

Original citation:

Couper, Keith and Perkins, Gavin D.. (2016) Improving outcomes from in-hospital cardiac arrest. *BMJ (Clinical research ed.)*, 353 . i1858.

Permanent WRAP URL:

<http://wrap.warwick.ac.uk/79064>

Copyright and reuse:

The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions. Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

Publisher's statement:

<http://dx.doi.org/10.1136/bmj.i1858>

A note on versions:

The version presented here may differ from the published version or, version of record, if you wish to cite this item you are advised to consult the publisher's version. Please see the 'permanent WRAP URL' above for details on accessing the published version and note that access may require a subscription.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk

Improving outcomes from in-hospital cardiac arrest

Keith Couper,^{1 2} postdoctoral research fellow, Gavin D Perkins,^{1 2} professor

¹Warwick Medical School, University of Warwick, Coventry CV4 7AL, UK

²Heart of England NHS Foundation Trust, Birmingham B9 5SS, UK

Correspondence to: G D Perkins g.d.perkins@warwick.ac.uk

Research, doi:[10.1136/bmj.i1653](https://doi.org/10.1136/bmj.i1653)

Research, doi:[10.1136/bmj.i1577](https://doi.org/10.1136/bmj.i1577)

Make sure local practice is informed by the latest guidelines

Over 200 000 adults a year sustain a cardiac arrest while in hospital in the United States.¹ Most trials have taken place outside hospital,² yet the aetiology, patient characteristics, time to treatment, and outcomes are quite different to cardiac arrests occurring in inpatients. Clinical guidelines for in-hospital resuscitation are therefore mainly drawn from the extrapolation of findings from out-of-hospital trials, observational studies, and consensus of expert opinion coordinated through the International Liaison Committee for Resuscitation.³

Given the cost, logistical, and ethical challenges of conducting randomised trials in cardiac arrest, the use of high quality observational data to provide insights into the effectiveness of treatments is attractive. The main limitation of observational studies is the risk that the outcome is affected by both the treatment allocation and other factors that influence the treatment allocation. Propensity scoring methods have been growing in popularity as a way of reducing confounding related to measured variables.

In critically ill patients, well conducted propensity score analyses generally agree with findings from randomised controlled trials, although the effect size may vary.⁴ A key limitation nevertheless remains the bias caused by unmeasured confounders. This was illustrated in two propensity analyses using data from the same registry on the effect of adrenaline on survival from out-of-hospital cardiac arrest. The studies yielded diametrically opposing results through small differences in the variables included in the propensity scoring model.⁵

In The BMJ, two linked research papers^{6 7} use propensity score analyses of data from the American Heart Association's (AHA) Get With The Guidelines-Resuscitation (GWTG-R) registry to examine the association between different treatment strategies for cardiac arrest and patient outcomes in in-hospital patients with shock refractory ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT).

Bradley and colleagues⁶ explored differences in outcomes between defibrillator shocks delivered in rapid succession (stacked shocks), which formed part of the AHA guidelines in 2000, and the strategy of delivering a single shock strategy followed by 2 minutes of chest compressions, which was introduced in 2005 (fig 1).⁸ Their analysis showed slow adoption of the single shock sequence (increase from 30% in 2006 to 60% in 2012). Although unadjusted analyses showed better hospital survival with stacked shocks, there was no difference after adjustment for propensity scoring (adjusted risk ratio 0.89, 95% confidence interval 0.78 to 1.01).

Fig 1 Difference between defibrillator shock strategies (stacked shocks v single shock sequence), as recommended in the AHA guideline before and after 2005 [A: Legend OK?] [A: The illustrator left out the chart because he thought it looked a bit superfluous, but he can add it back if necessary]

The change in shock sequence from stacked to single shocks was introduced concurrently with the recommendation that adrenaline (epinephrine) administration was deferred until after 2 minutes of cardiopulmonary resuscitation (CPR) after the time of rhythm re-analysis and close to delivery of a second shock (fig 1). The premise for deferring adrenaline was to avoid giving it blindly before determining the response to initial defibrillation and potentially precipitating refrillation.

Andersen and colleagues⁷ explored the association between early (within 2 minutes) and deferred (or no) adrenaline in patients enrolled in the registry from 2006 (to avoid contamination with changes in shock sequences). In contrast to previous work from the GWTG-R group where early adrenaline seemed to improve outcomes in patients with non-shockable rhythms,⁹ the early administration of adrenaline to patients with shock refractory VF or VT was associated with reduced survival to hospital discharge (adjusted odds ratio 0.70, 95% confidence interval 0.59 to 0.82).

The key strength of both studies are the use of the high quality GWTG-R registry, which collates data from over 300 hospitals in the USA and serves as a rich source of high quality information on treatments and outcomes from in-hospital cardiac arrest.¹⁰ While the breadth of coverage across the USA is a major strength, its primary purpose as a quality improvement registry necessarily limits the depth and specificity of information that is available for analysis. In both studies, researchers were reliant on using timings to draw inferences on the treatments being administered rather than extracting specific information about single versus stacked shocks or about timing of adrenaline in relation to shock sequence. Without such granular information, the slow adoption of deferred shock strategy identified by Bradley and colleagues and its interaction with the timing of adrenaline and other unmeasured and potentially confounding variables (eg, changes in ratio of compressions to ventilations, CPR quality introduced in 2005) make it difficult to conclude a casual association between the studied interventions and survival.

So should the findings from these studies alter your practice? Yes, the finding of widespread non-adherence with clinical guidelines should prompt those responsible for organising or delivering advanced life support to review their practice and ensure that it is informed by the latest clinical guidelines. While the jury remains out on the overall safety or effectiveness of adrenaline in cardiac arrest,¹¹ these data suggest that if adrenaline is given, in accordance with current guidelines, it should be deferred until at least after the second shock has been delivered.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: KC is supported by a National Institute for Health Research (NIHR) postdoctoral fellowship; GDP is supported as a NIHR senior investigator.

Provenance and peer review: Commissioned, not externally peer reviewed.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide licence to the Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution, iii) create any other derivative work(s) based on the Contribution, iv) to exploit all subsidiary rights in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.

1 Mozaffarian D, Benjamin EJ, Go AS, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation* 2016;133:e38-360. PubMed doi:10.1161/CIR.0000000000000366

2 Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. *Resuscitation* 2015;88:150-7. PubMed

3 Nolan JP, Hazinski MF, Aickin R, et al. Part 1: Executive summary: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation* 2015;95:e1-31. PubMed doi:10.1016/j.resuscitation.2015.07.039

4 Kitsios GD, Dahabreh IJ, Callahan S, Paulus JK, Campagna AC, Dargin JM. Can We Trust Observational Studies Using Propensity Scores in the Critical Care Literature? A Systematic Comparison With Randomized Clinical Trials. *Crit Care Med* 2015;43:1870-9. PubMed doi:10.1097/CCM.0000000000001135

5 Olasveengen TM. Adrenaline for out of hospital cardiac arrest? *BMJ* 2013;347:f7268. PubMed doi:10.1136/bmj.f7268

6 Bradley SM, Liu W, Chan PS, et al. Defibrillation time intervals and outcomes of cardiac arrest in hospital: retrospective cohort study from Get With The Guidelines-Resuscitation registry. *BMJ* 2016;353:i1653.

7 Andersen LW, Kurth T, Chase M, et al. Early administration of epinephrine (adrenaline) in patients with cardiac arrest with initial shockable rhythm in hospital: propensity score matched analysis. *BMJ* 2016;353:i1577.

8 Hazinski MF, Nadkarni VM, Hickey RW, O'Connor R, Becker LB, Zaritsky A. Major changes in the 2005 AHA Guidelines for CPR and ECC: reaching the tipping point for change. *Circulation* 2005;112(Suppl):IV206-11. PubMed doi:10.1161/CIRCULATIONAHA.105.170809

9 Donnino MW, Saliccioli JD, Howell MD, et al; American Heart Association's Get With The Guidelines-Resuscitation Investigators. Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: retrospective analysis of large in-hospital data registry. *BMJ* 2014;348:g3028. PubMed doi:10.1136/bmj.g3028

10 Peberdy MA, Kaye W, Ornato JP, et al. Cardiopulmonary resuscitation of adults in the hospital: a report of 14720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. *Resuscitation* 2003;58:297-308. PubMed doi:10.1016/S0300-9572(03)00215-6

11 Perkins GD, Cottrell P, Gates S. Is adrenaline safe and effective as a treatment for out of hospital cardiac arrest? *BMJ* 2014;348:g2435. PubMed doi:10.1136/bmj.g2435