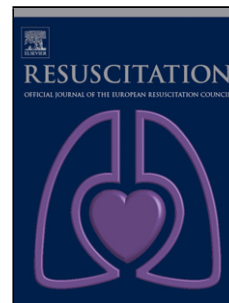# Accepted Manuscript

Title: The cost-effectiveness of a mechanical compression device in out of hospital cardiac arrest

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The cost-effectiveness of a mechanical compression device in out of hospital cardiac arrest

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Abstract

Aim: To assess the cost-effectiveness of LUCAS-2, a mechanical device for cardiopulmonary resuscitation (CPR) as compared to manual chest compressions in adults with non-traumatic, out-of-hospital cardiac arrest.

Methods: We analysed patient-level data from a large, pragmatic, multi-centre trial linked to administrative secondary care data from the Hospital Episode Statistics (HES) to measure healthcare resource use, costs and outcomes in both arms. A within-trial analysis using quality adjusted life years derived from the EQ-5D-3L was conducted at 12-month follow-up and results were extrapolated to the lifetime horizon using a decision-analytic model.

Results: 4471 patients were enrolled in the trial (1652 assigned to the LUCAS-2 group, 2819 assigned to the control group). At 12 months, 89 (5%) patients survived in the LUCAS-2 group and 175 (6%) survived in the manual CPR group. In the vast majority of analyses conducted, both within-trial and by extrapolation of the results over a lifetime horizon, manual CPR dominates LUCAS-2. In other words, patients in the LUCAS-2 group had poorer health outcomes (i.e. lower QALYs) and incurred higher health and social care costs.

Conclusion: Our study demonstrates that the use of the mechanical chest compression device LUCAS-2 represents poor value for money when compared to standard manual chest compression in out-of-hospital cardiac arrest.

Introduction

National Health Service (NHS) Ambulance Services attend approximately 60,000 cardiac arrests each year in the UK. (1) Resuscitation is attempted in only under half of the cases and the overall survival to hospital discharge is only approximately 8%. While functional survival after cardiac arrest is generally good (2), survivors may experience post-arrest problems, including anxiety, depression, posttraumatic stress, and difficulties with cognitive function.(3) However, despite the annual death toll exceeding that of dementia, stroke or lung cancer, there has been relatively little investment in research in this condition. This has created a relatively weak evidence base compared to other diseases. (4) High mortality and the challenges of accurate prediction of patient outcomes mean that important resources are invested in treating cardiac arrest patients without clear assessment of the potential benefits. A recent single-centre micro-costing study has estimated that the cost per survivor to hospital discharge was £50,000, with a cost per quality-adjusted life years (QALY) of £16,000 among patient with good neurological outcomes. (5) Overall, only a few studies assessed the costs of out-of-hospital of cardiac arrest and the cost-effectiveness of related interventions. (6-11)

A critical step of the resuscitation process is early cardiopulmonary resuscitation (CPR), i.e. the combination of chest compressions and ventilations. CPR can be started by bystanders and is typically taken over by emergency services. (12) Current resuscitation guidelines highlight the importance of high quality CPR for ensuring optimal outcomes from cardiac arrest. (13) In this context, several mechanical devices have been proposed that are able to provide compressions of a standard depth and frequency for long periods without interruption or fatigue. In addition, these devices free emergency medical personnel for other tasks. The LUCAS-2 (Lund University Cardiopulmonary Assistance System) is a mechanical device that provides automatic chest compressions, manufactured in Sweden by PhysioControl. It delivers sternal compression at a constant rate to a fixed depth and has been on the market since 2002 in Europe. The primary objective of this study was to assess the cost-effectiveness of the LUCAS-2 device versus manual CPR using data from a large pragmatic multi-centre trial. (14) While several other studies have assessed the effectiveness of mechanical chest compression devices in out-of-hospital cardiac arrest (15-18), this study is the first comprehensive economic evaluation in this area. The analysis also provides useful costs and health-related quality-of-life (HRQoL) estimates that will be of use in future economic models.

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Methods

Overview of the analysis

The study was based on costs and outcomes from a large multi-centre randomised controlled trial of mechanical versus manual chest compression (CPR), the PARAMEDIC trial. (19) Briefly, this 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, Wales, South Central). Ninety one 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 CPR or manual CPR according to the first trial vehicle to arrive on scene. The trial was approved in accordance with the requirements of the Mental Capacity Act (2005) for England and Wales by the Coventry Research Ethics Committee (ref 09/H1210/69). Enrolment proceeded with waiver of informed consent; patients discharged from hospital were invited to take part in the follow up and written consent obtained. (14) The economic evaluation was conducted to assess the cost-effectiveness of LUCAS-2 compared to manual CPR during resuscitation by ambulance staff after out-of-hospital cardiac arrest. It consisted of two complementary sets of analyses: a within-trial analysis over the 12 months trial period and a decision-analytic model built to extrapolate the results over the expected lifetime of trial participants. The analyses followed best practice guidelines (20), were conducted from the UK NHS perspective and report cost per incremental quality-adjusted life year (QALY) of LUCAS-2 compared to usual care (i.e. manual CPR). Missing data for both resource use and health outcomes were handled using multiple imputation (see Technical Appendix).

Resource use and costs

The costs considered in this analysis included intervention costs and the costs associated with the use of health care services along the patient pathway. Intervention costs were defined as the additional costs of the LUCAS-2 device as compared to manual CPR. Micro-costing was used to establish the cost of LUCAS-2 and determine the relevant cost per application. The following cost elements were considered: 1) the cost of purchasing the device and accessories; 2) the cost of fitting the device to the ambulance; 3) maintenance costs; and 4) initial and on-going staff training costs. A product lifespan of eight years was assumed in the calculations. Total costs were divided by the total number of applications estimated from trial data to obtain an estimate of the cost per application (Supplementary Table S1).

Resource use included hospital inpatient stays, A&E admissions and outpatient visits, and the use of primary care-based and community-based health and social care services, such as GP and social worker visits. Various data sources were combined to obtain a patient-level estimate of resource use

along the care pathway. Data on the use of hospital services were obtained through linkage with the Hospital Episode Statistics (HES) data set (Copyright © 2014, re-used with the permission of the Health and Social Care Information Centre. All rights reserved). We extracted data from the HES for study participants from cardiac arrest to 12 months after randomisation. The dataset records information on inpatient length of stay (LOS) (ICU and general ward), in-person and telephone outpatient visits, and A&E admissions. As intensive care is likely to account for a large share of the costs of cardiac arrest, data on ICU LOS were also extracted from the Intensive Care National Audit and Research Centre (ICNARC) dataset and complementary analyses were conducted using this alternative data source. Patients who died in hospital within 24 hours (i.e. LOS<1) were considered as having spent one day in ICU.

Following hospital discharge, healthcare resource use questionnaires were completed by surviving patients at three and twelve months post cardiac arrest. Patients were asked about their use of health and social services during the previous 3 months, including further inpatient and outpatient care and primary- and community-based health and social services. We used the average resource utilisation between the initial (0-3 months) and final (9-12 months) period to impute resources utilisation for the 6 months period during which post-discharge resource use data were not collected (i.e. between 3 and 9 months post cardiac arrest). Patients who died within 3 months were assumed to have incurred no post-discharge costs. Of note, this represents only a small proportion of patients as most patients either died within days, or survived beyond 3 months. Resource use was multiplied by the relevant unit costs extracted from national reference costs. (21, 22) (Supplementary Table S2).

Health outcomes

Quality-adjusted life years (QALYs) reflect both duration and quality of life and their estimation requires the production of utility weights for each health state observed in the trial population. HRQoL was assessed using the EQ-5D-3L which has been validated for use in the critical care patient group. (23) Surviving patients completed the EQ-5D-3L at three and twelve months post cardiac arrest. The EQ-5D-3L responses were converted to health-state utility values using the UK tariff. (24) Utility values were combined with survival information to calculate QALYs for the trial period using an area under the curve (AUC) approach. As patients were unable to complete the measure at baseline (i.e. cardiac arrest), estimates had to be made of their baseline utility level. Following strategies previously employed in studies that had dealt with this scenario (25-27), we assumed that patients who experienced a cardiac arrest had a baseline utility value of '0', which is equivalent to dead. We then assumed a linear transition from '0' to the 3-month utility value and similarly from the 3-month to the 12-month utility value. A utility weight of '0' was assigned to patients who died within 3 months. Alternative assumptions were explored in sensitivity analyses.

Cost-effectiveness analysis

The within-trial analysis aimed to determine the cost-effectiveness of LUCAS-2 compared to manual chest compression over the period of the trial, i.e. from cardiac arrest to 12 months follow-up. Neither costs nor QALYs were discounted given the 12-month time period. To extrapolate costs and outcomes over a lifetime horizon, we built a decision-analytic model (28), whose structure, parameters and assumptions are presented is detail in the Technical Appendix. Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the difference in mean cost between the two arms by the difference in mean QALYs between the two arms. Thus the ICER represents the cost per QALY gained. ICERs below the NICE willingness to pay threshold of £20,000 indicate cost-effectiveness. Sensitivity analyses were performed for both the within-trial and long-term analyses (see Technical Appendix).

Results

Trial participants

Among the 4771 patients enrolled in the study, 1652 were assigned to the intervention group (LUCAS-2) and 2819 were assigned to the control group (manual CPR). During the trial, 985 (60%) patients in the intervention group received LUCAS-2 and 11(<1%) patients in the control group received mechanical CPR. (14) At 3 months, 96 (6%) patients survived in the LUCAS-2 group and 182 (6%) survived in the control group. At 12 months, 89 (5%) patients survived in the LUCAS-2 group and 175 (6%) survived in the manual CPR group. Of the 278 surviving patients at 3 months, 146 (53%) completed the EQ-5D questionnaire and 145 (52%) completed the resource use questionnaire. At 12 months, among the 266 surviving patients, 143 (54%) completed the EQ-5D-3L questionnaire and 139 (52%) completed the resource use questionnaire.

Costs

Table 1 provides an overview of the costs along the care pathway for both trial arms. In the complete case analysis, the mean cost to the NHS at one year was higher in the LUCAS-2 group (£1,400) than in the control group (£1,294), giving rise to an incremental cost of £107, with ICU costs being the main cost driver. Overall, mean costs in each category was higher in the LUCAS-2 group than in the manual CPR group. Multiple imputation gave rise to higher cost estimates in both groups. Using the imputed data, we calculated the total cost in each patient group (i.e. the sum of all costs across all patients) that we divided by the number of one-year survivors in each group (i.e. 175 in the manual CPR arm and 89 patients in the LUCAS-2 arm) and obtained an estimate of the cost per one-year

survivor of £32,560 in the manual CPR arm and of £52,548 in the LUCAS-2 arm. This difference is driven by the difference in one-year survival rates (i.e. 6.2% vs. 5.4%) and mean one-year cost (i.e. £2,021 vs. £2,831) between the two arms.

Health-related quality of life

HRQoL scores derived from the 3 months and 12 months EQ-5D-3L questionnaires are shown in Table 2. At both follow-up periods, HRQoL was higher in the manual CPR group than in the LUCAS-2 group (p<0.05). Overall, changes in utility between the 3 month and 12 month assessments were not statistically significant. The table also reports the mean QALYs over one year accrued by patients in both groups based on the AUC approach and calculated using both the complete case analysis and the imputed data. The mean one-year QALYs is small due to the high one-year mortality rate in the sample (>95%). As expected, multiple imputation gave rise to higher mean QALYs in both groups. The difference in mean QALYs between groups is small, with patients in the manual CPR group having a higher average QALYs than patients in the LUCAS-2 group. HRQoL of survivors at 12 months was also estimated by neurological outcome status (i.e. CPC score). We found a significant difference in HRQL between patients with good neurological outcome (CPC score of 1 or 2) (mean: 0.75) and patients with poor neurological outcome (CPC of 3 or 4) (mean: 0.47).

Cost-effectiveness

Table 3 presents the cost-effectiveness results, showing the incremental costs and QALYs for each arm of the trial, as well as the corresponding ICER. At one-year, we found an incremental QALY of -0.0072 and an incremental cost of £107, which indicates that LUCAS-2 is dominated by manual chest compression (dominance means that LUCAS-2 is more costly and less effective than manual chest compression). When a per-protocol analysis was conducted instead, manual compression still dominated and the conclusions remain unchanged when QALYs were derived using SF-12 instead of EQ-5D-3L, and when the ICNARC dataset instead of HES was used to derive ICU costs. Overall, the results consistently suggest that manual chest compression dominates LUCAS-2 in this patient group. Interpretation should however be tempered by the very small between-group QALY differences and the relatively small differences in costs. In Figure 1, we present the results of the 10,000 bootstrap replications in the cost-effectiveness plane for the analysis based on multiple imputation. The 10,000 estimates are spread mainly in the north-west quadrant of the cost-effectiveness plane; it is, however, worth noting that QALY losses are minimal.

The lifetime cost-effectiveness results obtained using the Markov model are presented in Table 4. The base case analysis is based on a cohort of patients aged 60, followed over 40 years, which corresponds to the average age of patients who survived at one year. Results suggest that LUCAS-2 is dominated

by manual CPR, with an incremental cost of £ 2,376.4 and an incremental QALY of -0.1286. This finding is robust to a range of sensitivity analyses as shown in the table. Figure 2 shows results from the probabilistic sensitivity analysis that takes parameter uncertainty into account. The CEAC indicate that the probability that LUCAS-2 is cost-effective is about 25 per cent, irrespective of the value of the threshold used. The flat shape of the CEAC is explained by the fact that most iterations lie in the North-West quadrant of the cost-effectiveness plane. (29)

Discussion

This study is the first to provide evidence on the cost-effectiveness of mechanical chest compression as compared to manual CPR. It demonstrates that the use of the mechanical chest compression device LUCAS-2 represents poor value for money in out-of-hospital cardiac arrest. In the vast majority of analyses conducted, both within-trial and by extrapolation of the results over a lifetime horizon, manual CPR dominates LUCAS-2. In other words, patients in the LUCAS-2 group had poorer health outcomes and incurred higher health and social care costs. The cost-effectiveness results are driven by worse neurological outcomes and lower survival in the LUCAS-2 group as compared to manual CPR. Results resonate with previously published short-term clinical outcomes observed in the PARAMEDIC trial (14) and are in line with several other randomised trials that have investigated the effectiveness of mechanical chest compression (15-18) and that found no consistent evidence of survival benefits and highly heterogeneous effects in terms of neurological outcomes. On the basis of there being approximately 28,000 resuscitation attempts in England annually, introducing mechanical CPR across English Ambulance Services would likely cost £6.5m per year. Such costs in the absence of evidence of effectiveness are unlikely to be justifiable.

Potential explanations for worse outcomes in the LUCAS-2 group include interruptions in CPR during device deployment that could cause reduced cardiac and cerebral perfusion and possible delay in the time to first shock due to the deployment of LUCAS-2. The pragmatic design of the PARAMEDIC trial meant that paramedics received focus training (average 1 hour) similar to the approach that would be taken to introducing new technology into NHS Ambulance Services. More intensive initial training, regular re-training adopting a "pit-stop" approach with on-going CPR quality monitoring may reduce potentially deleterious interruptions to CPR associated with device deployment. (30, 31) In the CIRC trial paramedics received 4 hour initial training, supplemented by refresher training and continuous CPR quality monitoring and feedback throughout the study period. (32) This additional training will have increased costs associated with mechanical CPR. The on-going CPR quality monitoring programme in the CIRC trial demonstrated that the device was deployed with minimal

interruptions to chest compressions, but similar to PARAMEDIC and LINC trial found no difference in overall survival. (18)

Our analysis was primarily based on high quality data collected alongside a large cluster randomised trial, and therefore has high internal validity compared to economic studies that rely exclusively on modelling. In addition, linkage with large administrative datasets, including the Hospital Episodes Statistics data was used to obtain resource use estimates that are more accurate than those obtained using retrospective surveys of patients. The importance of such data is crucial given the high mortality rate in the trial. The long-term decision model relied on a number of assumptions and existing evidence was scarce for some parameters. However, the majority of the key parameters were derived from trial data. We are therefore confident that our analyses captured the most relevant relative costs and outcomes of LUCAS-2 as compared to manual CPR. Also, our study provides costs and quality-of-life estimates that can be used in other economic evaluations in cardiac arrest patients/cardiac arrest interventions/technology.

One aspect of costs not considered in our study was the influence of mechanical chest compression and injuries to staff involved in the resuscitation attempt. Manual CPR is a physically demanding tasks and a survey reported in the literature indicate that approximately 25% of staff sustain back injuries during CPR. (33, 34) Advantages of a mechanical CPR device are that they have the potential to limit the exposure of staff to periods of prolonged CPR, although require additional heavy equipment to be carried to and from the scene of the cardiac arrest. Ambulance vehicle crashes, although fortunately rare (no incidents were reported during our study), have the potential to cause significant injuries to staff, particularly if un-restrained by a seat belt. A mechanical CPR device provides staff with the opportunity to use safety belts unlike performing manual CPR. Also, availability and deployment of LUCAS-2 may also mean fewer staff are required at scene to manage the resuscitation attempt, therefore releasing resources. As our data did not allow us to capture these potential benefits of mechanical CPR, there is a risk that our study slightly overestimates the net cost of the technology. However, it is unlikely that the presence of the compression device means that only one paramedic would be required on scene and that therefore a lower cost would be necessarily associated with that scenario. Even if that were the case, the associated cost savings would be below £100 per application, considering average intervention time observed in the trial. Also, it is unclear whether the effectiveness observed in the trial would be comparable with only one paramedic operating the device.

Meta-analysis from four large and one smaller randomised trial provide consistent evidence that the routine use of mechanical CPR in out of hospital cardiac arrest does not improve clinical outcomes (35). These findings are consistent with the International Liaison Committee On Resuscitation (ILCOR) treatment recommendation against the routine use of mechanical CPR devices. (36) ILCOR

suggest that mechanical CPR devices may continue to have a role where manual chest compressions are impossible or compromise rescuer safety. Future research could usefully focus on refining the indications and cost effectiveness of mechanical CPR in these settings.

Conclusions

This study provides evidence that the use of the mechanical chest compression device LUCAS-2 represents poor value for money in out-of-hospital cardiac arrest.

Conflicts of interest

The authors have no conflict of interest to declare.

Acknowledgments

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Legends to Figures

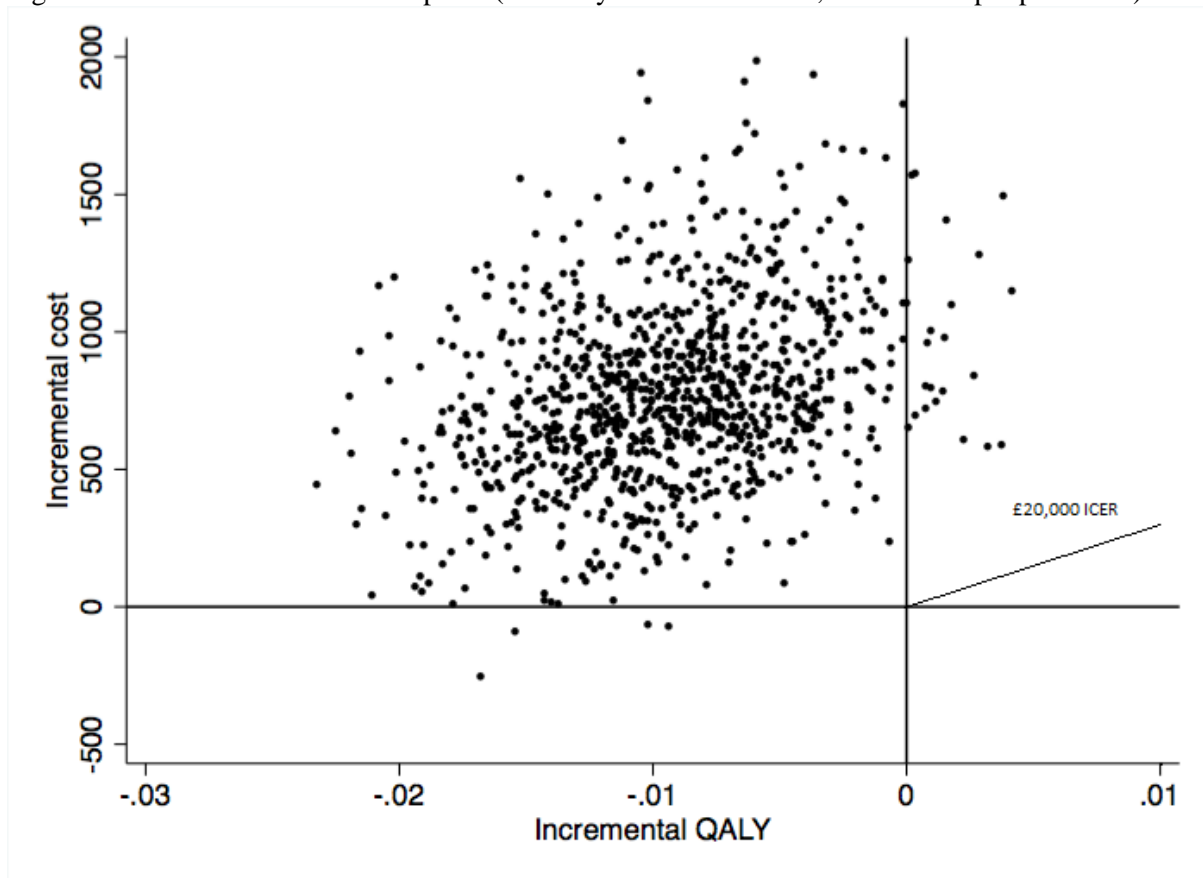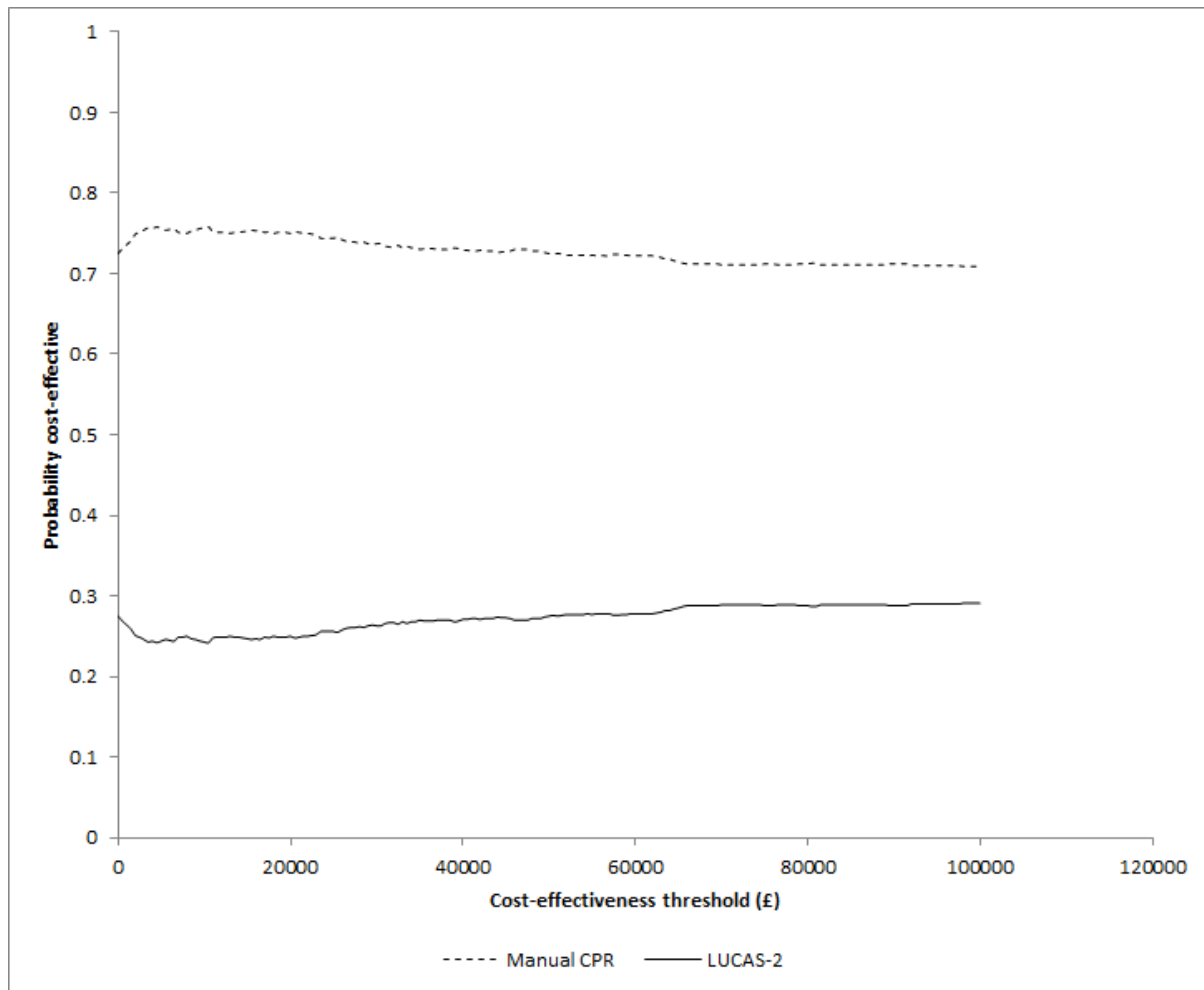Figure 1:   Cost-effectiveness plane (MI analysis – Based on 10,000 Bootstrap replications)

Figure 2:   Cost-effectiveness acceptability curves for LUCAS-2 compared with manual CPR

Tables

Table 1 One-year costs by treatment arm

	Manual CPR						LUCAS					
	n	n missing	mean (£)	95% CI	min	Max	n	n missing	mean (£)	95% CI	min	Max
Complete-case data												
Costs to the NHS over 1 year	2,690	129	1,294.0	1,152.4-1,435.7	0	41,945	1,577	75	1,400.7	1,131.2-1,670.3	0	123,660
ICU costs	2,762	57	959.2	826.8-1,091.6	0	59,426	1,622	30	1,221.8	766.2-1,677.5	0	317,860
Other hospital costs (A&E, outpatient, general ward)	2,772	47	521.5	428.6-614.3	0	75,767	1,619	33	585.0	386.0-784.0	0	74,276
Hospital costs	2,732	87	1,318.0	1,136.3-1,499.8	0	101,928	1,599	53	1,540.3	1,083.4-1,997.2	0	318,327
Community-based health and social care costs	2,716	103	31.9	23.1-40.6	0	8,834	1,593	59	91.1	21.2-160.9	0	50,138
Imputed data												
Costs to the NHS over 1 year	2,819	-	2,021.3	1,772.3-2,270.2	0	41,945	1,652	-	2,831.0	2,149.6-3,512.3	0	123,660
ICU costs	2,819	-	1,102.1	947.0-1,257.2	0	59,426	1,652	-	1,447.3	883.4-2,011.1	0	317,860
Other hospital costs (A&E, outpatient, general ward)	2,819	-	604.0	478.8-729.1	0	75,767	1,652	-	724.6	507.5-941.7	0	74,276
Hospital costs	2,819	-	1,706.1	1,477.5-1,934.6	0	101,928	1,652	-	2,171.8	1,525.6-2,818.0	0	318,327
Community-based health and social care costs	2,819	-	108.8	37.9-179.6	0	8,834	1,652	-	287.4	111.8-463.0	0	50,138
Total costs to the NHS divided by the number of 1 year survivors	175	-	32,560	28,551-36,569			89	-	52,548	39,908-65,188		

Table 2 – HRQL by treatment arm

		Manual CPR			LUCAS-2	
	n	Mean	95% CI	n	Mean	95% CI
Utility score among survivors						
3 months	99	0.780	0.732-0.828	47	0.647	0.555-0.738
12 months	95	0.761	0.712-0.810	48	0.639	0.542-0.736
QALY over 12 months						
Complete case	2,741	0.026	0.021-0.031	1,609	0.018	0.013-0.024
Imputed	2,818	0.042	0.036-0.048	1,652	0.033	0.026-0.040

Table3 – ICERS: within-trial analysis

Analysis	n	Incremental cost (£)	Incremental QALY	ICER
Multiple imputation (ITT)	4,771	809.6	-0.0093	Manual CPR dominates[b]
Complete case (ITT)	4,267	106.7	-0.0072	Manual CPR dominates
Complete case (ITT, average group cost for outliers)	4,267	39.2	-0.0067	Manual CPR dominates
Multiple imputation (per-protocol)	3,793	495.9	-0.0142	Manual CPR dominates
Complete case (per-protocol)	3,391	296.4	-0.0070	Manual CPR dominates
Alternative QALY calculation[a]	4,771	809.6	-0.0091	Manual CPR dominates
ICU resource use derived using ICNARC dataset	4,771	934.2	-0.0093	Manual CPR dominates
QALY derived with SF-12 (complete case)	4,267	106.7	-0.0046	Manual CPR dominates
CACE (complete case)	4,267	177.8	-0.012	Manual CPR dominates

a) Instead of incurring 0 QALYs, patients who died within 3 months were imputed QALYs based on their total number of survival days to which we assigned a utility corresponding to the average 3-month utility in our sample.

b) A technology/treatment is said to dominate an alternative when it is less expensive and more effective than the alternative.

Table 4 – ICERS: Markov model

Analysis	Incremental cost (£)	Incremental QALY	ICER
Base case analysis (age 60 cohort)	£2,376.4	-0.1286	Manual CPR dominates
One-way sensitivity analyses			
Sensitivity to costs			
+20% of costs	£2,851.6	-0.1286	Manual CPR dominates
-20% of costs	£1,901.1	-0.1286	Manual CPR dominates
Sensitivity to QALY			
+20% of QALY	£2,376.4	-0.1543	Manual CPR dominates
-20% of QALY	£2,376.4	-0.1029	Manual CPR dominates
Sensitivity to one-year mortality			
+20% one-year mortality	-£3,987.5	-0.0187	£213,014 per QALY
-20% one-year mortality	£10,603.8	-0.2401	Manual CPR dominates