is associated with an increase in proportion of emergency crew–witnessed cases and bystander cardiopulmonary resuscitation. *Circulation*. 2008;118:389–396.
18. Wissenberg M, Lippert FK, Folke F, Weeke P, Hansen CM, Christensen EF, Jans H, Hansen PA, Lang-Jensen T, Olesen JB, Lindhardsen J, Fosbol EL, Nielsen SL, Gislason GH, Kober L, Torp-Pedersen C. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. *JAMA*. 2013;310:1377–1384.
19. Rea TD, Fahrenbruch C, Culley L, Donohoe RT, Hambly C, Innes J, Bloomingdale M, Subido C, Romines S, Eisenberg MS. CPR with chest compression alone or with rescue breathing. *N Engl J Med*. 2010;363:423–433.
20. Travers AH, Rea TD, Bobrow BJ, Edelson DP, Berg RA, Sayre MR, Berg MD, Chameides L, O'Connor RE, Swor RA. Part 4: CPR overview: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 Suppl 3):S676–S684.
21. Peberdy MA, Callaway CW, Neumar RW, Geocadin RG, Zimmerman JL, Donnino M, Gabrielli A, Silvers SM, Zaritsky AL, Merchant R, Vanden Hoek TL, Kronick SL; American Heart Association. Part 9: post-cardiac arrest care: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 Suppl 3):S768–S786.

CLINICAL PERSPECTIVE

Over the past several decades, the United States has made little progress in improving the overall rate of survival from out-of-hospital cardiac arrest, with survival rates remaining relatively unchanged at 7.6%. In recent years, advances in resuscitation science and a renewed focus on early delivery of high-quality cardiopulmonary resuscitation (CPR) offered hope for improvements in survival. In this article by Chan and colleagues, the authors leveraged contemporary data from a large, prospective U.S. registry for out-of-hospital cardiac arrest and examined whether survival for this condition has indeed increased. The authors found that rates of overall survival (ie, to hospital discharge) for out-of-hospital cardiac arrest between 2005 and 2012 have increased by ≈50%, and these gains were attributable to both improvements in prehospital and in-hospital survival. Among those surviving to hospital discharge, the authors also found that there was a temporal trend for less severe neurological disability. Rates of bystander CPR and use of automated external defibrillators modestly increased during this study period and, in part, accounted for the gains in prehospital survival. Collectively, these findings indicate that the dismal rates of out-of-hospital cardiac arrest survival that have persisted for so long in the United States are not immutable, and they suggest the possibility of achieving further gains in survival.

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Out-of-hospital cardiac arrest: manual or mechanical CPR?

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The appropriate role for mechanical chest compression devices in pre-hospital care has been debated in recent years.[1] The quality of manual cardiopulmonary resuscitation (CPR) during out-of-hospital cardiac arrest is often less than optimum, and affects survival.[2] Mechanical compression devices are an attractive alternative: they never get tired, give consistent chest compressions, and allow CPR to continue during transfer of the patient. Results from two studies[3,4] of implementation of mechanical CPR devices in the so-called real world showed higher rates of return of spontaneous circulation and survival to discharge with mechanical CPR than with manual CPR. However, results from three randomised trials[5-7] did not show significant survival benefit for mechanical CPR compared with manual CPR.

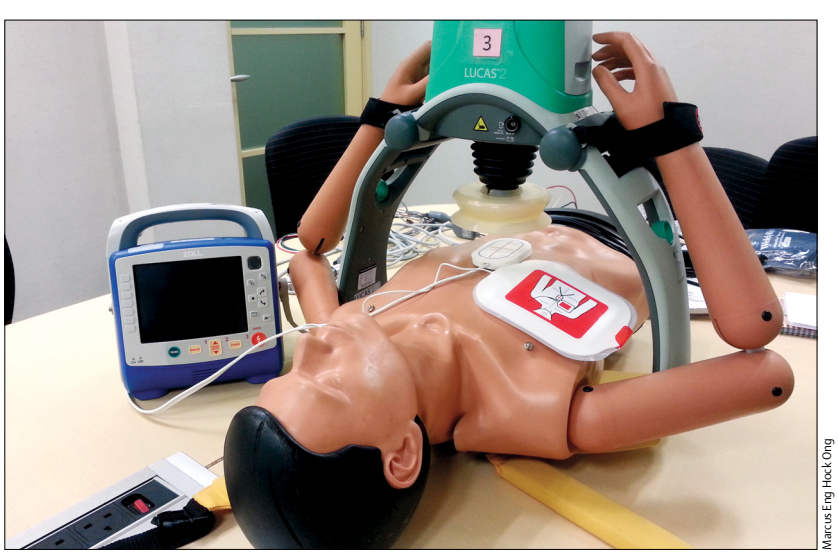
In *The Lancet*, Gavin Perkins and colleagues[8] describe a pragmatic, cluster-randomised trial including adults with non-traumatic out-of-hospital cardiac arrest from four UK ambulance services. Ambulances were randomly assigned to either mechanical CPR (with the LUCAS-2 device, figure) or manual CPR. The investigators enrolled 4471 patients (1652 patients in the LUCAS-2 group, and 2819 patients in the control group). However, only 985 (60%) patients in the mechanical CPR group actually received the LUCAS-2 intervention, as did 11 (<1%) in the control group. 30 day survival (analysed by intention to treat) was similar for mechanical CPR (104 [6%] of 1652 patients) and manual CPR (193 [7%] of 2819 patients; adjusted OR 0·86, 95% CI 0·64–1·15). Neurological survival with favourable neurological outcome at 3 months was lower in the mechanical CPR group than in the manual CPR group (adjusted OR 0·72, 95% CI 0·52–0·99).

The authors should be commended for attempting a real-world clinical trial on an important issue for Emergency Medical Services (EMS) systems worldwide. This study portrays the complexities and difficulties surrounding large-scale resuscitation trials, and the importance of attention to implementation and training in the assessment of any new technology. The somewhat low device usage rate (60%) reported in this study was due to difficulties in device use (15%), unknown reasons (6%), and non-compliance (16%). Even with apparent compliance, whether operational issues resulted in implementation delays with the mechanical device is unknown. The absence of difference (or even inferiority) in outcomes in the trial group might not be due to the treatment or device itself, but to attention to training, compliance to protocols, and implementation.

When implementing a programme with a mechanical device that has weight and bulk, we cannot presume that ambulance crews would always carry the device with them when attending to a call. It would be relevant to know whether the LUCAS device was immediately started at the site or later, including in the ambulance. If later, substantial time delays in initiating mechanical CPR might have negated potential for benefit in device use.

The time from emergency call to arrival of the vehicle or ambulance crew at the patient's side, as an indicator of duration of collapse before intervention by ambulance crew, might underestimate collapse intervals. This study[8] did not calculate collapse time or collapse duration before application of interventions. Conventional therapies for cardiac arrest seem to have minimum effect after long collapse intervals. Long intervals in the intervention group might conceal the effect of these interventions. Assessment of the effect of this collapse interval on outcomes after mechanical CPR might throw light on the relative usefulness of this mode of resuscitation.

About 60% of cardiac arrests attended were deemed not eligible and had no resuscitation attempted



Marcus Eng Hock Ong

Figure: LUCAS-2 mechanical chest compression device

(6482 of 11 171). This proportion is rather high compared with that in many EMS systems internationally. This finding raises questions of selective resuscitation by ambulance crews, although the study team did monitor for enrolment bias and noted no difference between study groups.

Quality of implementation is an especially important issue with regard to the benefit or harm of mechanical CPR. Interruptions to CPR and delays in application of mechanical CPR devices are major factors that affect outcomes.[9] Wang and colleagues showed that human error and lack of training with mechanical CPR led to prolonged intervals without chest compression.[10]

Attention to team training and focusing on quality of deployment of mechanical CPR devices alone can greatly improve outcomes.[11] The absence of quality implementation measures in this study,[8] such as data on delays in application of the device or CPR interruptions, makes it difficult to refute the hypothesis that the outcomes noted are possibly more an effect of the quality of implementation rather than the therapy in question.

Although this study does not give us a definitive answer to the debate between manual and mechanical CPR, it does throw a spotlight on implementation and quality. EMS services should aim to provide the best quality of CPR possible. High-quality manual CPR requires EMS commitment to training and quality review. Mechanical CPR requires the same commitment to training and attention to deployment practices. Mechanical CPR is also more costly than manual CPR. EMS systems worldwide routinely transport patients with cardiac arrest to hospital with ongoing manual CPR of doubtful quality.[12] Safety concerns for unrestrained crew using manual CPR in a moving ambulance are real. Mechanical CPR allows crews to be safely belted up and is a logical choice from the safety perspective.[13]

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MEHO is principal investigator of an industry-funded study involving a mechanical CPR device; has received grants from Laerdal Medical, grants and personal fees from Zoll Medical Corporation, and non-financial support from Bard Medical and Zoll Medical Corporation; and has a patent method of predicting patient survival licensed to Zoll Medical Corporation, and a patent system and method of determining a risk score for triage pending. VA is principal investigator in an industry-funded study on use of a mechanical CPR device in the out-of-hospital situation; has received non-financial support from Physio-Control Inc; and is a member of the Medical Advisory Board of Falck Foundation.

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1 Ong ME, Mackey KE, Zhang ZC, et al. Mechanical CPR devices compared to manual CPR during out-of-hospital cardiac arrest and ambulance transport: a systematic review. *Scand J Trauma Resusc Emerg Med* 2012; **20:** 39.
2 Wik L, Kramer-Johansen J, Myklebust H, et al. Quality of cardiopulmonary resuscitation during out-of-hospital cardiac arrest. *JAMA* 2005; **293:** 299–304.
3 Casner M, Andersen D, Isaacs SM. The impact of a new CPR assist device on rate of return of spontaneous circulation in out-of-hospital cardiac arrest. *Prehosp Emerg Care* 2005; **9:** 61–67.
4 Ong MEH, Ornato JP, Edwards DP, et al. Use of an automated, load-distributing band chest compression device for out-of-hospital cardiac arrest resuscitation. *JAMA* 2006; **295:** 2629–37.
5 Hallstrom A, Rea TD, Sayre MR, et al. Manual chest compression vs use of an automated chest compression device during resuscitation following out-of-hospital cardiac arrest. *JAMA* 2006; **295:** 2620–28.
6 Rubertsson S, Lindgren E, Smekal D, et al. Mechanical chest compressions and simultaneous defibrillation vs conventional cardiopulmonary resuscitation in out-of-hospital cardiac arrest: the LINC randomized trial. *JAMA* 2014; **311:** 53–61.
7 Wik L, Olsen JA, Persse D, et al. Manual vs integrated automatic load-distributing band CPR with equal survival after out of hospital cardiac arrest. The randomized CIRC trial. *Resuscitation* 2014; **85:** 741–48.
8 Perkins GD, Lall R, Quinn T, et al. Mechanical versus manual chest compression for out-of-hospital cardiac arrest (PARAMEDIC): a pragmatic, cluster randomised controlled trial. *Lancet* 2014; published online Nov 16. http://dx.doi.org/10.1016/S0140-6736(14)61886-9.
9 Ong ME, Annathurai A, Shahidah A, et al. Cardiopulmonary resuscitation interruptions with use of a load-distributing band device during emergency department cardiac arrest. *Ann Emerg Med* 2010; **56:** 233–41.
10 Wang HC, Chiang WC, Chen SY, et al. Video-recording and time-motion analyses of manual versus mechanical cardiopulmonary resuscitation during ambulance transport. *Resuscitation* 2007; **74:** 453–60.
11 Ong ME, Quah JL, Annathurai A, et al. Improving the quality of cardiopulmonary resuscitation by training dedicated cardiac arrest teams incorporating a mechanical load-distributing device at the emergency department. *Resuscitation* 2013; **84:** 508–14.
12 Russi CS, Kolb LJ, Myers LA, Hess EP, White RD. A comparison of chest compression quality delivered during on-scene and transport cardiopulmonary resuscitation. *Prehosp Emerg Care* 2011; **15:** 106.
13 Ong MEH, Shin SD, Soon SS, et al. Recommendations on ambulance cardiopulmonary resuscitation in basic life support systems. *Prehosp Emerg Care* 2013; **17:** 491–500.

Original Investigation | LESS IS MORE

Outcomes After Out-of-Hospital Cardiac Arrest Treated by Basic vs Advanced Life Support

Prachi Sanghavi, BS; Anupam B. Jena, MD, PhD; Joseph P. Newhouse, PhD; Alan M. Zaslavsky, PhD

IMPORTANCE Most out-of-hospital cardiac arrests receiving emergency medical services in the United States are treated by ambulance service providers trained in advanced life support (ALS), but supporting evidence for the use of ALS over basic life support (BLS) is limited.

OBJECTIVE To compare the effects of BLS and ALS on outcomes after out-of-hospital cardiac arrest.

DESIGN, SETTING, AND PARTICIPANTS Observational cohort study of a nationally representative sample of traditional Medicare beneficiaries from nonrural counties who experienced out-of-hospital cardiac arrest between January 1, 2009, and October 2, 2011, and for whom ALS or BLS ambulance services were billed to Medicare (31 292 ALS cases and 1643 BLS cases). Propensity score methods were used to compare the effects of ALS and BLS on patient survival, neurological performance, and medical spending after cardiac arrest.

MAIN OUTCOMES AND MEASURES Survival to hospital discharge, to 30 days, and to 90 days; neurological performance; and incremental medical spending per additional survivor to 1 year.

RESULTS Survival to hospital discharge was greater among patients receiving BLS (13.1% vs 9.2% for ALS; 4.0 [95% CI, 2.3-5.7] percentage point difference), as was survival to 90 days (8.0% vs 5.4% for ALS; 2.6 [95% CI, 1.2-4.0] percentage point difference). Basic life support was associated with better neurological functioning among hospitalized patients (21.8% vs 44.8% with poor neurological functioning for ALS; 23.0 [95% CI, 18.6-27.4] percentage point difference). Incremental medical spending per additional survivor to 1 year for BLS relative to ALS was $154 333.

CONCLUSIONS AND RELEVANCE Patients with out-of-hospital cardiac arrest who received BLS had higher survival at hospital discharge and at 90 days compared with those who received ALS and were less likely to experience poor neurological functioning.

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Invited Commentary

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American emergency medical services (EMS) respond to an estimated 380 000 out-of-hospital cardiac arrests of primary cardiac etiology annually.[1] Although 90% of these patients do not survive to hospital discharge, community training, rapid and appropriate delivery of prehospital care, and high-quality hospital cardiac care may substantially improve survival rates.[2-7] In the United States and in other developed countries, an important strategy for responding to out-of-hospital cardiac arrest has been the delivery of advanced life support (ALS) by ambulance service providers.[8]

Advanced life support providers, or paramedics, are trained to use sophisticated, invasive interventions to treat cardiac arrest, including endotracheal intubation, intravenous fluid and drug delivery, and semiautomatic defibrillation.[9] In contrast, basic life support (BLS) providers, or emergency medical technicians, use simple devices such as bag valve masks and automated external defibrillators. As a result, ALS providers tend to spend substantially more time at the location of the cardiac arrest than BLS providers.[10] Reflecting ALS's additional training and equipment, insurance reimbursement for it is higher.[11]

However, ALS has no established benefit over BLS for patients with cardiac arrest.[10,12] Of the few high-quality comparisons that exist, the most robust is a before-after study[10] from Ontario, Canada, which found that ALS did not improve survival to hospital discharge compared with a BLS system that optimized the time to defibrillation. Research from the United States is scant, but observational studies[13,14] from urban areas of other high-income countries have also failed to find a benefit of prehospital ALS. Similarly, studies[15,16] on the effective-

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ness of airway management favor BLS, and evidence of the benefits of intravenous drug delivery in the prehospital setting is limited.[17-21] Understanding the comparative effects of ALS and BLS on health outcomes and medical spending after out-of-hospital cardiac arrest is important not only for countries such as the United States with developed ALS-based emergency response systems but also for developing countries in the process of designing cost-effective prehospital emergency response systems.

Methods

Study Population and Data Linkage

This research was approved by institutional review boards at Harvard University and the National Bureau of Economic Research. Informed consent was not required because the analysis is based on deidentified Medicare claims. We analyzed a 20% simple random sample of fee-for-service Medicare beneficiaries from nonrural counties who experienced out-of-hospital cardiac arrest between January 1, 2009, and October 2, 2011. We identified ground emergency ambulance rides by Health Care Financing Administration Common Procedural Coding System codes A0429 (BLS emergency), A0427 (ALS level 1 emergency), and A0433 (ALS level 2)[11] with origin and destination codes RH (residence to hospital), SH (scene of accident or acute event to hospital), NH (skilled nursing facility [SNF] to hospital), or EH (residential, domiciliary, or custodial facility or nursing home other than SNF to hospital). We linked 95.7% of these rides to inpatient and outpatient claims by matching on beneficiary identification numbers and dates of service.

For 43 760 ambulance rides, an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnosis code of 427.5 for cardiac arrest was present on an outpatient claim or an inpatient claim marked as "present on admission." To focus on cardiac arrests arising from a nontraumatic etiology and to allow comparison with other studies,[10] we removed observations with an injury *ICD-9-CM* diagnosis code (800-999 or E800-E900). We also removed cases (3.1%) from Connecticut, Delaware, Hawaii, and the District of Columbia, where billing practices make it difficult to determine whether ALS provided the service. For example, in Delaware, ALS is supported by local government funds and does not generally bill Medicare. We excluded observations (approximately 10% of the sample) from rural counties as defined by the US Bureau of the Census because they exhibited large differences on baseline characteristics. Finally, we removed cases from North Dakota, Vermont, and Wyoming because they had no BLS cases in nonrural areas. Our final sample size was 32 935 ambulance rides (**Figure 1**). We linked each observation to beneficiary data on demographics, death, and chronic conditions. Using claims for services during the 1 year before cardiac arrest, we constructed combined Charlson and Elixhauser comorbidity scores.[22] We ascertained total Medicare spending from claims. We obtained demographic data from the 2009 Population Estimates for Zip Code Tabulation Areas,[23] county-level demographic and health information for the most recent year available before 2011 for each variable from the Area Health Resources Files,[24] and hospital process measures and mortality rates for 2009 to 2011 from the Hospital Compare data sets.[25]

Comparison Groups

We compared BLS and ALS transports defined by the service level billed on the Medicare ambulance claim, as indicated by the Health Care Financing Administration Common Procedural Coding System code. This code reflects the level of service that was deemed medically necessary. Crucially for our purposes, Medicare allows billing at the ALS level if assessment by ALS-trained providers was considered necessary at dispatch, even if ALS providers delivered only BLS interventions. Medicare pays a single amount for the service level that is inclusive of all items, and there is no itemized list of interventions in the claims. Therefore, although we cannot observe the specific combination of provider training, local protocols, or clinical interventions that a patient experienced, the ambulance crew level is an indicator for the set of interventions and scene and transport times that are characteristic of that level.

Guidelines and training for ALS providers direct them to provide ALS care for cardiac arrest or its antecedent conditions.[8,20] Still, a potential concern may be that, after evaluating a patient, ALS-trained providers will deliver BLS interventions to patients who appear healthier and therefore bill at the BLS level. However, as noted above, ALS providers can still bill at the ALS level in these cases, and it is unlikely that they would not do so given the reimbursement differences. Therefore, it is unlikely that BLS cases in our sample were treated by providers trained in ALS.

A second potential concern with comparing outcomes for patients receiving ALS vs BLS is that, if more severe cases were to be triaged by dispatchers toward ALS, our analyses may be confounded by making ALS outcomes appear worse than they would be if patients were randomized to ALS. However, based on telephone interviews with EMS officials in 45 states, we established that existing dispatch protocols generally lead to BLS dispatch for cardiac arrest or any of its prodromal symptoms (eg, chest pain, breathing difficulty, or fainting) only if ALS is unavailable within a reasonable amount of time, either due to travel distance, attendance at another call, or a staffing shortage.

Outcome Measures

Our primary outcome measures were patient survival to hospital discharge, to 30 days, and to 90 days. Our secondary outcomes included neurological performance and medical spending. We inferred Cerebral Performance Categories Scale[26] item 4 (coma or vegetative state) and item 5 (brain death) by the presence of *ICD-9-CM* diagnosis codes for anoxic brain injury (348.1), coma (700.01), persistent vegetative state (780.03), or brain dead (348.82). We combined these items to create an indicator for poor neurological functioning. For cardiac arrests that occurred in 2009 and 2010, we computed total medical spending up to 1 year after the cardiac arrest or until death.

Statistical Analysis

We first modeled the probability (P) that a beneficiary received ALS using logistic regression. The predicted propen-

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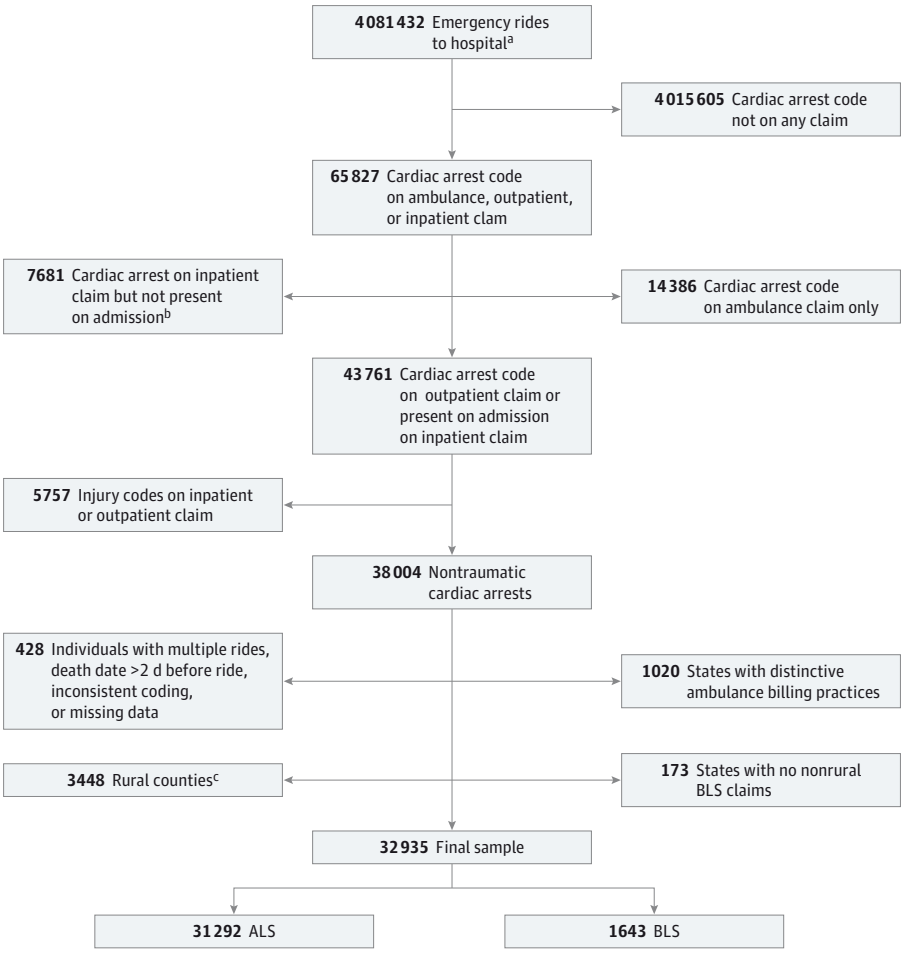
Figure 1. Flowchart of Cardiac Arrest Sample Construction



Codes refer to *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes. ALS indicates advanced life support; BLS, basic life support.

[a] Pickup locations included residence, scene of accident or acute event, skilled nursing facility, and non–skilled nursing facility residential, domiciliary, custodial, or nursing home facility.

[b] Present on admission status for cardiac arrest is either no or unknown.

[c] Rural areas are defined as counties that do not meet the metropolitan or micropolitan criteria as defined by the US Bureau of the Census. Metropolitan counties have at least 1 urbanized area of 50 000 or more population, and micropolitan counties have at least 1 urban cluster of at least 10 000 but less than 50 000 population. Both types have adjacent territory that has a high degree of social and economic integration with the core as measured by commuting ties.

sity scores P were used to derive balancing weights.[27] Because ALS cases outnumbered BLS cases, we chose weights to adjust the ALS distribution to the observed BLS distribution over the set of covariates. Therefore, each BLS observation received a weight of 1, and each ALS observation received a weight of $(1 - P)/P$. We chose this approach over propensity score–based matching or stratifying because it provided exact balance most efficiently. Furthermore, unlike using the propensity score as a covariate in a multivariable model, it allowed balance checking.

We tested the following individual-level variables in the propensity score regression: ambulance mileage, history of 27 chronic conditions, and a 6-category zip code–level indicator combining high (>$40 000) or low median household income and racial/ethnic composition (>80% black, >80% white, or integrated).[28] To account for differences in the quality of hospital care that may be correlated with both outcomes and the propensity of a beneficiary to receive prehospital ALS, we also created zip code–level hospital quality measures, as described in the eAppendix in the Supplement.

Our final propensity score model adjusted for age (linear spline), sex, race/ethnicity, pickup location, and 3 chronic conditions at the individual level (the model coefficients are summarized in the eAppendix in the Supplement). At the zip code level, we adjusted for race/ethnicity, the median household income, and hospital quality (eAppendix in the Supplement). We also adjusted for urbanicity, percentage older than 25 years with 4 or more years of college, percentage of primary care practitioners, and the presence of any medical school–affiliated hospital at the county level. We included binary variables for all states with 15 or more BLS observations (ie, state fixed effects) and created groups by region defined by the US Bureau of the Census for the remaining states. The Hosmer-Lemeshow test was not statistically significant for this model, suggesting that the link function was appropriate.

We used statistical software to construct (SAS version 9.3) and analyze (R version 3.1.0) the sample. All statistical tests were 2-sided at the 5% level. All differences were evaluated using t tests. Kaplan-Meier survival curves were prepared from the weighted observations, with end points defined by death or survival beyond the end of our data on December 31, 2011. Medical spending included Medicare and any non-Medicare primary insurer payments, as well as beneficiary payments, geographically adjusted using the Medicare Hospital Wage Index for an estimated 70% labor share of inputs. For medical spending and survival to 1 year, we used balancing weights es-

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Table 1. Comparison of Medicare Claims–Based Sample and Primary Data–Based Samples on Mortality at Discharge for Individuals Brought to a Hospital

Variable	Medicare[a]	CARES	ROC	OPALS Study
No. of patients who arrived at the hospital via EMS	32 935	24 843	7486	4247
Inpatients who died before discharge, %	66	63	NA	NA
Inpatients and outpatients who died before discharge, %	90	88	87	95

Abbreviations: CARES, Cardiac Arrest Registry to Enhance Survival[29]; EMS, emergency medical services; NA, not available; OPALS, Ontario Prehospital Advanced Life Support[10]; ROC, Resuscitation Outcomes Consortium.[30]

[a] Discharge status for Medicare outpatient claims was approximated using 2-day mortality because discharge status was poorly coded.

timated for observations in 2009 and 2010, and for survival to 2 years, we used only 2009 data.

Sensitivity Analyses

We conducted several sensitivity analyses, described in the eAppendix in the Supplement. First, to assess the extent to which unmeasured disease severity could confound our results, we estimated potential unmeasured confounding by introducing incremental changes to comorbidity scores. Second, we assessed the sensitivity of our results to alternative analytic methods by regressing survival on a binary indicator for ambulance type and other variables from our main analysis. Third, we assessed sensitivity to the inclusion of beneficiaries who appeared to have died en route to the hospital. We excluded this group in the main analysis because diagnosis is only available from ambulance claims and coding may be inaccurate. Fourth, we used other data sets to check the sensitivity of our results to the exclusion of individuals who may have died at the scene and therefore were not transported. Fifth, we estimated the effect of ALS, excluding patients from nursing homes who may have received different on-site care compared with other patients. Sixth, we assessed the sensitivity of our results to situations in which BLS called for ALS backup by calculating the number of BLS cases that would have to have been incorrectly attributed to ALS to reverse the direction of our findings. Seventh, we estimated the effect of ALS compared with BLS for patients with a primary cardiac etiology by excluding patients with acute respiratory failure codes. Eighth, we assessed the robustness of our results to a less sensitive but more specific definition of poor neurological functioning that included only patients with persistent vegetative state or brain death.

Results

Out-of-hospital cardiac arrest mortality rates were high (**Table 1**) and comparable to those of other studies[10,29,30] that used primary data. Beneficiaries who received ALS were slightly younger, were more likely to be male, and were less likely to have most chronic conditions (**Table 2**). They were more often picked up at a residence, whereas patients receiving BLS were more often picked up at a skilled nursing facility. The distributions of household income and race/ethnicity, urbanicity, and the presence of medical school-affiliated hospitals differed (**Table 3**). Beneficiaries receiving ALS services were taken to hospitals that had somewhat better performance on process measures but had slightly worse 30-day mortality from acute myocardial infarction, heart failure, or pneumonia. After applying the propensity score-derived balancing weights to the ALS observations, there were no meaningful differences on any observed measure between the BLS and ALS groups.

Differences in Patient Survival

Unadjusted survival to hospital discharge was 3.5 (95% CI, 1.9-5.2) percentage points higher among patients receiving BLS (13.1% vs 9.6% for ALS) (**Table 4**). Unadjusted survival after BLS was also greater at 30 days (9.6% vs 6.5% for ALS; 3.1 [95% CI, 1.6-4.5] percentage point difference) and at 90 days (8.0% vs 5.8% for ALS; 2.2 [95% CI, 0.9-3.6] percentage point difference).

After propensity score adjustment, survival to hospital discharge was 4.0 (95% CI, 2.3-5.7) percentage points, or 43%, higher among patients receiving BLS (13.1% vs 9.2% for ALS) (Table 4). Survival after BLS was also greater at 30 days (9.6% vs 6.2% for ALS; 3.4 [95% CI, 1.9-4.8] percentage point difference) and at 90 days (8.0% vs 5.4% for ALS; 2.6 [95% CI, 1.2-4.0] percentage point difference). Kaplan-Meier estimates show that much of the difference in survival between ALS and BLS is explained by higher mortality in the first few days after cardiac arrest for patients receiving ALS (**Figure 2**). After this period, the near constancy in the survival ratios to different time points suggests that patients receiving BLS survive at least as well as those receiving ALS. These findings were unaffected by various sensitivity analyses (eAppendix in the Supplement).

Differences in Neurological Performance

Among all individuals experiencing an out-of-hospital cardiac arrest, the percentage with poor neurological functioning after cardiac arrest was lower among those who received BLS vs ALS (6.1% vs 9.7%; 3.5 [95% CI, 2.2-4.8] percentage point difference). Among individuals who were admitted to the hospital, rates of poor neurological functioning were markedly lower for BLS compared with ALS (21.8% vs 44.8%; 23.0 [95% CI, 18.6-27.4] percentage point difference).

Differences in Medical Spending

The mean medical spending was higher among beneficiaries receiving BLS ($11 875 vs $9097 for ALS; $2778 [95% CI, $582-$4973] difference), in part because individuals who received BLS survived longer and had more opportunity to receive medical care (Table 4). Incremental medical spending per addi-

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Table 2. Differences in Patient Characteristics by Ambulance Service Level[a]

Variable	BLS	Unweighted ALS	*P* Value	Weighted ALS
Age, mean, y	77	75	<.001	77
Female sex, %	52	46	<.001	52
Race/ethnicity, %			<.001[b]	
White	72	77		72
Black	21	17		21
Hispanic	3	2		3
Asian	2	2		2
Other	2	2		2
Ambulance mileage, mean, km	8.7	9.5	.002	8.5
Pickup location, %			<.001[b]	
Residence	55	65		55
Skilled nursing facility	27	14		27
Scene	14	17		14
Non-skilled nursing facility nursing home[c]	5	4		5
Comorbidity score, mean	5.5	4.8	<.001	5.5
Chronic conditions, %				
Acute myocardial infarction	13	14	.17	14
Alzheimer disease	20	15	<.001	20
Alzheimer disease or dementia[d]	42	31	<.001	42
Atrial fibrillation	30	29	.25	31
Cataract	66	62	<.001	65
Chronic kidney disease	53	48	<.001	52
Chronic obstructive pulmonary disease	49	49	.69	49
Heart failure	66	62	.001	67
Diabetes mellitus	58	53	<.001	58
Glaucoma	27	22	<.001	25
Hip or pelvic fracture	9	8	.06	9
Ischemic heart disease	75	72	<.001	76
Depression	43	40	.005	43
Osteoporosis	24	20	<.001	23
Rheumatoid arthritis or osteoarthritis	59	55	<.001	58
Stroke or transient ischemic attack	32	27	<.001	31
Breast cancer	5	4	.14	5
Colorectal cancer	6	4	.02	5
Prostate cancer	7	7	.98	7
Lung cancer	5	4	.87	4
Endometrial cancer	1	1	.95	1
Anemia	80	72	<.001	79
Asthma	19	20	.31	19
Hyperlipidemia	76	75	.43	77
Benign prostatic hyperplasia	23	22	.68	21
Hypertension	91	90	.04	92
Acquired hypothyroidism	25	22	.004	24

Abbreviations: ALS, advanced life support; BLS, basic life support.

[a] Differences between BLS and unweighted ALS observations were tested for statistical significance using *t* test or χ^2 test, as appropriate. Because of missing data, some measures are based on less data than the full sample. Hospital-level measures are based on data from the Hospital Compare data sets.[25]

[b] χ^2 Test of independence was used for this categorical variable.

[c] This includes non-skilled nursing facility residential, domiciliary, custodial, or nursing home facilities.

[d] Alzheimer disease or dementia includes Alzheimer-related diseases and senile dementia.

tional survivor to 1 year for BLS relative to ALS was $154 333 ([$11 875 − $9097]/[6.2% − 4.4%]), less than the mean medical spending per survivor to 1 year for ALS ($206 775).

Sensitivity Analyses

With one exception, our results were robust to all the sensitivity analyses described above and in the eAppendix in the Supplement. The exception is that, after restricting the definition of poor neurological functioning to only persistent vegetative state or brain death, there was no observed difference in neurological functioning between patients receiving ALS vs BLS.

Discussion

Using a nationally representative sample of traditional Medicare beneficiaries from nonrural counties who experienced out-

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Table 3. Differences in Community and Hospital Characteristics by Ambulance Service Level[a]

Variable	BLS	Unweighted ALS	*P* Value	Weighted ALS
Zip Code Level, %				
Household income/race/ethnicity group[b]			<.001[c]	
High/white	37	43		38
Low/white	7	8		7
High/black	2	1		2
Low/black	3	2		3
High/integrated	35	30		34
Low/integrated	16	16		16
Female sex	51	51	<.001	51
Age ≥65 y	14	14	.30	14
County Level, %				
Metropolitan[d]	87	85	.01	87
Persons with ≥4 y of college	24	23	<.001	24
General practice physicians	14	16	<.001	14
Any hospital with medical school affiliation	70	63	<.001	69
Hospital Level, %				
Given aspirin at arrival[e]	98	98	.58	98
Given aspirin at discharge[e]	98	98	.63	98
Given β-blocker at discharge[e]	97	98	.003	98
Given evaluation for LVSD[f]	97	98	<.001	98
Given angiotensin-converting enzyme inhibitor or angiotensin receptor blocker for LVSD[f]	94	95	.05	95
Initial blood culture performed before first dose of antibiotics[g]	95	96	<.001	96
Given the most appropriate initial antibiotic[g]	93	93	.01	93
Heart failure 30-d mortality rate	11	11	<.001	11
Myocardial infarction 30-d mortality rate	15	16	<.001	15
Pneumonia 30 d mortality rate	11	12	<.001	11

Abbreviations: ALS, advanced life support; BLS, basic life support; LVSD, left ventricular systolic dysfunction.

[a] Differences between BLS and unweighted ALS observations were tested for statistical significance using *t* test or χ^2 test, as appropriate. Because of missing data, some measures are based on less data than the full sample. Hospital-level measures are based on data from the Hospital Compare data sets.[25]

[b] This was high if the median household income exceeded $40 000 (otherwise low) and predominantly black if more than 80% black, predominantly white if more than 80% white, and otherwise integrated.

[c] χ^2 Test of independence was used for this categorical variable.

[d] Metropolitan counties have at least 1 urbanized area of 50 000 or more population, and micropolitan counties have at least 1 urban cluster of at least 10 000 but less than 50 000 population. Both types have adjacent territory that has a high degree of social and economic integration with the core as measured by commuting ties.

[e] The denominator for these measures is patients with myocardial infarction.

[f] The denominator for these measures is patients with heart failure.

[g] The denominator for these measures is patients with pneumonia.

of-hospital cardiac arrest between 2009 and 2011 and for whom EMS were billed to Medicare, we compared the effects of out-of-hospital BLS and ALS on survival, neurological performance, and medical spending. Ninety-day survival and neurological performance were substantially better among beneficiaries who received out-of-hospital BLS rather than ALS. Our estimates suggest that each year 1479 (95% CI, 683-2276) additional Medicare beneficiaries who experience out-of-hospital cardiac arrest would survive to 90 days if provided BLS instead of ALS. Furthermore, incremental medical spending per additional survivor to 1 year for BLS relative to ALS was $154 333, substantially less than the mean medical spending per survivor to 1 year for ALS ($206 775).

Prehospital care is complex, expensive, and critical to survival after out-of-hospital cardiac arrest, making it crucial to understand the combined effect on morbidity and mortality of the medical interventions, transport time, and training that characterize the 2 dominant models of prehospital care. Results of our study, to our knowledge the first large-scale systematic comparison of BLS and ALS in the United States, are consistent with those of international studies,[10,13,14] which found that ALS does not improve survival to hospital discharge after cardiac arrest. In contrast, our results suggest that the use of ALS is associated with higher mortality than the use of BLS in patients with cardiac arrest. However, most out-of-hospital cardiac arrests treated by EMS in the United States are provided with ALS care.

Although ALS is often assumed to improve clinical outcomes by providing advanced airway management and intravenous drug therapy, other studies have described mechanisms by which ALS may lead to the worse outcomes that we found. First, prehospital endotracheal intubation entails risks, including unrecognized esophageal intubation, aspiration of gastric contents, aggravation of existing injuries such as cervical spine damage, and interference with chest compressions.[31] Furthermore, successful intubation requires

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Table 4. Health and Payment Outcomes by Ambulance Service Level[a]

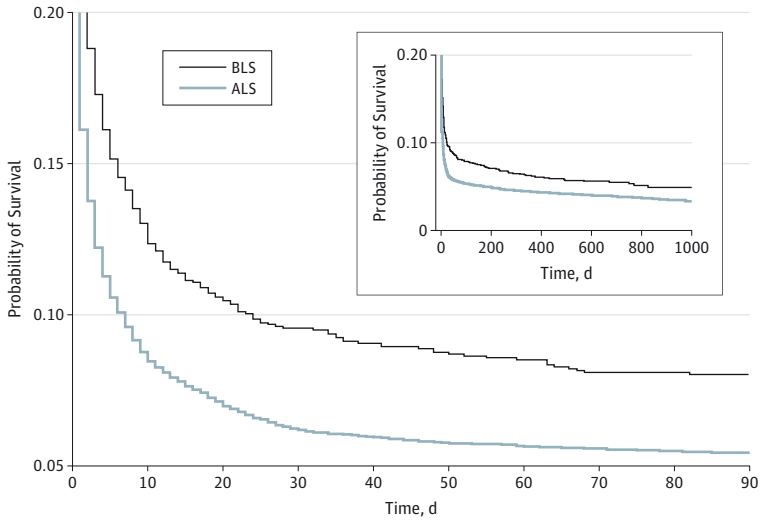
Variable	% (95% CI) BLS	% (95% CI) ALS	Percentage Point Difference[b]	Ratio (95% CI)
Unadjusted Outcomes				
Survival to hospital discharge	13.1 (11.5-14.8)	9.6 (9.3-9.9)	3.5 (1.9-5.2)	1.4 (1.2-1.5)
Survival to 30 d	9.6 (8.1-11.0)	6.5 (6.2-6.8)	3.1 (1.6-4.5)	1.5 (1.2-1.7)
Survival to 90 d	8.0 (6.7-9.3)	5.8 (5.5-6.1)	2.2 (0.9-3.6)	1.4 (1.2-1.6)
Adjusted Outcomes				
Survival				
Survival to hospital discharge	13.1 (11.5-14.8)	9.2 (8.7-9.7)	4.0 (2.3-5.7)	1.4 (1.2-1.6)
Survival to 30 d	9.6 (8.1-11.0)	6.2 (5.8-6.6)	3.4 (1.9-4.8)	1.5 (1.3-1.8)
Survival to 90 d	8.0 (6.7-9.3)	5.4 (5.0-5.8)	2.6 (1.2-4.0)	1.5 (1.2-1.8)
Survival to 1 y	6.2 (4.9-7.6)	4.4 (4.0-4.8)	1.8 (0.4-3.3)	1.4 (1.1-1.8)
Survival to 2 y	6.8 (4.8-8.9)	3.9 (3.3-4.5)	2.9 (0.8-5.0)	1.7 (1.2-2.4)
Other health measures				
Poor neurological performance	6.1 (5.0-7.3)	9.7 (9.1-10.2)	3.5 (2.2-4.8)	0.6 (0.5-0.8)
Admission to hospital	25.4 (23.3-27.5)	20.5 (19.8-21.2)	4.9 (2.7-7.1)	1.2 (1.1-1.4)
Payments, mean, $				
1-y Medical spending for all beneficiaries	11 875 (9754-13 995)	9097 (8527-9666)	2778 (582-4973)	1.3 (1.1-1.6)
1-y Medical spending per additional survivor to 1 y	190 153 (150 041-230 265)	206 775 (189 909-223 641)	NA	NA

Abbreviations: ALS, advanced life support; BLS, basic life support; NA, not applicable.

[a] Unless noted otherwise, estimates are adjusted by propensity score–based balancing weights. Estimates for survival to 1 year used only data from 2009 and 2010, and estimates for survival to 2 years used only data from 2009. Medical spending includes total payments to the provider by Medicare, the beneficiary, and a non-Medicare primary payer if one exists. Payments are geographically adjusted using the Medicare Hospital Wage Index for an estimated 70% labor share of inputs.

[b] Discrepancies in differences are due to rounding.

Figure 2. Kaplan-Meier Analysis of Survival After Cardiac Arrest by Ambulance Service Level



The main plot shows survival probability during the first 90 days, and the inset shows survival probability over the full observational period. Survival analysis was based on cardiac arrests that occurred between January 1, 2009, and October 2, 2011. Mortality was observed until December 31, 2011, when the data were censored; thus, there was follow-up to at least 90 days for each beneficiary. ALS indicates advanced life support; BLS, basic life support.

high levels of competency and regular practice, but in a Pennsylvania study[32] paramedics performed a median of only one intubation per year. Therefore, bag valve mask ventilation may improve outcomes over endotracheal intubation in out-of-hospital cardiac arrest.[15,16] Consistent with these risks of prehospital intubation, a large study[15] of cardiac arrests in Japan found greater neurologically favorable survival with the use of bag valve masks compared with advanced airways. Similarly, an analysis of out-of-hospital cardiac arrests in Los Angeles, California, found that advanced airway methods were associated with decreased survival to hospital discharge compared with bag valve mask ventilation.[16] Second, evidence on the benefits of intravenous drug delivery in out-of-hospital cardiac arrest is limited.[17-21] Third, and perhaps most important, ALS may entail delays in hospital care[10] that would otherwise offer definitive clinical management of the underlying dis-

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ease (eg, percutaneous coronary intervention for acute myocardial infarction).

Because a randomized controlled trial of ALS vs BLS is unlikely to occur, we performed an observational analysis. Although our analysis is the largest to date in the United States to our knowledge, it has several limitations. Patients receiving ALS may be at higher risk of mortality irrespective of the intervention, which would confound our estimates. This would be most likely to occur if ALS was dispatched to patients with higher preexisting mortality risk based either on symptoms or preexisting conditions. However, telephone interviews with 45 state EMS agencies demonstrated that if ALS was available it would always be provided in cases of known cardiac arrest or for any typical prodromal symptoms (eg, chest pain, syncope, etc) that would be known to the dispatcher at the time of dispatch. In other words, BLS would only be dispatched when ALS is unavailable, leaving no clear remaining mechanisms to explain why less severely ill patients would be preferentially dispatched BLS. Moreover, beneficiaries who received BLS had on average more preexisting comorbidities than those who received ALS, suggesting that outcomes among patients receiving BLS would (if anything) be worse and not better. Finally, in analyses of sensitivity to unmeasured confounding, our findings that outcomes under BLS were better than under ALS would continue to hold unless an implausibly high difference in unobserved severity was postulated.

An additional source of confounding may be that individuals who can be more easily resuscitated at the scene (eg, those with ventricular fibrillation) might be overrepresented among BLS cases, while individuals who cannot be resuscitated by BLS wait to be treated by ALS rather than undergoing direct transport to the hospital. Advanced life support would then be spuriously associated with worse outcomes that should have been attributed to BLS. However, our sensitivity analysis of situations in which BLS waits for ALS backup found that this would have to occur in an implausibly high proportion of BLS cases to change the direction of our effect (eAppendix in the Supplement).

Additional factors that influence outcomes after cardiac arrest may potentially confound our analysis. For example, shorter ambulance response times to the scene[33] and the presence of a shockable rhythm[29] are associated with improved outcomes. However, no evidence exists that these factors differ between patients receiving ALS vs BLS. However, ALS providers on average spend significantly more time at the scene,[10] which suggests how BLS may improve outcomes over ALS via rapid transport to the hospital. Other factors such as the quality of cardiopulmonary resuscitation (CPR) and the use of endotracheal intubation or intravenous drugs are similarly potential mediators of ALS and BLS treatment effects and, like scene and travel time, should not be viewed as confounders. Finally, although bystander-initiated CPR has been associated with improved outcomes,[28] we could not directly control for bystander-initiated CPR and defibrillation. However, we adjusted for area-level race/ethnicity and household income, which have been shown to be important determinants of bystander-initiated treatment.[28]

An additional limitation is that we used administrative claims, which may be inaccurate and subject to coding errors in diagnoses and procedures. For example, our identification of ALS and BLS exposures may not accurately reflect the service level of the ambulance. However, Medicare policy allows billing at the ALS level if assessment by an ALS-trained crew was considered necessary at dispatch. Based on telephone interviews with state EMS officials, we found some instances of joint BLS and ALS response in which Medicare is billed for only BLS. However, states with distinctive billing practices such as this comprise about 3% of the sample, and our findings were unaffected by their exclusion. Nonetheless, services provided by EMS may differ across areas, which may not be reflected in the level of billing to Medicare. Because we could not identify specific interventions provided to each patient, our conclusions are limited to differences in outcomes associated with the overall practices of BLS and ALS providers.

Conclusions

Our study calls into question the widespread assumption that advanced prehospital care improves outcomes of out-of-hospital cardiac arrest relative to care following the principles of BLS, including rapid transport and basic interventions such as effective chest compressions, bag valve mask ventilation, and automated external defibrillation. It is crucial to evaluate BLS and ALS use in other diagnosis groups and settings and to investigate the clinical mechanisms behind our results to identify the most effective prehospital care strategies for saving lives and improving quality of life conditional on survival.

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REFERENCES

1. Roger VL, Go AS, Lloyd-Jones DM, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2012 update: a report from the American Heart Association [published correction appears in *Circulation*. 2012;125(22):e1002]. *Circulation*. 2012;125(1):e2-e220. doi:10.1161/CIR.0b013e31823ac046.

2. Hallstrom AP, Ornato JP, Weisfeldt M, et al; Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351(7):637-646.

3. Stiell IG, Wells GA, Field BJ III, et al. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS study phase II: Ontario Prehospital Advanced Life Support. *JAMA*. 1999;281(13):1175-1181.

4. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002;346(8):557-563.

5. Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med*. 2002;346(8):549-556.

6. Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation*. 2007;74(2):227-234.

7. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73(1):29-39.

8. Travers AH, Rea TD, Bobrow BJ, et al. Part 4: CPR overview: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;122(18)(suppl 3):S676-S684.

9. National Highway Traffic Safety Administration. National EMS scope of practice model. 2007. http://www.ems.gov/education/EMSScope.pdf. Accessed January 7, 2014.

10. Stiell IG, Wells GA, Field B, et al; Ontario Prehospital Advanced Life Support Study Group. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351(7):647-656.

11. Medicare Payment Advisory Committee (MedPAC). Ambulance services payment system: payment basics. October 2013. http://www.medpac.gov/documents/payment-basics/ambulance-services-payment-system.pdf?sfvrsn=0. Accessed September 11, 2014.

12. Isenberg DL, Bissell R. Does advanced life support provide benefits to patients? a literature review. *Prehosp Disaster Med*. 2005;20(4):265-270.

13. Bur A, Kittler H, Sterz F, et al. Effects of bystander first aid, defibrillation and advanced life support on neurologic outcome and hospital costs in patients after ventricular fibrillation cardiac arrest. *Intensive Care Med*. 2001;27(9):1474-1480.

14. Ma MH, Chiang WC, Ko PC, et al. Outcomes from out-of-hospital cardiac arrest in metropolitan Taipei: does an advanced life support service make a difference? *Resuscitation*. 2007;74(3):461-469.

15. Hasegawa K, Hiraide A, Chang Y, Brown DF. Association of prehospital advanced airway management with neurologic outcome and survival in patients with out-of-hospital cardiac arrest. *JAMA*. 2013;309(3):257-266.

16. Hanif MA, Kaji AH, Niemann JT. Advanced airway management does not improve outcome of out-of-hospital cardiac arrest. *Acad Emerg Med*. 2010;17(9):926-931.

17. Gueugniaud PY, David JS, Chanzy E, et al. Vasopressin and epinephrine vs. epinephrine alone in cardiopulmonary resuscitation. *N Engl J Med*. 2008;359(1):21-30.

18. Stiell IG, Wells GA, Hebert PC, Laupacis A, Weitzman BN. Association of drug therapy with survival in cardiac arrest: limited role of advanced cardiac life support drugs. *Acad Emerg Med*. 1995;2(4):264-273.

19. Nolan JP, De Latorre FJ, Steen PA, Chamberlain DA, Bossaert LL. Advanced life support drugs: do they really work? *Curr Opin Crit Care*. 2002;8(3):212-218.

20. Neumar RW, Otto CW, Link MS, et al. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care [published corrections appear in *Circulation*. 2013;128(25):e480 and 2011;123(6):e236]. *Circulation*. 2010;122(18)(suppl 3):S729-S767.

21. Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. *JAMA*. 2012;307(11):1161-1168.

22. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. *J Clin Epidemiol*. 2011;64(7):749-759.

23. Center for Health Policy Research, The Dartmouth Institute for Health Policy and Clinical Research. 2009 Population estimates for Zip Code Tabulation Areas (ZCTAs) and Primary Care Service Areas (PCSAs). http://datawarehouse.hrsa.gov/DataDownload/PCSA/2009/Population%20Estimates%202009.pdf. Accessed September 10, 2014.

24. US Department of Health and Human Services, Health Resources and Services Administration. Area Health Resources Files (AHRF). http://arf.hrsa.gov. Accessed January 7, 2014.

25. Centers for Medicare and Medicaid Services. Hospital Compare. http://www.medicare.gov/hospitalcompare/Data/About.html. Accessed January 7, 2014.

26. Safar P. *Resuscitation After Brain Ischemia: Brain Failure and Resuscitation*. New York, NY: Churchill Livingstone; 1981:155-184.

27. Hirano K, Imbens GW. Estimation of causal effects using propensity score weighting: an application to data on right heart catheterization. *Health Serv Outcomes Res Methodol*. 2001;2(3-4):259-278.

28. Sasson C, Magid DJ, Chan P, et al; CARES Surveillance Group. Association of neighborhood characteristics with bystander-initiated CPR. *N Engl J Med*. 2012;367(17):1607-1615.

29. McNally B, Robb R, Mehta M, et al; Centers for Disease Control and Prevention. Out-of-hospital cardiac arrest surveillance: Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005—December 31, 2010. *MMWR Surveill Summ*. 2011;60(8):1-19.

30. Nichol G, Thomas E, Callaway CW, et al; Resuscitation Outcomes Consortium Investigators. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300(12):1423-1431.

31. Wang HE, Mann NC, Mears G, Jacobson K, Yealy DM. Out-of-hospital airway management in the United States. *Resuscitation*. 2011;82(4):378-385.

32. Wang HE, Yealy DM. Managing the airway during cardiac arrest. *JAMA*. 2013;309(3):285-286.

33. Pell JP, Sirel JM, Marsden AK, Ford I, Cobbe SM. Effect of reducing ambulance response times on deaths from out of hospital cardiac arrest: cohort study. *BMJ*. 2001;322(7299):1385-1388.

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Mechanical versus manual chest compression for out-of-hospital cardiac arrest (PARAMEDIC): a pragmatic, cluster randomised controlled trial

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Summary

Background Mechanical chest compression devices have the potential to help maintain high-quality cardiopulmonary resuscitation (CPR), but despite their increasing use, little evidence exists for their effectiveness. We aimed to study whether the introduction of LUCAS-2 mechanical CPR into front-line emergency response vehicles would improve survival from out-of-hospital cardiac arrest.

Methods The pre-hospital randomised assessment of a mechanical compression device in cardiac arrest (PARAMEDIC) trial was a pragmatic, cluster-randomised open-label trial including adults with non-traumatic, out-of-hospital cardiac arrest from four UK Ambulance Services (West Midlands, North East England, Wales, South Central). 91 urban and semi-urban ambulance stations were selected for participation. Clusters were ambulance service vehicles, which were randomly assigned (1:2) to LUCAS-2 or manual CPR. Patients received LUCAS-2 mechanical chest compression or manual chest compressions according to the first trial vehicle to arrive on scene. The primary outcome was survival at 30 days following cardiac arrest and was analysed by intention to treat. Ambulance dispatch staff and those collecting the primary outcome were masked to treatment allocation. Masking of the ambulance staff who delivered the interventions and reported initial response to treatment was not possible. The study is registered with Current Controlled Trials, number ISRCTN08233942.

Findings We enrolled 4471 eligible patients (1652 assigned to the LUCAS-2 group, 2819 assigned to the control group) between April 15, 2010 and June 10, 2013. 985 (60%) patients in the LUCAS-2 group received mechanical chest compression, and 11 (<1%) patients in the control group received LUCAS-2. In the intention-to-treat analysis, 30 day survival was similar in the LUCAS-2 group (104 [6%] of 1652 patients) and in the manual CPR group (193 [7%] of 2819 patients; adjusted odds ratio [OR] 0·86, 95% CI 0·64–1·15). No serious adverse events were noted. Seven clinical adverse events were reported in the LUCAS-2 group (three patients with chest bruising, two with chest lacerations, and two with blood in mouth). 15 device incidents occurred during operational use. No adverse or serious adverse events were reported in the manual group.

Interpretation We noted no evidence of improvement in 30 day survival with LUCAS-2 compared with manual compressions. On the basis of ours and other recent randomised trials, widespread adoption of mechanical CPR devices for routine use does not improve survival.

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Introduction

The burden of cardiac arrest out of hospital is substantial, with an estimated 424 000 cardiac arrests occurring each year of about in the USA[1] and 275 000 in Europe.[2] As few as one in 12 victims of cardiac arrest out of hospital survive to return home.[3,4] High-quality chest compressions of sufficient depth[5] and rate,[6] with full recoil of the chest between compressions[7] and avoidance of interruptions[8] are crucial to survival. Maintenance of high-quality compressions during out-of-hospital resuscitation is difficult because of the small number of crew present, fatigue, patient access, competing tasks (eg, defibrillation, vascular access) and difficulty of performing resuscitation in a moving vehicle.[9]

Mechanical compression devices suitable for use in the pre-hospital environment have been developed to automate and potentially improve this process. At the time of initiating this study, one large randomised trial of a load distributing band mechanical device had been done and was terminated early because of the worsened long-term outcomes in patients allocated to mechanical compression.[10] The subsequent Cochrane review reported insufficient evidence to conclude that mechanical chest compressions are associated with benefit or harm and their widespread use is not supported.[11] Since then, two further large randomised efficacy trials have been reported. The CIRC trial[12] assessed the load distributing band and reported it was equivalent to manual cardiopulmonary resuscitation

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See Online for appendix

(CPR). The LINC trial[13] assessed the LUCAS device and concluded that mechanical CPR did not result in improved outcomes compared with manual CPR.[13]

Previous trials were designed as efficacy (explanatory) trials, which aim to answer the question "Can this intervention work under ideal conditions?". We sought to study mechanical CPR use under real life conditions, and therefore adopted a pragmatic design for the pre-hospital randomised assessment of a mechanical compression device in cardiac arrest (PARAMEDIC) trial. The trial sought to assess whether LUCAS-2 was better than manual CPR for the improvement of 30 day survival in adults receiving resuscitation for non-traumatic, out-of-hospital cardiac arrest.

Methods

Trial design and participants

The PARAMEDIC trial was a pragmatic, cluster randomised trial, with ambulance service vehicles as the unit of randomisation. The trial protocol has been published previously.[14]

The trial was done in partnership with four UK National Health Service (NHS) Ambulance Services (West Midlands, North East England, Wales, South Central). These sites serve a total population of 13 million people spread over 62 160 km². We selected 91 ambulance stations for participation based on their location (urban and semi-urban settings, representing 25% of stations). A dispatch centre in each region coordinated the emergency response. The nearest available rapid response vehicle (RRV) or ambulance was dispatched to cases of suspected cardiac arrest. Back-up was provided by a second vehicle as soon as possible. If there was clear evidence that life was extinct (eg, rigor mortis, post-mortem staining; see appendix for full details) or the patient had a do-not-attempt-resuscitation order, ambulance staff were authorised to recognise death and withhold CPR. Where resuscitation was indicated, ambulance staff had been trained in advanced airway management, drug administration, and external defibrillation, and follow standardised national guidelines based on the European Resuscitation Council Guidelines.[15,16] If the patient did not respond despite full ALS intervention and remained asystolic for more than 20 min then the resuscitation attempt could be discontinued. Unless these criteria were met, resuscitation was continued and the patient was transported to the nearest emergency department with continuous CPR. CPR quality and feedback technology was not available in any of the participating ambulance services.

We chose broad eligibility criteria, indicating the pragmatic nature of the trial. Individual patients were included in the study if a trial vehicle was the first ambulance service vehicle on scene, the patient was in cardiac arrest outside of a hospital, resuscitation was attempted, and the patient was known or believed to be aged 18 years or older. Exclusion criteria were cardiac arrest caused by trauma, and known or clinically apparent pregnancy.

Ambulance services recorded cardiac arrest data according to variables contained in the Utstein template.[17] Every ambulance service submitted these data to a central trial database.

Enrolment proceeded with a waiver of informed consent, in line with the Mental Capacity Act 2005. The trial team contacted patients who were discharged from hospital to let them know of their enrolment and to invite them to take part in the follow-up 3 months and 12 months after cardiac arrest. Those willing to take part provided written informed consent. For those who did not have capacity, a personal consultee completed the questionnaires on behalf of the patient.

The Coventry Research Ethics Committee (reference 09/H1210/69) approved the study, and University of Warwick, UK sponsored it. The study was done in accordance with the principles of Good Clinical Practice and the Mental Capacity Act (2005).

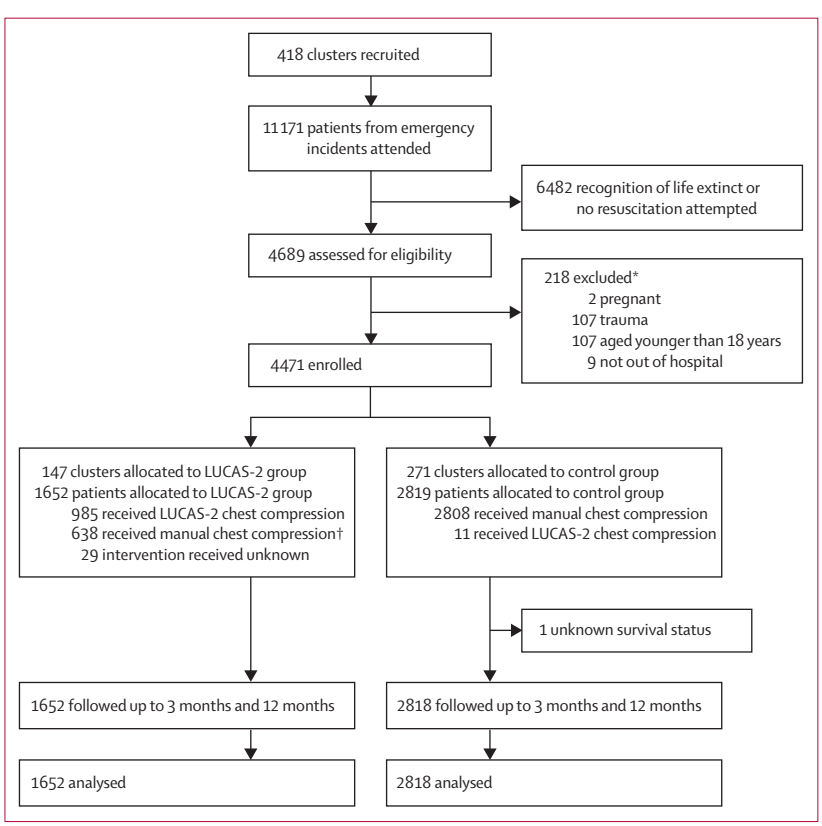

Figure 1: **Trial profile**
*Seven met more than one exclusion criteria. †Reasons LUCAS-2 not used: 78 because of crew not trained; 168 because of crew error; 26 no device in vehicle; 102 unsuitable patients (58 patient too large, 22 patient too small, 22 other reason–eg, chest deformity), 14 device issues, 140 not possible to use device; 110 reason unknown. Reasons for LUCAS-2 use in control group were crew error.

Randomisation and masking

Because the number of LUCAS devices available to the trial was limited to 143, we used a ratio of about 1 LUCAS to 2 control to optimise efficiency. Individual ambulance

vehicles (clusters) were assigned with a computer-generated randomisation sequence, which stratified by station and vehicle type (ambulance or RRV).

Individual patients were allocated to the LUCAS-2 or control (standard manual chest compression) group according to the first trial vehicle on scene. We obtained information from ambulance services on all potential cardiac arrests attended by trial vehicles, and included all eligible patients in the trial, thereby minimising selection bias.

Ambulance dispatch staff were unaware of the randomised allocations. Masking of ambulance clinicians was not possible, since they gave the intervention. Vehicles randomly assigned to LUCAS-2 were identified to ambulance clinical staff at the start of the shift during vehicle checks and through stickers contained in the cab of the vehicle and on the outside of the vehicle. We extracted short-term outcomes from ambulance or hospital records. We obtained survival status at 30 days, 3 months, and 12 months from the NHS Information Centre's central death register. Trial staff who assessed patient neurological outcome were unaware of the randomised allocation or the treatment received.

Procedures

Paramedics seconded to work on the trial and clinical educator staff trained all operational ambulance staff to use LUCAS-2. Because of the vehicle movements and staff rotations, staff serviced vehicles that were randomly assigned to both LUCAS-2 and manual groups. Training was carefully designed by the ambulance services on the basis of the manufacturers guidance. Because of the pragmatic design of this trial, training was developed in accordance with the process by which new technology would be introduced in routine practice into NHS Ambulance Services. This preparation included access to online training resources and included 1–2 h face-to-face training, updated annually. Training covered the study protocol and procedures, how to operate the LUCAS-2 device, and the importance of high-quality CPR. Training included hands-on device deployment practice, with a resuscitation manikin, and emphasised the importance of rapid deployment with minimum interruptions in CPR. A competency checklist was completed before authorising staff to deploy the LUCAS-2 device. Research paramedics reviewed all cases and provided feedback to individual staff as required. The rate of device use and reasons for non-use were fed back to participating services on a quarterly basis.

LUCAS-2 (Physio-Control Inc/Jolife AB, Lund, Sweden) provides chest compressions between 40–53 mm in depth (according to patient size) at a rate of 102 min^{-1} and ensures full chest recoil between compressions and an equal time in compression and decompression. In the LUCAS-2 group, staff initiated manual CPR and switched the device on. Once powered up manual compressions were paused briefly while the back plate was inserted. CPR was restarted while the central arms were positioned until locked in place, suction cup was deployed and device activated. After this procedure, ECG monitoring was

	LUCAS-2 (n=1652)	Manual CPR (n=2819)
Age, years (mean [SD])	71·0 (16·3)	71·6 (16·1)
Male	1039 (63%)	1774 (63%)
Aetiology		
Presumed cardiac	1417 (86%)	2445 (87%)
Respiratory	125 (8%)	191 (7%)
Submersion	5 (<1%)	7 (<1%)
Unknown	48 (3%)	74 (3%)
Other (non-cardiac)	57 (3%)	102 (4%)
Location		
Home	1336 (81%)	2336 (83%)
Public place	225 (14%)	362 (13%)
Other	91 (6%)	121 (4%)
Witnessed cardiac arrest	1001 (61%)	1749 (62%)
Bystander	704 (43%)	1223 (43%)
EMS	250 (15%)	449 (16%)
Non-EMS health care	47 (3%)	75 (3%)
Not known	0	2 (<1%)
Bystander CPR before EMS arrival		
CPR n (%)	716 (43%)	1238 (44%)
Not known	90 (5%)	168 (6%)
Median time from emergency call to vehicle arrival, min (IQR)	6·5 (4·8–9·1)	6·3 (4·6–9·2)
Initial rhythm		
VF	364 (22%)	597 (21%)
VT	12 (1%)	18 (1%)
PEA	398 (24%)	707 (25%)
Asystole	824 (50%)	1384 (49%)
Not known	54 (3%)	113 (4%)
Defibrillation before EMS arrival	19 (1%)	40 (2%)
Treatment of cardiac arrest		
Intravenous drugs given	1366 (83%)	2255 (80%)
Not known	8 (<1%)	14 (<1%)
Intubation		
Intubated	749 (45%)	1297 (46%)
Not known	33 (2%)	48 (2%)
LMA or supraglottic airway device		
LMA or supraglottic airway device used	435 (26%)	736 (26%)
Not known	29 (2%)	47 (2%)
Transport to hospital	1099 (67%)	1868 (66%)
Transport to hospital status at handover		
ROSC	377 (23%)	658 (23%)
CPR in progress	640 (39%)	1081 (38%)
Unknown	82 (5%)	129 (5%)

Data are n (%) or mean (SD). CPR=cardiopulmonary resuscitation. EMS=emergency medical services. VF=ventricular fibrillation. VT=ventricular tachycardia. PEA=pulseless electrical activity. LMA=laryngeal mask airway. ROSC=return of spontaneous circulation.

Table 1: **Baseline characteristics and treatment**

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established and LUCAS-2 was briefly paused to check the ECG rhythm. If the patient was in a shockable rhythm LUCAS-2 was restarted and defibrillation was attempted with continuous mechanical CPR.

Patients in the control group received manual CPR aiming for a target compression depth of 50–60 mm, rate 100–120 min^{-1}, full recoil between compressions and an equal time in compression and decompression in line with guidelines. CPR was started on arrival and ECG monitoring established. Chest compressions were paused briefly to allow rhythm analysis and if appropriate, attempted defibrillation. Both groups received compression to ventilation ratio of 30:2 before intubation and continuous compressions with asynchronous ventilation after intubation.

Outcomes

The primary outcome of the study was survival to 30 days after the cardiac arrest event. The main secondary clinical outcomes were survived event (return of spontaneous circulation [ROSC] sustained until admission and transfer of care to medical staff at the receiving hospital), survival to 3 months, survival to 12 months, and survival with favourable neurological outcome at 3 months. The initial trial protocol originally specified survival to hospital discharge as an additional outcome; this outcome is not reported here because survival to 30 days is more clinically meaningful, and these data could not be obtained from all hospitals included in the trial because of logistical and governance difficulties. We have reported ROSC as an additional (non-prespecified) outcome since it is part of the Utstein template.[17]

We defined favourable neurological outcome as a Cerebral Performance Category (CPC) score[17] of 1 or 2 at 3 months. CPC was extracted from medical records or assessed at a face-to-face visit done by research staff.

	LUCAS-2 (n=1652)	Control (n=2819)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Survival to 30 days				
Survived to 30 days	104 (6%)	193 (7%)	0·91 (0·71–1·17)	0·86 (0·64–1·15)
Not known	0	1 (<1%)	··	··
ROSC				
ROSC	522 (32%)	885 (31%)	1·02 (0·89–1·16)	0·99 (0·86–1·14)
Not known	58 (4%)	82 (3%)	··	··
Survived event				
Survived event	377 (23%)	658 (23%)	0·97 (0·83–1·14)	0·97 (0·82–1·14)
Not known	82 (5%)	129 (5%)	··	··
Survival to 3 months				
Survived to 3 months	96 (6%)	182 (6%)	0·89 (0·69–1·15)	0·83 (0·61–1·12)
Not known	0	1 (<1%)	··	··
Survival to 12 months	89 (5%)	175 (6%)	0·86 (0·60–1·12)	0·83 (0·62–1·11)
Survival with favourable neurological outcome (CPC 1–2)	77 (5%)	168 (6%)	0·77 (0·59–1·02)	0·72 (0·52–0·99)
CPC			··	··
1	67 (4%)	153 (5%)	··	··
2	10 (1%)	15 (1%)	··	··
3	14 (1%)	10 (<!%)	··	··
4	2 (<1%)	1 (<1%)	··	··
5	1556 (94%)	2636 (94%)	··	··
Not known	3 (<1%)	4 (<1%)	··	··

Data are n (%) unless otherwise indicated. OR=odds ratio. ROSC=return of spontaneous circulation. CPC=cerebral performance category score.

Table 2: **Outcomes**

Statistical analysis

At the time of the design of this study, there were no randomised trials using the LUCAS device on which to base the likely treatment effect. We determined the minimally important difference to our decision makers (the NHS) through discussion with partner ambulance services and subsequent agreement with the funder. The study had 80% power to find a significant result (with threshold two-sided p value of 0·05) if the incidence of survival to 30 days was 5% in the manual CPR group and 7·5% in the LUCAS-2 group. Using an intracluster correlation coefficient of 0·01 to allow for clustering, and a cluster size of 15, we aimed to recruit 245 clusters (3675 patients) into the trial.

The target sample size was revised in September, 2012, after recruitment of 2469 patients, to take account of the frequency of use of LUCAS-2 and updated information on the cluster size. With the agreement of the Data Monitoring Committee and the Trial Steering Committee, we increased the target sample size to 4344 patients. We estimated this sample size to have a sufficient number of cases of LUCAS-2 use to maintain the originally specified power. The sample size re-estimation did not use any information from comparisons between the trial groups.

The primary analysis was by intention to treat. This analysis explores if the treatment works under the usual conditions, with all the noise inherent therein. We used complier average causal effect (CACE) analyses, to estimate the effect in cardiac arrest where the protocol was followed.[18,19] CACE estimates the treatment effect in people randomly assigned to the intervention who actually received it, by comparing compliers in the intervention group with those participants in the control group who would have been compliers if they had been allocated to the intervention group. This analysis retains the advantages of randomisation and avoids introducing bias, hence CACE is preferred to per-protocol analysis. We did two CACE analyses, defining compliers in different ways. In CACE1, we treated as non-compliant those cases in which LUCAS-2 was not used for unknown or trial-related reasons that would not occur in real-life clinical practice (eg, crew were not trained in trial procedures, crew misunderstood the trial protocol, the device was missing from the vehicle). This analysis omits trial-related non-use and might be a better estimate of the treatment effect in real-world clinical practice analysis by intention to treat. In the CACE2 analysis, we only treated as compliant those

cases in which LUCAS-2 was actually used, and this analysis therefore estimates efficacy—ie, the treatment effect in patients who received LUCAS-2.

For intention-to-treat analyses, we used fixed-effect logistic regression models to obtain unadjusted and adjusted odds ratios (ORs) and 95% CIs. The prespecified covariates used in the adjusted models were age, sex, response time, bystander CPR, and initial rhythm. We attempted adjusting for the clustering design using multilevel logistic models (using the GLIMMIX procedure with logit link function based on the binomial distribution). Because of the extremely low survival rates in each cluster (vehicle), the multilevel models could not be fitted with the vehicle random effect since this effect was not estimable. For this reason, we assumed that the intracluster correlation coefficient was negligible (0·001) and ordinary logistic regressions were fitted. We also did prespecified subgroup analyses, by: (1) initial rhythm (shockable *vs* non-shockable); (2) cardiac arrest witnessed versus not witnessed; (3) type of vehicle (RRV versus ambulance); (4) bystander CPR versus no bystander CPR; (5) region, and (6) aetiology (presumed cardiac, or non-cardiac); (7) age and (8) response time. We fitted logistic regression models for the primary outcome measure with the inclusion of an interaction term to examine whether the treatment effect differed between the subgroups. Age and response times are continuous variables and we assessed these using multivariate fractional polynomials.

We did all analyses using Statistical Analysis Software (SAS) version 9·3 (SAS Institute, Marlow, UK). This trial is registered on the International Standard Randomised Controlled Trial Number Register, number ISRCTN08233942.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. RL had full access to all data in the study. GDP and SG had final responsibility for the decision to submit for publication.

Results

We recruited 418 emergency vehicles (287 dual-manned ambulances and 131 single-manned rapid response vehicles) and randomly assigned them to either the LUCAS-2 group (147 clusters) or the control group (271 clusters; ratio 1:1·8; figure 1). In the 3 years of the study, individual ambulance staff attended on average 4·1 (3·6) arrests in the control group and 3·0 (2·3) in the LUCAS group.

The trial ran between April 15, 2010, and June 10, 2013 (with a 12 months' follow-up) during which time trial vehicles attended 11171 emergency incidents (figure 1). The trial finished when the revised target sample size was exceeded. Cardiac arrest was confirmed and resuscitation attempted in 4689 cases of which 218 cases were ineligible and excluded. The proportion of arrests for which resuscitation was attempted did not differ between groups (1737 [41%] of 4192 for the LUCAS-2 group; 2953 [42%] of 6980 for the control group).

4471 patients were enrolled in the study. 985 (60%) of the 1652 patients in the LUCAS-2 group received mechanical chest compression. The reasons for non-use of LUCAS-2 were trial related (n=272), not possible (n=256), or unknown (n=110; figure 1). We did not note any major imbalances in baseline characteristics between the trial groups (table 1). One patient in the control group was lost to follow-up. No patient requested to withdraw their data from the study.

For the primary outcome, 30 day survival was similar in the LUCAS-2 and control groups (104 [6%] of patients in the LUCAS-2 group, 193 [7%] of patients in the control group, adjusted OR 0·86 [95% CI 0·64–1·15]; table 2)

The proportion of patients achieving any ROSC and sustained ROSC with spontaneous circulation until admission and transfer of care to the medical staff at the receiving hospital (survived event) was very similar in the two groups (table 2). Survival at 3 months was also similar to the primary outcome, indicating that little mortality occurs between 30 days and 3 months.

The number of patients with a favourable neurological outcome (CPC 1 or 2) was lower in the LUCAS-2 group than in the control group (table 2).

Both CACE analyses had similar results to those of the intention-to-treat analysis and are presented in table 3. LUCAS-2 had almost no effect on ROSC and survival of event, and 30 day survival did not differ between groups. The ORs for 30 day survival were similar to those for the intention-to-treat analysis, but the 95% CIs were slightly wider (table 2). However, survival with CPC1-2 was lower in the LUCAS-2 group

	CACE 1			CACE 2		
	LUCAS-2	Control	OR (95% CI)	LUCAS-2	Control	OR (95% CI)
Survival to 30 days	81/1241 (7%)	153/2155 (7%)	0·92 (0·69–1·21)	50/985 (5%)	99/1710 (6%)	0·87 (0·61–1·23)
CPC 1–2	62/1238 (5%)	142/2151 (7%)	0·76 (0·56–1·03)	38/983 (4%)	101/1701 (6%)	0·65 (0·45–0·96)
Survived event	297/1241 (24%)	537/2026 (27%)	0·90 (0·77–1·06)	232/985 (24%)	415/1704 (24%)	0·97 (0·81–1·16)
ROSC	410/1212 (34%)	702/2104 (33%)	1·01 (0·88–1·17)	318/971 (33%)	538/1680 (32%)	1·02 (0·87–1·19)

CPC=cerebral performance category score. ROSC=return of spontaneous circulation. CACE=complier average causal effect.

Table 3: **CACE analyses**

	LUCAS-2	Control	OR (95% CI)
Initial rhythm			
VF or VT	69/376 (18%)	148/615 (24%)	0·71 (0·52–0·98)*
PEA or asystole	24/1222 (2%)	30/2090 (1%)	1·38 (0·80–2·36)
Rhythm not known	54	113	..
Witnessed status			
Witnessed	89/1001 (9%)	163/1749 (9%)	0·96 (0·73–1·25)
Not witnessed	10/528 (2%)	21/864 (2%)	0·78 (0·36–1·66)
Witnessed status not known	123	205	..
Bystander CPR			
Given	42/716 (6%)	68/1238 (5%)	1·07 (0·72–1·59)
Not given	59/846 (7%)	115/1413 (8%)	0·86 (0·61–1·17)
Not known	90	167	..
Type of vehicle			
Ambulance	60/1063 (6%)	127/1773 (8%)	0·78 (0·56–1·06)
Rapid response car	44/589 (7%)	66/1045 (6%)	1·20 (0·81–1·78)
Region			
A	16/186 (9%)	23/357 (6%)	1·37 (0·70–2·66)
B	9/148 (6%)	33/359 (9%)	0·64 (0·30–1·37)
C	19/346 (5%)	22/352 (6%)	0·87 (0·46–1·64)
D	60/972 (6%)	115/1750 (7%)	0·94 (0·68–1·29)
Aetiology			
Presumed cardiac	91/1417 (6%)	173/2445 (7%)	0·90 (0·69–1·17)
Other	9/130 (7%)	7/198 (4%)	2·03 (0·74–5·59)

Data are n/N (%) unless otherwise indicated. VT=ventricular tachycardia. PEA=pulseless electrical activity. CPR=cardiopulmonary resuscitation. VF=ventricular fibrillation. *Interaction effect of subgroup p<0·05.

Table 4: **Subgroup analyses for primary outcome (30 day survival)**

than in the control group in both CACE analyses. The appendix includes patient characteristics for the CACE analyses.

Subgroup analyses according to whether the arrest was witnessed, type of vehicle (ambulance or solo responder car), whether the patient received bystander CPR, aetiology, and region showed no significant difference in 30 day survival between the subgroups (table 4).

The subgroup analysis by initial rhythm showed a difference in treatment effect between patients with a shockable initial rhythm and those with PEA or asystole; survival was lower in the LUCAS-2 group in those with shockable initial rhythms than in the control group.

Seven clinical adverse events were reported in the LUCAS-2 group (three events of chest bruising, two of chest laceration, and two of blood in mouth). No serious adverse events were reported. 15 device incidents occurred during operational use (four incidents in which alarms sounded, seven in which the device stopped working, and four other device incidents). No adverse or serious adverse events were reported in the control group.

Panel: **Research in context**

Systematic review

We searched PubMed and The Cochrane Library from 2002, to September, 2014, for randomised trials assessing LUCAS for out of hospital cardiac arrest, using a combination of text (LUCAS, LUCAS-2, cardiac arrest, mechanical chest compression, mechanical CPR) and medical subject headings terms (out-of-hospital cardiac arrest; death, sudden, cardiac; heart arrest). We identified two randomised trials: LINC,[13] which was sponsored by the manufacturer of LUCAS and recruited 2593 patients, and a much smaller pilot study[20] done by the same investigators. We assessed bias risk of the trials using the Cochrane risk of bias method. Both of the included trials were at low risk of bias for randomisation methods, completeness of data, and selective reporting. Masking of clinicians, participants, and outcome assessment was not possible, but mortality and CPC score were very unlikely to have been influenced by knowledge of trial allocations. We noted some important differences between LINC and PARAMEDIC. First, the intervention assessed in LINC was a new treatment algorithm including mechanical chest compression, whereas in PARAMEDIC, mechanical chest compression was simply used to replace manual chest compression. Second, survivors in LINC were treated with hypothermia, whereas in PARAMEDIC post-resuscitation care was given according to hospitals' usual practice.

Interpretation

Meta-analysis of the outcomes survived event and survival to hospital discharge or 30 days showed no evidence of inconsistency between the three trials' results, and no evidence of improvement with LUCAS (survived event odds ratio [OR] 1·00, 95% CI 0·90–1·11; survival OR 0·96, 0·80–1·15). The two trials that reported survival with CPC 1–2 had inconsistent results (I^2=69%), but overall did not suggest that outcomes were better with LUCAS than with manual chest compression (random effects model OR 0·93, 0·64–1·33). The reasons for the inconsistency are unclear, but could be related to the differences between the trials, particularly in relation to the implementation strategies adopted. PARAMEDIC supports the finding from LINC that use of LUCAS does not lead to an improvement in survival, but additionally found that neurological outcomes might be worse.

Discussion

In this pragmatic, cluster randomised trial, the introduction of LUCAS-2 did not improve the primary outcome of survival to 30 days. Meta-analysis of the present study's findings alongside the results of the two previous randomised trials including the LUCAS mechanical CPR device showed no evidence of superiority in 30 day survival, survival to discharge, or neurological function at 3 months (panel, figure 2).

This study was designed to assess the effectiveness of LUCAS-2 when implemented in a real life setting. As such it differed from recent industry sponsored efficacy

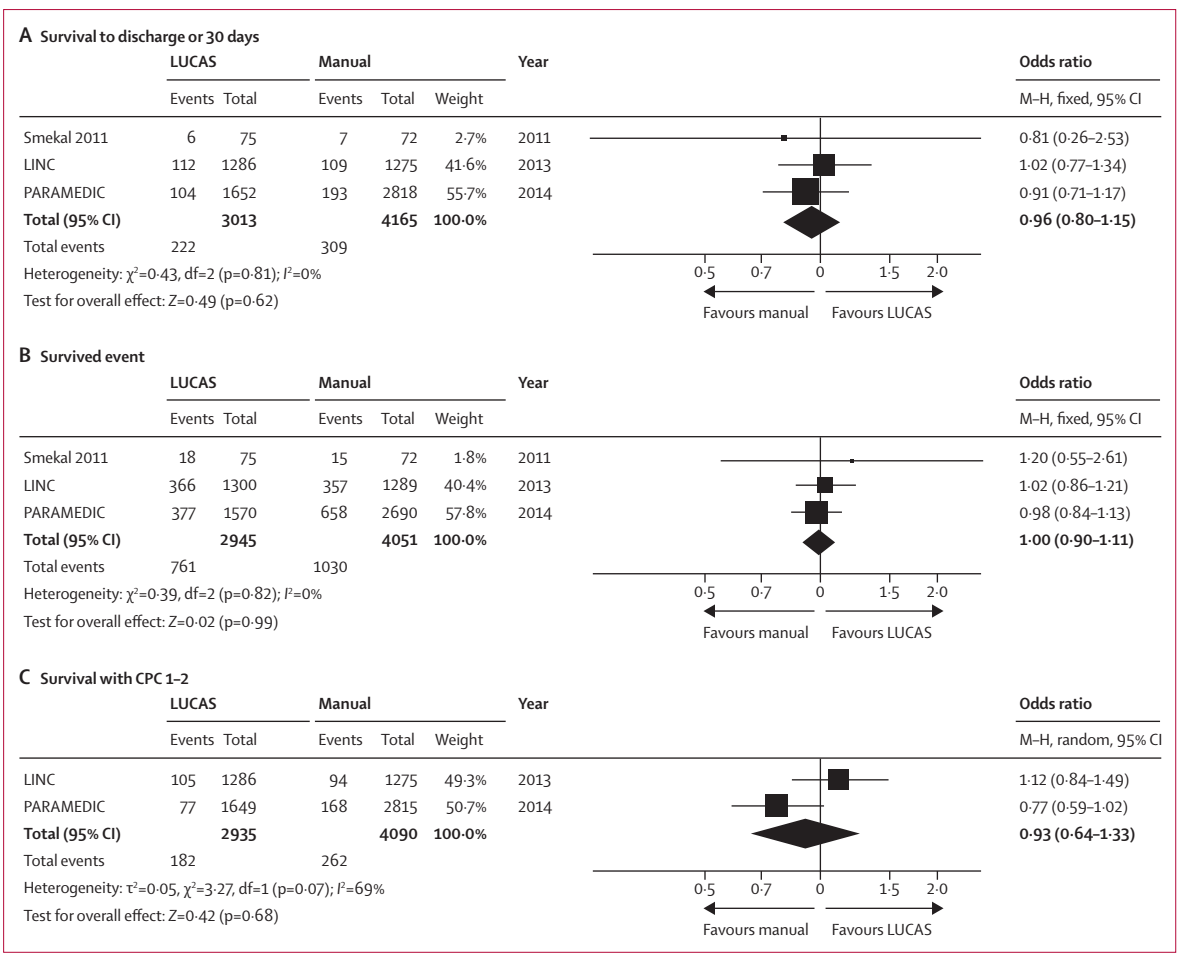

Figure 2: **Meta-analysis of the outcomes survived event and survival to hospital discharge or 30 days**
(A) Survival to discharge or 30 days. (B) Survived event. (C) Survival with CPC 1–2.

trials[12,13] which included more intensive initial and re- training, a run-in period; and in one study,[12] a statistical inclusion phase whereby patients were excluded from analysis if quality of implementation fell below a predefined threshold. Our pragmatic approach to training, developed by experienced ambulance training staff, portrayed the training that would be delivered when rolling out new technology across UK ambulance services. In this setting, the average ambulance paramedic only encounters one to two cardiac arrests annually[21] and CPR update training is provided annually, so it is unlikely that individuals became expert in the use of the device.

The success of implementation is particularly important when balancing the benefit versus harm potential for mechanical chest compression devices since interruptions in CPR and delays in device deployment are a major factor that can impact outcomes.[22] In the present study 985 (60%) of 1652 patients randomly assigned to LUCAS received the allocated intervention. While some cases of non-use were due to patient-related and device-related factors, a proportion (15%) arose because of difficulties inherent with implementation of new equipment and the training and quality issues associated with this. Another key difference between our study and other recent trials was the absence of CPR feedback technology in the participating ambulance services. CPR feedback devices allow the measurement and adjustment of CPR quality at the bedside.[23] Although international guidelines published in 2010[24] suggested the devices could be considered as part of an overall strategy to improve CPR quality, their adoption into clinical practice has been variable. The scarcity of this technology limited our ability to report on the quality of CPR and monitor the performance of our implementation strategy. These findings serve to highlight the potential limitations of expecting the findings from efficacy trials to translate to real life practice without applying the same degree of rigor, attention and assessment applied during the index trials.

The sample size was increased to maintain the power of the study on the basis of the rate at which the intervention was used in practice. The intention-to-treat

analysis provides the answer to our primary question of the effectiveness of implementation of mechanical CPR into routine clinical practice. The two CACE analyses estimate the treatment effect of LUCAS in participants who were compliant with the trial protocol, and those where LUCAS was actually used. Since this approach retains the initial randomised assignment, it overcomes the issues related to per-protocol and on-treatment analyses. These analyses served to confirm the direction of findings from the intention-to-treat analysis.

The findings of marginally worse neurological outcomes and lower survival in patients presenting with an initially shockable rhythm was unexpected. Although these analyses were defined a priori, they were not the primary objective of the trial and should be interpreted with caution and deemed as hypothesis generating. One of these hypotheses is that interruptions in CPR during device deployment could cause reduced cardiac and cerebral perfusion. Alternatively, slightly more patients received adrenaline after randomisation in the LUCAS group than in the control group, which might increase cardiac instability and impair cerebral microcirculation.[25] Finally, deployment of LUCAS before the first shock is likely to have led to a delay in the time to first shock, which might in itself reduce survival.[26]

We chose to use a cluster randomised design with vehicles as the unit of randomisation. This design allowed us to include all cardiac arrests where a trial vehicle was first on scene, because recruitment to the trial was not dependent on a paramedic making a decision to randomise. This means that one of the major potential drawbacks of cluster randomisation, selection bias, was avoided because we have included in the trial all of the eligible patients. It is possible that selection bias could be introduced by paramedics having a lower threshold for initiation of resuscitation, in view of the knowledge that a LUCAS device was present. The independent data monitoring committee monitored this throughout the trial, by looking at the proportions of patients resuscitated when LUCAS and control vehicles were first on scene, and the characteristics of patients recruited to the two trial groups. No evidence of different resuscitation thresholds was found.

The implementation process was tailored to reflect how such technology would be implemented in the NHS and the study findings should be considered in that context. Health-care systems will need to consider carefully the findings from this and previous studies when considering the role of mechanical CPR during out-of-hospital cardiac arrest. Deployment across entire services will require substantial capital investment. This investment must be balanced against the accepted role such devices will continue to have when manual CPR is impractical or increased risk (eg, in a moving ambulance). Where organisations decide to adopt mechanical CPR it seems essential that sufficient resources are made available to support initial and regular refresher training and ongoing quality assurance. Future research should look to define the optimum method and frequency of such training.

In conclusion, this trial was unable to show any superiority of mechanical CPR and highlights the difficulties of training and implementation in real world EMS systems.

Contributors

GDP, RL, TQ, CDD, MWC, SEL, AMS, MW, RW and SG designed the trial. JH, AC, MS, RW, AW, HP, JB, JW, KH led recruitment and data collection. RL analysed the data which was interpreted by the co-authors. GDP, RL, TQ, CDD and SG drafted the paper with input from co-authors. The final paper has been approved by all authors.

Collaborators

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Declaration of interests

GDP, RL, TQ, CDD, MWC, SEL, A-MS, MW, RW and SG report grants from NIHR HTA Programme during the conduct of the study. The other authors declare no competing interests.

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References

1 Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation* 2014; **129:** e28–e292.

2 Atwood C, Eisenberg MS, Herlitz J, Rea TD. Incidence of EMS-treated out-of-hospital cardiac arrest in Europe. *Resuscitation* 2005; **67:** 75–80.

3 Perkins GD, Cooke MW. Variability in cardiac arrest survival: the Ambulance Service Quality Indicators. *Emerg Med J* 2012; **29:** 3–5.

4 Wang HE, Devlin SM, Sears GK, et al. Regional variations in early and late survival after out-of-hospital cardiac arrest. *Resuscitation* 2012; **83:** 1343–48.

5 Vadeboncoeur T, Stolz U, Panchal A, et al. Chest compression depth and survival in out-of-hospital cardiac arrest. *Resuscitation* 2014; **85:** 182–88.

6 Idris AH, Guffey D, Aufderheide TP, et al. Relationship between chest compression rates and outcomes from cardiac arrest. *Circulation* 2012; **125:** 3004–12.

7 Zuercher M, Hilwig RW, Ranger-Moore J, et al. Leaning during chest compressions impairs cardiac output and left ventricular myocardial blood flow in piglet cardiac arrest. *Crit Care Med* 2010; **38:** 1141–46.

8 Christenson J, Andrusiek D, Everson-Stewart S, et al. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. *Circulation* 2009; **120:** 1241–47.

9 Krarup NH, Terkelsen CJ, Johnsen SP, et al. Quality of cardiopulmonary resuscitation in out-of-hospital cardiac arrest is hampered by interruptions in chest compressions—a nationwide prospective feasibility study. *Resuscitation* 2011; **82:** 263–69.

10 Hallstrom A, Rea TD, Sayre MR, et al. Manual chest compression vs use of an automated chest compression device during resuscitation following out-of-hospital cardiac arrest: a randomized trial. *JAMA* 2006; **295:** 2620–28.

11 Brooks SC, Hassan N, Bigham BL, Morrison LJ. Mechanical versus manual chest compressions for cardiac arrest. *Cochrane Database Syst Rev* 2014; **2:** CD007260.

12 Wik L, Olsen JA, Persse D, et al. Manual vs. integrated automatic load-distributing band CPR with equal survival after out of hospital cardiac arrest. The randomized CIRC trial. *Resuscitation* 2014; **85:** 741–48.

13 Rubertsson S, Lindgren E, Smekal D, et al. Mechanical chest compressions and simultaneous defibrillation vs conventional cardiopulmonary resuscitation in out-of-hospital cardiac arrest: the LINC randomized trial. *JAMA* 2014; **311:** 53–61.

14 Perkins GD, Woollard M, Cooke MW, et al. Prehospital randomised assessment of a mechanical compression device in cardiac arrest (PaRAMeDIC) trial protocol. *Scand J Trauma Resusc Emerg Med* 2010; **18:** 58.

15 Koster RW, Baubin MA, Bossaert LL, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 2. Adult basic life support and use of automated external defibrillators. *Resuscitation* 2010; **81:** 1277–92.

16 Deakin CD, Nolan JP, Soar J, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 4. Adult advanced life support. *Resuscitation* 2010; **81:** 1305–52.

17 Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). *Resuscitation* 2004; **63:** 233–49.

18 Dunn G, Maracy M, Dowrick C, et al. Estimating psychological treatment effects from a randomised controlled trial with both non-compliance and loss to follow-up. *Br J Psychiatry* 2003; **183:** 323–31.

19 Hewitt CE, Torgerson DJ, Miles JN. Is there another way to take account of noncompliance in randomized controlled trials? *CMAJ* 2006; **175:** 347.

20 Smekal D, Johansson J, Huzevka T, Rubertsson S. A pilot study of mechanical chest compressions with the LUCAS™ device in cardiopulmonary resuscitation. *Resuscitation* 2011; **82:** 702–06.

21 Deakin CD, King P, Thompson F. Prehospital advanced airway management by ambulance technicians and paramedics: is clinical practice sufficient to maintain skills? *Emerg Med J* 2009; **26:** 888–91.

22 Ong ME, Annathurai A, Shahidah A, et al. Cardiopulmonary resuscitation interruptions with use of a load-distributing band device during emergency department cardiac arrest. *Ann Emerg Med* 2010; **56:** 233–41.

23 Yeung J, Meeks R, Edelson D, Gao F, Soar J, Perkins GD. The use of CPR feedback/prompt devices during training and CPR performance: a systematic review. *Resuscitation* 2009; **80:** 743–51.

24 Nolan JP, Hazinski MF, Billi JE, et al. Part 1: executive summary: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Resuscitation* 2010; **81** (suppl 1)**:** e1–25.

25 Perkins GD, Cottrell P, Gates S. Is adrenaline safe and effective as a treatment for out of hospital cardiac arrest? *BMJ* 2014; **348:** g2435.

26 Stiell IG, Nichol G, Leroux BG, et al. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. *N Engl J Med* 2011; **365:** 787–97.

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