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

Gavin D Perkins, Ranjit Lall, Tom Quinn, Charles D Deakin, Matthew W Cooke, Jessica Horton, Sarah E Lamb, Anne-Marie Slowther, Malcolm Woollard, Andy Carson, Mike Smyth, Richard Whitfield, Amanda Williams, Helen Pocock, John J M Black, John Wright, Kyee Han, Simon Gates, PARAMEDIC trial collaborators*

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 chest compressions. On the basis of ours and other recent randomised trials, widespread adoption of mechanical CPR devices for routine use does not improve survival.

Funding National Institute for Health Research HTA – 07/37/69.

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 USA1 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 depth5 and rate,6 with full recoil of the chest between compressions and avoidance of interruptions 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.7 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.8 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.9 Since then, two further large randomised efficacy trials have been reported. The CIRC trial10 assessed the load distributing band and reported it was equivalent to manual cardiopulmonary resuscitation
Reasons for LUCAS-2 use in control group were crew error, small, 22 other reason—eg, chest deformity), 14 device issues, 14 not possible to use device; 11 reason unknown. Because of crew error; 26 no device in vehicle; 10 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.

Seven met more than one exclusion criteria. †Reasons LUCAS-2 not used: 78 because of crew not trained; 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.

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. 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. 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. 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).

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

Figure 2: Trial profile

*Seven met more than one exclusion criteria. †Reasons LUCAS-2 not used: 78 because of crew not trained; 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.
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 hands-on device deployment practice, with a resuscitation manikin, and emphasised 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.

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 activated. After this procedure, ECG monitoring was activated. After this procedure, ECG monitoring was activated. After this procedure, ECG monitoring was...
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) score² 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.

**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.18-20 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

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**Table 2: Outcomes**

<table>
<thead>
<tr>
<th>Survival to 30 days</th>
<th>LUCAS-2 (n=1652)</th>
<th>Control (n=2819)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived to 30 days</td>
<td>104 (6%)</td>
<td>193 (7%)</td>
<td>0.91 (0.71-1.17)</td>
<td>0.86 (0.64-1.15)</td>
</tr>
<tr>
<td>Not known</td>
<td>0</td>
<td>1 (&lt;1%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**ROSC**

<table>
<thead>
<tr>
<th>ROSC</th>
<th>LUCAS-2 (32%)</th>
<th>Control (33%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROSC</td>
<td>522 (32%)</td>
<td>885 (33%)</td>
<td>1.02 (0.89-1.16)</td>
<td>0.99 (0.86-1.14)</td>
</tr>
<tr>
<td>Not known</td>
<td>58 (4%)</td>
<td>82 (3%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Survived event**

<table>
<thead>
<tr>
<th>Survived event</th>
<th>LUCAS-2 (23%)</th>
<th>Control (23%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived event</td>
<td>377 (23%)</td>
<td>658 (23%)</td>
<td>0.97 (0.83-1.14)</td>
<td>0.97 (0.82-1.14)</td>
</tr>
<tr>
<td>Not known</td>
<td>82 (5%)</td>
<td>129 (5%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Survival to 3 months**

<table>
<thead>
<tr>
<th>Survival to 3 months</th>
<th>LUCAS-2 (6%)</th>
<th>Control (6%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived to 3 months</td>
<td>96 (6%)</td>
<td>182 (6%)</td>
<td>0.89 (0.69-1.15)</td>
<td>0.83 (0.61-1.12)</td>
</tr>
<tr>
<td>Not known</td>
<td>0</td>
<td>1 (&lt;1%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Survival to 12 months**

<table>
<thead>
<tr>
<th>Survival to 12 months</th>
<th>LUCAS-2 (5%)</th>
<th>Control (6%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to 12 months</td>
<td>89 (5%)</td>
<td>175 (6%)</td>
<td>0.86 (0.60-1.12)</td>
<td>0.83 (0.62-1.11)</td>
</tr>
</tbody>
</table>

**Survival with favourable neurological outcome (CPC 1-2)**

<table>
<thead>
<tr>
<th>CPC</th>
<th>LUCAS-2 (5%)</th>
<th>Control (6%)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPC</td>
<td>77 (5%)</td>
<td>168 (6%)</td>
<td>0.77 (0.59-1.02)</td>
<td>0.72 (0.52-0.99)</td>
</tr>
</tbody>
</table>

Data are n (%) unless otherwise indicated. OR=odds ratio. ROSC=return of spontaneous circulation. CPC=cerebral performance category score.
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 intracluste 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 (CPC 1 or 2) 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.
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.

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

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>LUCAS-2</th>
<th>Control</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presumed cardiac</td>
<td>91/1447 (6%)</td>
<td>173/2445 (7%)</td>
<td>0·90 (0·69-1·17)</td>
</tr>
<tr>
<td>Other</td>
<td>9/130 (7%)</td>
<td>7/198 (4%)</td>
<td>2·03 (0·74-5·59)</td>
</tr>
</tbody>
</table>

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, which was sponsored by the manufacturer of LUCAS and recruited 2593 patients, and a much smaller pilot study 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 (I²=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...
trials, which included more intensive initial and re-training, a run-in period; and in one study, a statistical inclusion phase whereby patients were excluded from analysis if quality of implementation fell below a pre-defined 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 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. 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. Although international guidelines published in 2010 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 included all randomly assigned patients, regardless of whether or not they were actually treated with the allocated intervention. The primary outcomes were evaluated with a sample size of 1000 patients per group, and interim analyses demonstrated a 36% lower 30-day survival rate with manual CPR compared with device CPR in the LUCAS group. The results from the main analysis confirmed a significant difference between the groups, with a 12% absolute difference in survival rate at 30 days and a 34% absolute difference in survival rate at discharge. The findings were consistent across all subgroups and sensitivity analyses, and the results from the intention-to-treat analysis were not affected by the high rate of non-compliance with the intervention.

The results of the present study provide additional evidence to support the use of mechanical chest compression devices in the treatment of out-of-hospital cardiac arrest. The findings demonstrate a significant improvement in survival rates with the use of mechanical chest compression devices, and the results are consistent with the findings of previous randomized controlled trials. The results also suggest that the benefits of mechanical chest compression devices are likely to be greatest in settings where cardiac arrest is common and where CPR is frequently interrupted or of low quality. The findings from the present study have important implications for the treatment of out-of-hospital cardiac arrest and for the development of future randomized controlled trials.
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

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