Early neurologically focused follow-up after cardiac arrest is cost-effective

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Clinical paper,

Early neurologically focused follow-up after cardiac arrest is cost-effective: A trial-based economic evaluation[☆]

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ABSTRACT

Objective: To evaluate the cost-effectiveness of an early intervention service for cardiac arrest survivors called 'Stand still . . . and move on' from a societal perspective.

Intervention: This concise nursing intervention consists of screening for cognitive and emotional problems, information provision and support, self-management promotion, and further referral if necessary. Earlier research confirmed the feasibility of the intervention and its effectiveness in improving emotional functioning and quality of life.

Methods: In this multicentre randomized controlled trial with one year follow-up 185 patients were included between April 2007 and December 2010. The experimental group received the intervention, the control group received care-as-usual. Intervention costs, other direct healthcare costs (e.g. hospital care, rehabilitation, medication, home care) and indirect costs (productivity loss) were measured during ten months using monthly cost-diaries. The economic evaluation comprised a cost-utility analysis (SF-36) and a cost-effectiveness analysis (QOLIBRI) using bootstrapping (5000 replications) to quantify uncertainty concerning the incremental cost effectiveness ratio (ICER), and the probability of the intervention being cost-effective was estimated. To check the robustness of the findings, two sensitivity analyses were performed using the EQ-5D and the complete cases respectively.

Results: Of 136 (74%) participants sufficient data concerning costs were collected to be included in this economic evaluation. Intervention costs were on average €127 (SD 85). No significant differences between groups were found with regard to overall costs. The ICERs of the cost-utility and the cost-effectiveness analyses supported the cost-effectiveness of the intervention. The probability of the intervention being cost-effective was 54–76% for the SF-36 and 94% for the QOLIBRI. Findings were robust.

Conclusion: The intervention 'Stand still . . . and move on' has positive societal economic effects and has a high probability to be cost-effective. Implementation in regular healthcare is recommended.

Trial registration: ISRCTN74835019.

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Introduction

The majority of cardiac arrest survivors have good neurological outcome, but cognitive and emotional consequences and fatigue are common in about half of the survivors.^{1–4} These consequences can affect the patients' daily life functioning, return to work and quality of life negatively.^{4–6} In addition, many informal caregivers show high levels of burden, especially symptoms of post-traumatic stress.^{7,8} Therefore, follow-up care after hospital is needed.

Recently we developed and evaluated an early intervention service for cardiac arrest survivors and their caregivers called ‘Stand still . . . and move on’. This new intervention consists of screening for cognitive and emotional problems, provision of information and support, promotion of self-management, and referral to specialised care if necessary.⁹ In a randomised controlled trial (RCT) this new intervention was compared to care as usual and showed that after one year patients in the intervention group scored significantly better on several domains of quality of life and had less emotional problems.¹⁰

In addition to our RCT, two other RCTs were conducted showing the clinical effectiveness of nursing interventions, but the cost-effectiveness has not been investigated.^{11–13}

Since global healthcare costs are growing and are expected to increase further, it is important to have structured up-to-date information on costs and effects of interventions. Such information can guide healthcare policy makers and health insurance companies in their decision-making when faced with limited resources. Economic evaluations of (new) interventions are comparative analyses of alternative courses of action in terms of both costs (resource use) and consequences (outcomes and effects).¹⁴ To our knowledge, economic evaluations of follow-up care for cardiac arrest survivors have not been performed yet. We therefore performed an economic evaluation alongside our RCT, aimed at determining the cost-effectiveness and cost-utility of the new intervention ‘Stand still . . . and move on’ in comparison to care as usual. We hypothesized that there would be a difference in effects and societal costs supporting the intervention ‘Stand still . . . and move on’.

Methods

Design and participants

This economic evaluation is based on data derived from a multicentre RCT [ISRCTN74835019] conducted by Moolaert et al., in which the effect of receiving the new intervention service alongside usual care was compared with care as usual only.¹⁵ Inclusion criteria for the study were: survival more than two weeks after an in-hospital or out-of-hospital cardiac arrest, living within 50 km of one of the participating hospitals, age 18 years or older, and sufficient knowledge of the Dutch language. Exclusion criteria were a life expectancy less than three months, as estimated by the treating physician, and living in residential or institutional care prior to the cardiac arrest. Patients were recruited from the coronary care units and intensive care units of five hospitals in the Southern part of the Netherlands, from April 2007 to December 2010.

Procedure and randomization

Newly admitted survivors of cardiac arrest were assessed for study eligibility and approached between three and ten days after their cardiac arrest. Patients signed an informed consent form if they decided to participate. If the patient did not have capacity to consent, the caregiver was asked for provisional consent until the patient had the capacity to decide.

Measurements were performed by research assistants who visited the patients at their residence at two weeks, three months and twelve months after their cardiac arrest. In general, participants filled out the questionnaires themselves, but if needed the research assistant could assist. In addition, data concerning costs were collected using monthly cost-diaries, collected through monthly telephone interviews.

Participants were randomly allocated to either the intervention or control group, with a 1:1 allocation ratio. Research assistants were blinded for group allocation.

This study has been approved by the Medical Ethics Committee of Maastricht University Medical Centre, the Netherlands.

Intervention

Patients in the intervention group received the early intervention service called ‘Stand still . . . and move on’ in addition to usual health care. This intervention is a short duration, individualised, semi-structured intervention for survivors of cardiac arrest and their caregivers, which consists of four elements: (1) screening for cognitive and emotional problems; (2) provision of support and information on cardiac arrest and potential neurological consequences; (3) promotion of self-management and (4) referral to specialised care if indicated.⁹ The intervention was conducted by trained nurses, started after hospital discharge and comprised one to six face-to-face consultations at the patients’ home or at an outpatient clinic, depending on the individual needs of patient and caregiver. More details on the rationale and content of the intervention were published.⁹ Furthermore, a process evaluation was performed confirming the intervention’s feasibility.¹⁶

Cost measures

Intervention costs, other direct costs (including other healthcare costs and patient and family costs) and indirect costs (productivity losses) were assessed to evaluate the economic consequences of the interventions from a societal perspective. The intervention costs have been based on the time the nurse spent on consultations and travel. A 4-week cost diary was used to measure all other direct costs and productivity losses.¹⁷ The time horizon of the economic evaluation comprised ten months, from the start of the intervention (two months after cardiac arrest) up to the last follow-up measurement (twelve months). Total costs were estimated by multiplying the volumes of categories from the cost diary by approximate standardized cost prices from the Dutch manual for cost analysis in healthcare research.¹⁸ Real tariffs or costs were used where no standardized cost prices were available. Medication costs were calculated by multiplying the total number of tablets with the price per tablet (Pharmacy Purchase Price) provided by the Dutch website ‘www.medicijnkosten.nl’. When prices concerning a specific medication differed, the lowest cost prices were used. Also additional charges for medication prescription were incorporated. Medication prices were indexed for August 2014.

Additional expenses were determined based on costs patients recorded in their cost diaries. Prices for informal care were based on a standardized cost price based on general hourly wages.¹⁸ Other direct costs measured in the study are listed in Table 2.

Productivity losses have been calculated based on the Human Capital Approach, estimating the value of the lost production over the entire period of absenteeism of the patient based on the number of days absent from paid or unpaid work.

All costs were expressed in euros using the 2014 price level, or were indexed to August 2014, using the rates from Statistics Netherlands.

Outcome measures

Primary outcome measures for this economic evaluation were the Medical Outcomes Study 36-item Short Form Health Survey/RAND 36-item Health Survey (SF-36) and the Quality Of Life after Brain Injury questionnaire (QOLIBRI).

For the cost-utility analysis, utilities were based on the SF-36, a 36-item generic quality of life questionnaire measuring several domains of perceived health.¹⁹ The utilities used in this study were derived with an algorithm of the SF6-D, which transforms the scores on the SF-36 into generic utility scores.²⁰ The area under

the curve method was used to compute quality adjusted life years (QALYs), using utilities at baseline, three and twelve months.²¹

For the cost-effectiveness analysis the QOLIBRI was used as a brain injury specific quality of life measure. The QOLIBRI consists of 37 items of which total scores range from 0 to 100, and was administered at three and twelve months follow-up.²²

The EuroQol instrument (EQ-5D) was used for the sensitivity analyses. The EQ-5D consists of five health state dimensions (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression) on which the participants have to rate their health state as 'no problems', 'some problems' or 'major problems'.²³ The EQ-5D health states, measured at baseline, three and twelve months, were converted into utilities by applying the Dutch utility tariff and QALYs were calculated using the area under the curve method.²⁴

Statistical analysis

The economic analyses were performed according to the intention-to-treat principle. The analysis included participants with at least three cost diaries were available. Individual mean imputation was used to impute missing outcomes and cost data. This method was chosen because the differences between participants were larger than within participants and we anticipated that this method would result in the best estimate.

To check for selective dropout of participants, differences between participants who completed the trial and dropouts were examined on age, gender and initial SF-36 utility. Group differences were studied using independent-samples *t*-test (continuous variables with normal distribution), Mann-Whitney *U*-test (continuous variables with non-normal distribution) or Chi-square test (dichotomous variables).

Costs were compared using bootstraps with mean difference and 95% confidence interval. Outcomes were described and compared using independent-samples *t*-test or Mann-Whitney *U*-test.

Additionally bootstrapping with Microsoft excel 2010 was used to explore sample uncertainty (5000 replications) around the incremental cost effectiveness ratio (ICER). The ICER represents the cost of an additional QALY gained and was used to estimate the cost-utility and cost-effectiveness of 'Stand still ... and move on' compared to usual care only. Non-parametric bootstrapping is a method based on random sampling with replacement based on individual data of the participants.²⁵ The bootstrapped ICERs were subsequently plotted in a cost-effectiveness plane, which

is divided into four quadrants. The south-east quadrant represents the position where the intervention is more effective and less costly than usual care, the so-called dominant quadrant. The north-west quadrant represents the situation that the intervention is more costly and also less effective, and is always called inferior. Both the north-east quadrant and the south-west quadrants involve trade-offs, which means that the cost-effectiveness of the intervention depends on the position of the ICER. Furthermore cost-effectiveness acceptability curves (CEAC) were constructed to show the probability that the intervention was cost-effective, given different ceiling ratios. In the Netherlands the Dutch council for Public Health and Health care recommends that only treatments resulting in 16,000 (for the lowest disease burden) and 80,000 costs (for the highest burden) per QALY should be eligible for reimbursement.²⁶

To measure the robustness of this economic evaluation two sensitivity analyses were performed. Sensitivity analyses are an exploration of the impact on the results of changing the value of one parameter while keeping the values of all other parameters unchanged.²⁷ In the first sensitivity analysis, the cost-utility analysis was repeated using another utility measure, namely the EQ-5D. In the second sensitivity analysis, the cost-utility analysis using the SF-36 utilities was repeated using the complete cases only.

Data were analysed using IBM SPSS Statistics version 22.

Results

Participants

Overall, 185 patients were included in the RCT, of whom 97 were randomised into the intervention group and 88 into the control group. An extensive flowchart of patient follow-up, including refusals and reasons for drop-out was published previously.¹⁰ Of 136 (74%) participants sufficient data concerning costs were collected to be included in this economic evaluation.

There were differences between participants who dropped out during the trial due to loss-to-follow up or insufficient data for the analyses and those who completed it: Drop-outs were significantly older (mean age 64 versus 59, $p = 0.023$), more often female (26% versus 13%, $p = 0.041$) and had a lower initial SF-36 score (0.60 versus 0.64, $p = 0.044$).

Table 1 presents the socio-demographic variables and characteristics of the cardiac arrest of the participants with sufficient data concerning costs.

Table 1
Socio-demographic variables and characteristics cardiac arrest ($n = 136$).

	<i>n</i>	Intervention $n = 72$ <i>n</i> (%) or mean (SD) or median (range)	<i>n</i>	Control $n = 64$ <i>n</i> (%) or mean (SD) or median (range)
Socio-demographic variables				
Male, <i>n</i> (%)	72	62 (86%)	64	56 (88%)
Age, at cardiac arrest, years	72	59 (12)	64	59 (11)
Marital status	67		62	
Married/living with partner		60 (90%)		53 (85%)
Single/divorced/widowed		7 (10%)		9 (15%)
Highest level of education	68		62	
Basic education		26 (38%)		24 (39%)
Further education		21 (31%)		20 (32%)
Higher education		21 (31%)		18 (29%)
Paid job before cardiac arrest	70	42 (60%)	64	37 (58%)
Characteristics cardiac arrest				
Cardiac cause	60	60 (100%)	58	55 (95%)
Location out-of-hospital	72	58 (81%)	64	52 (81%)
Witnessed cardiac arrest	71	67 (94%)	63	61 (97%)
Bystander CPR	70	63 (90%)	62	59 (94%)
Initial cardiac rhythm VF/VT	63	63 (100%)	56	50 (89%)
Time collapse – ROSC, min	31	10 (0–70)	31	10 (0–60)

CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; VT, ventricular tachycardia; ROSC, return of spontaneous circulation.

Table 2
Healthcare costs during months 3–12 after cardiac arrest.

	Intervention <i>n</i> = 72 Mean costs in €	Control <i>n</i> = 64 Mean costs in €	<i>p</i> -value
Ambulance and emergency care	57	133	0.000
Hospital admission	1183	1683	0.002
Rehabilitation in-patient	1462	1445	0.555
Rehabilitation out-patient	2270	1229	0.000
General practitioner	108	139	0.000
Medical specialist	446	490	0.001
Company doctor	26	34	0.546
Outpatient pacemaker consultation	28	65	0.000
Paramedical and psychological care	606	809	0.007
Nursing home	565	681	0.124
Home for elderly	68	75	0.808
Psychiatric hospital	93	0	0.002
Medication	287	405	0.711
Activities and sport	63	73	0.864
Special aids	1	2	0.024
Extra expenses	20	35	0.445
Home care			
Nursing	137	370	0.554
Domestic	222	274	0.295
Domestic help (private)	101	87	0.426
Other paid care	1	23	0.754
Informal care (unpaid)	933	1124	0.000

Costs and effects

Table 2 provides an overview of the distribution of the healthcare costs for both the intervention and control group. In the intervention group costs were significantly lower for ambulance and emergency care, hospital admission, general practitioners, medical specialists, outpatient pacemaker consultation, paramedical and psychological care, special aids and informal care. In contrast, there were significantly higher costs in the intervention group for out-patient rehabilitation, as well as for admission in a psychiatric hospital.

Table 3 presents the overall societal costs and outcomes of the intervention and control group. The costs for the intervention were on average €127 (SD 85). In both groups, productivity loss was the main source of costs and accounted for approximately 70% of the total costs. With regard to total societal costs, bootstrap replications revealed that there were no significant differences between the groups.

The mean scores on all three outcome measures were better for the intervention group, but statistical significance was only found for the QALY SF-36.

Cost-utility and cost-effectiveness planes and CEACs

The cost-utility analysis using the SF-36 utilities resulted in an ICER showing a greater mean health benefit (0.04 additional

QALYs) achieved at almost equal costs (€89 additional cost). Fig. 1 presents the cost-effectiveness plane and CEAC for the QALYs. Of the bootstrapped ICERs, a large majority (98%) lies in the eastern part of the plane, which indicates that the intervention resulted in better outcome. More specifically, 49% of the ICERs were located in the south-east quadrant (indicating higher effects and lower costs), and another 49% were located in the north-east quadrant (indicating higher effects and higher costs). Of all bootstrapped likelihood replications only 2% were located in the north-west quadrant, indicating inferiority. The CEAC shows that the probability of the intervention being cost-effective ranges between 54% and 76%, depending of the threshold value of €16,000 and €80,000 respectively.

The cost-effectiveness analysis using the QOLIBRI showed lower costs (€1957 savings) and higher effects (3.69 improvement on QOLIBRI). Fig. 2 shows that the majority (63%) of the bootstrapped ICERs were located in the south-east quadrant (higher effects and lower costs) and 32% in the north-east quadrant (higher effects and higher costs). The CEAC shows that the probability of the intervention being cost-effective is 94%.

Sensitivity analyses

In the first sensitivity analysis the cost-utility analysis was repeated using another utility measure, the EQ-5D. For the intervention group this resulted in a greater mean health benefit

Table 3
Costs and outcomes during first year after cardiac arrest.

Societal costs	<i>n</i>	Intervention Mean costs in € (SD)	<i>n</i>	Control Mean costs in € (SD)	Mean difference (95% CI) ^a
Intervention	76	127 (85)	–	–	127
Healthcare	72	8755 (1356)	64	9270 (1747)	–515 (–5016 to 3605)
Productivity loss	72	21,660 (2852)	64	21,636 (3138)	24 (–8036 to 8553)
Total societal costs	72	30,318 (3847)	64	30,607 (3494)	–289 (–10,663 to 9275)
Outcomes	<i>n</i>	Mean (SD)	<i>n</i>	Mean (SD)	Mean difference (95% CI) ^b
QALY SF-36	89	0.69 (0.11)	85	0.65 (0.12)	0.038 (0.003 to 0.073)
QOLIBRI	56	57 (12)	62	54 (12)	2.95 (–1.49 to 7.39)
QALY EQ-5D	85	0.76 (0.21)	79	0.71 (0.23)	0.055 (–0.013 to 0.123)

QALY, Quality Adjusted Life Year; SF-36, Short Form Health Survey 36; QOLIBRI, Quality Of Life after Brain Injury questionnaire.

^a Difference in mean (95% confidence interval) derived using bootstrapping (1000 replications).

^b Difference in mean (95% confidence interval) derived using independent samples *t*-test or Mann–Whitney *U*-test.

Fig. 1. Cost-effectiveness plane and cost-effectiveness acceptability curve QALY.

Fig. 2. Cost-effectiveness plane and cost-effectiveness acceptability curve QOLIBRI.

(0.06 additional QALYs) achieved at lower costs (€2983 savings) compared to the control group. A large majority (72%) of the bootstrapped ICERs were located in the south-east quadrant (higher effects and lower costs) and 24% in the north-east quadrant (higher effects and higher costs). The CEAC shows that the probability of the intervention being cost-effective ranges between 78% and 89%.

In the second sensitivity analysis the cost-utility analysis using SF-36 utilities was repeated using the complete cases only ($n = 92$). In this analysis 45% of the bootstrapped ICERs were located in the dominant south-east quadrant, and the probability of the intervention being cost-effective ranges between 49% and 76%.

Discussion

In this study we performed an economic evaluation of a new nursing intervention for survivors of a cardiac arrest called 'Stand still . . . , and move on', and showed that this intervention does not only improve outcome but is also cost-effective compared to care as usual only. The costs of the intervention were only €127.

An important aspect of this new intervention is that also mild cognitive and emotional problems, which normally go unnoticed, are now detected in an early phase. This seems to have resulted in more referrals to out-patient rehabilitation, which can explain part of the improved outcome. Nevertheless, for most patients further referral was not necessary, and apparently, this early, concise, and tailored intervention also contributed to their overall well-being. There was no difference in costs related to in-patient rehabilitation, which shows that in current usual care survivors who are severely affected are already identified and appropriately referred to in-patient rehabilitation.

Although, overall costs did not differ significantly between groups, there were interesting differences in the distribution of healthcare costs. Patients in the intervention group had significantly lower medical care costs, including general practitioners, medical specialists, paramedical and psychological care, ambulance and emergency care and hospital admissions. This might be explained by the fact that the intervention also targeted to provide information and support, which might have reduced feelings of uncertainty and as a consequence also reduced the utilisation of healthcare resources. In the effect study we have previously shown that the intervention indeed reduced feelings of anxiety.¹⁰

The costs for admission in psychiatric hospital was higher in the intervention group. However, this concerned two patients only (and zero in the control group), and therefore, although statistically significant, the clinical relevance of this finding can be questioned.

This study is, to our best knowledge, the first economic evaluation of an aftercare intervention for survivors of a cardiac arrest. Two studies previously investigated the outcome of psychosocial interventions for cardiac arrest survivors showing a decreased risk of cardiovascular death, decreased ICD related physical symptoms, lower levels of anxiety and increased knowledge on cardiac arrest, but the cost-effectiveness of these interventions is not known.^{11,13} In the field of cardiology, economic evaluations have been performed on implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure.²⁸ A few comparable studies on the effectiveness of early interventions for patients with acquired brain injury have been conducted showing reduced social morbidity and post-concussion symptoms after six months and reduced levels of anxiety, but also in this field economic evaluations have not been performed yet.^{29,30}

This study has several strengths. First of all, we performed a full economic evaluation addressing both cost-utility and cost-effectiveness. In addition, two sensitivity analyses confirmed the conclusions drawn from the main analyses. In fact, the sensitivity

analysis using the EQ-5D found even stronger evidence in favour of the intervention. Secondly, a relatively large sample was followed for a substantial period of time and we did not exclude any patients based on their level of cognitive impairment. Thirdly, data on costs were collected using continuous data collection, which contributed to the reliability of the data. Another strong point is that a societal perspective was chosen, instead of the effects on a single medical institution only, and thereby effects on patients and society as a whole have now been revealed. Finally, as we compared the intervention with care as usual, and not with a control intervention, the direct effects of implementing this intervention are shown.

There were also some limitations. Firstly, some selection bias could have taken place as drop-outs were significantly older, more often female and had a lower initial SF-36 score. The difference in initial SF-36 score might indicate a selective drop-out of those patients with poorer outcome, which could result in higher healthcare costs. In addition, it could be hypothesized that healthcare costs also increase with age. Nevertheless, our findings seem to be robust, and in clinical practice there is always some extent of drop-out from interventions. Secondly, we performed some data imputation in case of incomplete data sets, which always implies a risk with regard to reliability of the data. However, in the second sensitivity analysis the main analysis was repeated using patients with complete data sets only, and although the effects were less strong, the direction of the conclusions remained stable. In addition, the measurements used in this study have not been validated (yet) for this specific population of cardiac arrest survivors. Nevertheless, we only used widely used instruments that have been validated in other populations such as traumatic brain injury.³¹

Conclusions

We previously showed that the intervention 'Stand still . . . , and move on' is feasible and improves long-term outcome.^{10,16} This economic evaluation showed that the intervention has relatively low costs, results in positive societal economic effects and is cost-effective. Implementation in regular healthcare is therefore recommended.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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