Supplementary material

Technical appendix

Missing data

The primary analysis employed multiple imputation (MI) to handle missing data using baseline characteristics to impute missing follow-up utility and resource use information. Unlike more simple imputation approaches, MI reflects both the structural uncertainty related to the parameters of the imputation model and the uncertainty arising from missing data. (1-3) Practically, to obtain total costs and QALYs at one-year for each patient, missing data on utility and resource use was addressed using chained equations. We used truncated models to reflect the specific distribution of utility and resource use and generated ten datasets. Estimates from each imputed dataset were combined following Rubin's rule. (4) In the sensitivity analysis, we also report results from the complete case analysis where only patients with non-missing utility values were included. Overall, we expected higher costs and utility estimates using the imputed data as missing data disproportionally affected patients who survived to hospital discharge.

Decision-analytic model

The structure of the economic model is shown in Supplementary Figure S1. The model starts with a decision tree reflecting patients' risk of death at different time points from cardiac arrest to one-year follow-up and allocates one-year survivors to either good or poor neurological outcomes, based on the distribution of Cerebral Performance Category (CPC) score at the end of the trial. (5) The endpoints of the decision tree are the starting point of the lifetime Markov model. We chose to model the intervention impact from baseline application rather than simply extending outcomes and costs from 12 months onwards. The main motivation for this was to enable better capture of uncertainty during the trial period and allow propagation of this through the lifetime horizon. Beyond one year post cardiac arrest, costs, HRQL and survival were modelled in two subsets of patients: patients with good neurological outcomes at one year (CPC score=1 or 2) and patients with poor neurological outcomes at one year (CPC score>2). Relevant model parameters were extracted from the trial data and from the literature (Supplementary Table S2 and S3) and included relative survival rates that were applied to UK reference mortality rates (6) and annual cost and utility data for cardiac arrest survivors with good or poor neurological outcomes. Annual costs for patients in both neurological outcomes groups were obtained from trial data and included costs of outpatient visits and community-based health and social care. Residential care costs were added to the costs of patients with poor neurological outcomes given the level of support required by these patients. A discount rate of 3.5% was applied to costs and health outcomes in the lifetime Markov model. All analyses were conducted using STATA© (StataCorp LP) and Excel© (Microsoft).

Sensitivity analysis

In the within-trial analysis, uncertainty was explored by conducting non-parametric bootstrapping via 10,000 resampled analyses. Cost-effectiveness planes were created. (7, 8) Sensitivity analyses were conducted to determine the impact of assumptions on the cost-effectiveness results. While the main analyses used the intent-to-treat (ITT) principle, results of a per-protocol analysis were also reported due to the non-negligible number of non-compliers in the LUCAS-2 group. We compared results from complete-case analysis vs. multiple imputation and also carried out analyses using an average group cost for outliers with high costs. We finally explored the sensitivity of the results to the use of an alternative utility measure (i.e. SF-12) and to the use of an alternative data source (i.e. ICNARC) to estimate ICU and hospital LOS, the main cost drivers in our analysis.

The sensitivity of lifetime costs and utility estimates to parameter uncertainty was then assessed. We first performed several one-way sensitivity analyses by adding and subtracting 20 per cent of the main parameters of the model (i.e. costs, QALYs, and one-year mortality) and assessed the subsequent impact on the ICERs. The value of 20 per cent is arbitrary but was considered likely to represent any uncertainty that might exist in parameter values. A probabilistic sensitivity analysis was then conducted for a more comprehensive account of uncertainty. Cost-effectiveness acceptability curves (CEAC) that show the probability of cost-effectiveness across a range of values for the cost-effectiveness threshold were created using the net benefit approach. (9)

Supplementary tables and figures

Supplementary Table S1: Cost of the LUCAS-2 device

Cost item	**Assumptions**	**Cost for the trial period**	
Purchase cost (LUCAS-2 and accessories)	A one-off purchase cost the LUCAS device and necessary accessories were calculated using the purchase cost for the device itself, suction cups, battery, 12V car cable and power supply for inside the ambulance. The cost of each these items was multiplied by the number ambulances in the intervention trial arm. Battery chargers and a spare battery at each of the 90 stations with the LUCAS device were costed. For spare LUCAS parts it was assumed that 1 set of each spare would be required per 10 devices. Spare parts included a carry bag, stabilization strap, and wrist straps.	£ 148,504	
Cost of fitting LUCAS-2 to vehicles	The total cost of fitting the device to ambulance vehicles required the cost of screws, chair strap, clips and net. One hour of labour was estimated to fit the strap per ambulance. The cost of fitting the device to one ambulance was then multiplied by the number of vehicles in the intervention arm.	£ 783	
Maintenance (assuming no repairs)	The planned preventative maintenance service was estimated to cost £250 for each LUCAS device. This cost assumed no parts were needed and no repairs occurred.	£35,750	
Staff training (initial and on-going)	*Initial staff training:* It was estimated that each regional ambulance trust had a mandatory training program which paid paramedics 3 hours of overtime to attend. The per-paramedic cost was multiplied by the number of staff at each site that had been trained. *Ongoing staff training:* One regional ambulance site reported a 30 min training refresher for paramedics. It was assumed that paramedics in all sites would receive a similar 30 minute refresher course once per year. The cost per paramedic was multiplied by the total number of staff trained within the initial staff training.	£ 46,450	
Total costs		£ 231,488	
Number of applications		996	
Cost per application			**£232**

Supplementary Table S2: Unit costs

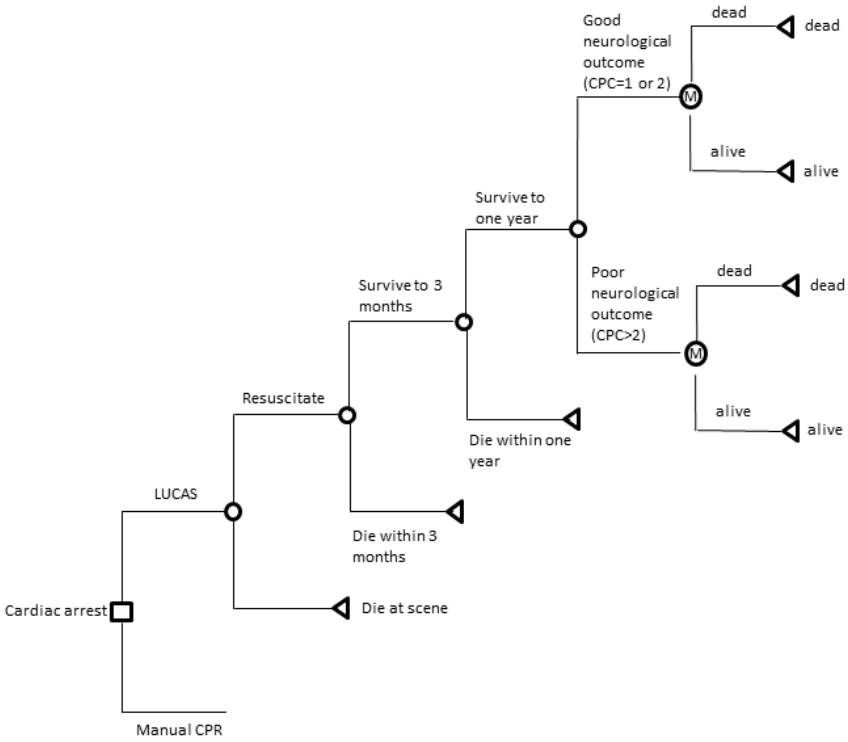
Resource Item	**Unit Cost**	**Source**	**Details/Assumptions**
LUCAS cost per application	£232	Own calculations see Appendix Table 1	Lifespan of 8 years was assumed.
Ambulance cost	£180	NHS Ref Costs	"See and treat" (if died on scene)
	£231	NHS Ref Costs	"See and treat and convey" (if did not die on scene)
Hospital based or residential care services			
Intensive care unit per day	£1,382	NHS Ref Costs	Non-specific general adult critical care patients predominate. Average cost of 0 to 6 or more organs supported SC:CCU01, CC XC01Z-XC07Z
Hospital inpatient stay per day	£275	NHS Ref Costs	Non-elective inpatients-Excess bed days
Hospital outpatient clinic appointment	£128	NHS Ref Costs	Outpatient-Consultant led
Hospital A&E visit	*£339*	NHS Ref Costs	*Emergency Medicine, Category 3 Investigation with Category 4 Treatment SC:T01A, CC:VB02ZZ*
Nursing/residential home per day	£157	Curtis L.	Local authority residential care for older people. Establishment cost per permanent resident week/7 days
Primary and community based health and social services			
GP- surgery visit	£46	Curtis L.	Per patient contact lasting 11.7 mins incl. direct care staff costs
GP- home visit	£92	Curtis L.	(Per patient contact lasting 11.7 mins + 12 min travel time) x£3.90/min cost of patient contact
District nurse/Health visitor visit	£45	NHS Ref Costs	Average of District Nurse, Face to face SC:NURS, CC;N02AF and Health Visitor, Face to Face SC:HVM, CC:N03G
Social worker visit	£79	Curtis L.	1 hour appointment
Counsellor appointment	£50	Curtis L.	1 hour appointment
Home help session	£24	Curtis L.	1 hour weekday session
Speech and language therapist appointment	£84	NHS Ref Costs	Speech and Language Therapist, Adult, One to One CC:A13A1
Psychologist appointment	£85	NHS Ref Costs	Non-Admitted Non-Face to Face Attendance, Follow-up SC:656 CC:WF01C

Day centre visit	£42	Curtis L.	Local authority day care for older people. Per client session lasting 3.5 hours.
Lunch or social club session	£7	Curtis L.	Same cost as 1 hour of befriending older adults program
Meals on Wheels	£7	Curtis L.	Assuming 1 contact=1 meal. Average cost of per meal on wheel for the local authority
Family Support session	£50	Curtis L.	Family support worker. Per hour of client related work
NHS- SC: Service Code CC: Currency Code			

Supplementary Table S3: Model parameters

	Group/arm	Mean value	Probability Distribution	Source
Decision tree parameters				
prob (die on scene)				
	Manual CPR	0.3274	Beta	Trial data
	LUCAS-2	0.3290	Beta	Trial data
prob (die within 3 months | didn't die on scene)				
	Manual CPR	0.9029	Beta	Trial data
	LUCAS-2	0.9134	Beta	Trial data
prob (die within 3-12 months | survived to 3 months)				
	Manual CPR	0.0380	Beta	Trial data
	LUCAS-2	0.0729	Beta	Trial data
prob (good neurological outcome | survive to 1 year)				
	Manual CPR	0.8605	Beta	Trial data
	LUCAS-2	0.7442	Beta	Trial data
Markov model parameters				
Annual mortality rate			Fixed	UK life tables (ONS, 2012)
Excess mortality for patients with poor neurological outcomes		1.67	lognormal	Phelps et al. 2013
Discount rate		3.5%	Fixed	
Annual cost				
	Good neurological outcome (CPC 1 or 2)	£ 3,315	lognormal	Trial data
	Poor neurological outcome (CPC 3 or 4)	£ 43,146	lognormal	Trial data and Curtis 2012
Utility				
	Good neurological outcome (CPC 1 or 2)	0.75	Beta	Trial data
	Poor neurological outcome (CPC 3 or 4)	0.47	Beta	Trial data

Supplementary Figure S1 – Structure of the decision-analytic model



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