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).

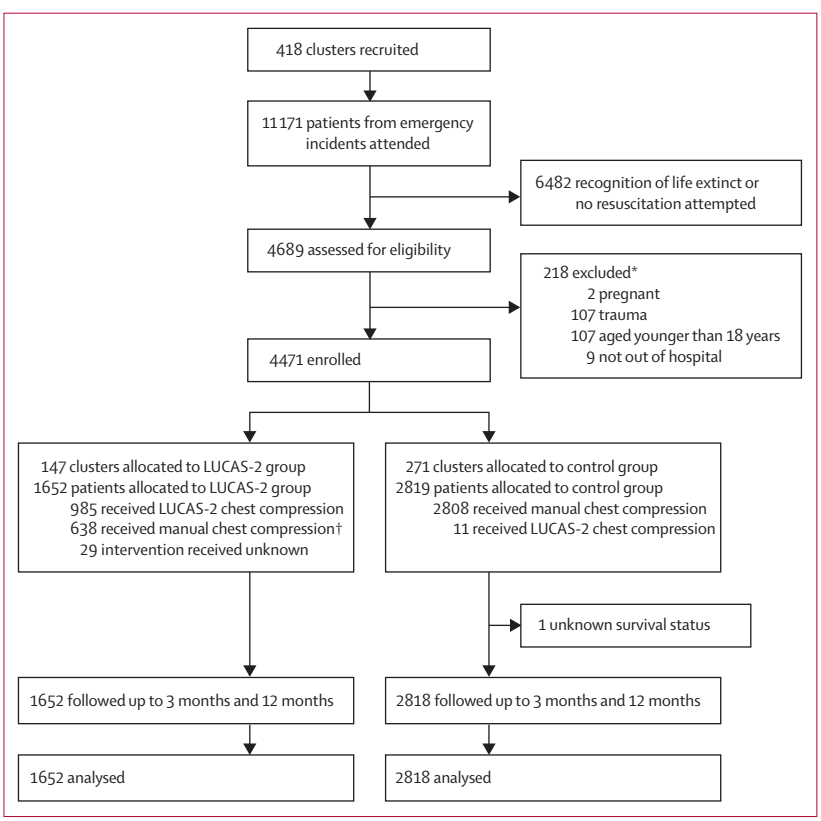

Figure 1: **Trial profile**
*Seven met more than one exclusion criteria. †Reasons LUCAS-2 not used: 78 because of crew not trained; 168 because of crew error; 26 no device in vehicle; 102 unsuitable patients (58 patient too large, 22 patient too small, 22 other reason–eg, chest deformity), 14 device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

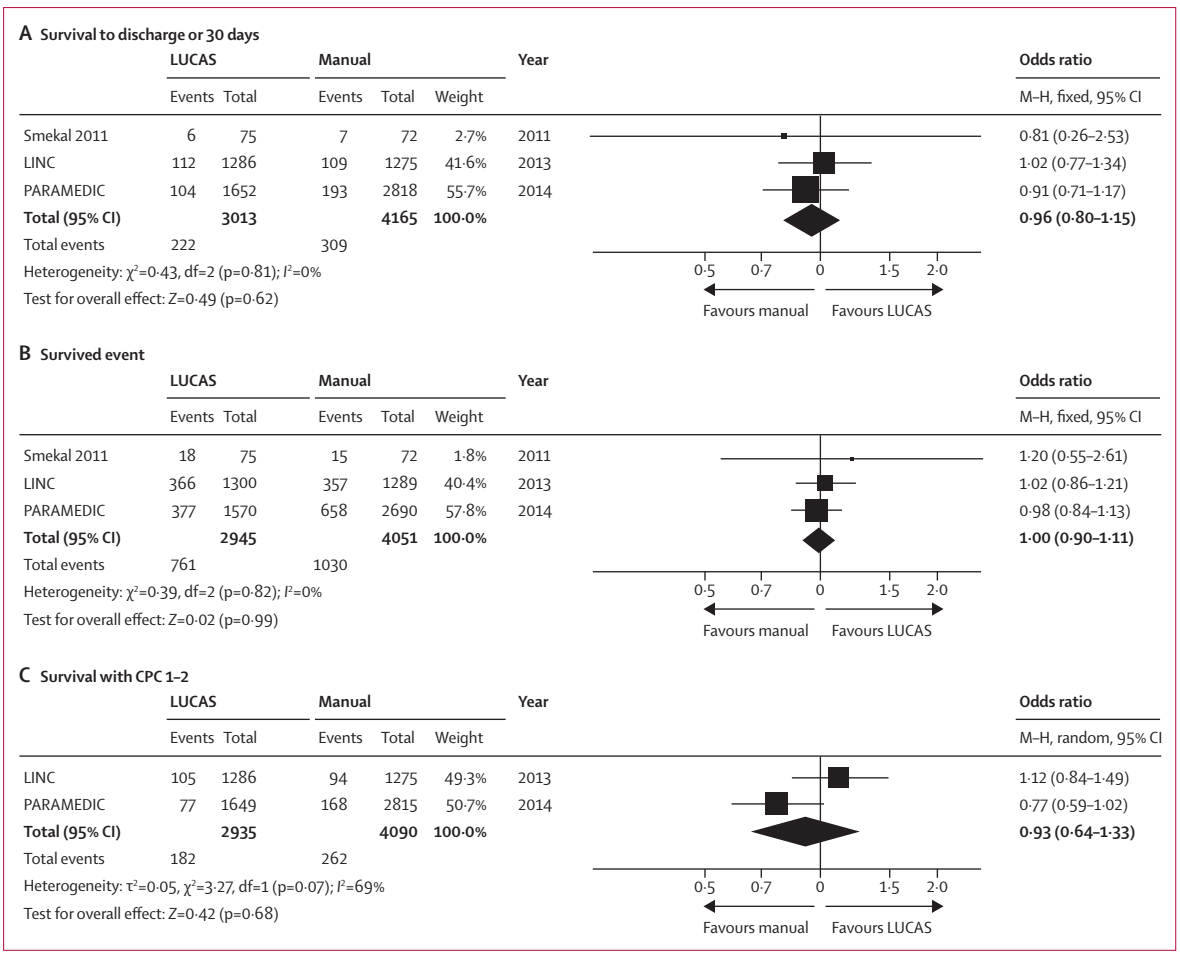

Figure 2: **Meta-analysis of the outcomes survived event and survival to hospital discharge or 30 days**
(A) Survival to discharge or 30 days. (B) Survived event. (C) Survival with CPC 1–2.

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

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