

# Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: A randomised controlled trial

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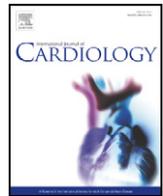
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## Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: A randomised controlled trial<sup>☆</sup>



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### ABSTRACT

**Background:** Survivors of a cardiac arrest frequently have cognitive and emotional problems and their quality of life is at risk. We developed a brief nursing intervention to detect cognitive and emotional problems, provide information and support, promote self-management, and refer them to specialised care if necessary. This study examined its effectiveness.

**Methods:** Multicentre randomised controlled trial with measurements at two weeks, three months and twelve months after cardiac arrest. 185 adult cardiac arrest survivors and 155 caregivers participated. Primary outcome measures were societal participation and quality of life of the survivors at one year. Secondary outcomes were the patient's cognitive functioning, emotional state, extended daily activities and return to work, and the caregiver's well-being. Data were analysed using 'intention to treat' linear mixed model analyses.

**Results:** After one year, patients in the intervention group had a significantly better quality of life on SF-36 domains Role Emotional (estimated mean differences (EMD) = 16.38,  $p = 0.006$ ), Mental Health (EMD = 6.87,  $p = 0.003$ ) and General Health (EMD = 8.07,  $p = 0.010$ ), but there was no significant difference with regard to societal participation. On the secondary outcome measures, survivors scored significantly better on overall emotional state (HADS total, EMD = -3.25,  $p = 0.002$ ) and anxiety (HADS anxiety, EMD = -1.79,  $p = 0.001$ ) at one year. Furthermore, at three months more people were back at work (50% versus 21%,  $p = 0.006$ ). No significant differences were found for caregiver outcomes.

**Conclusion:** The outcomes of cardiac arrest survivors can be improved by an intervention focused on detecting and managing the cognitive and emotional consequences of a cardiac arrest.

**Trial registration:** Current controlled trials, ISRCTN74835019.

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## 1. Introduction

Of those people who survive a cardiac arrest, about half suffer cognitive impairments and quality of life can be at risk for all of them [1–3]. The cognitive impairments arise from hypoxic–ischaemic brain injury

[4]. Emotional problems, such as anxiety and depression, are also frequently seen, as well as a reduced level of participation in society and a low return to work rate [5,6]. Caregivers may also feel highly burdened and they often have emotional problems, including symptoms of post-traumatic stress [7,8]. Because a cardiac arrest can affect patients and caregivers on all these domains, there is an urgent need for an effective intervention that guides patient and caregiver after survival of a cardiac arrest.

Although cognitive impairments are common after cardiac arrest and affect quality of life, these problems often remain undetected by health care professionals [9,10]. We therefore developed a new early intervention service for survivors and their caregivers called 'Stand still ..., and move on'.

<sup>☆</sup> All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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This brief intervention is directed at screening for cognitive and emotional problems, provision of information and support, promotion of self-management, and referral to specialised care if necessary [11].

The goal of this study was to evaluate the effectiveness of this new intervention for cardiac arrest survivors and their caregivers. We expected that the intervention would primarily result in a higher level of participation in society and better quality of life for the survivors and, in addition, would also improve the well-being of caregivers, compared with those who had only received usual care. We did not expect the intervention to affect cognitive impairments, as it did not include cognitive training.

## 2. Methods

### 2.1. Design overview

This study, named 'Activity and Life after Survival of a Cardiac Arrest' (ALASCA), was a multicentre single blind randomised controlled trial in which we compared the effect of receiving the new intervention alongside usual care to care as usual only. The study was registered in a trial register [ISRCTN74835019], and the protocol has been published [12]. There were only minor deviations from the protocol, which are reported in the following text.

### 2.2. Setting

Patients were recruited from the coronary care units and intensive care units of five hospitals in the southern part of the Netherlands, between April 2007 and December 2010. The participating hospitals serve approximately one million inhabitants. All the hospitals had protocols for care of resuscitation patients in line with international guidelines and performed therapeutic hypothermia and pacemaker implantations [13]. In addition, two of the hospitals undertook percutaneous coronary interventions, implantable cardioverter defibrillator (ICD) implantations, catheter ablations, and coronary artery bypass grafts. Throughout the study period, medical care for cardiac arrest patients in the participating hospitals remained unchanged.

### 2.3. Participants

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 of less than three months (as estimated by the treating physician) and living in residential or institutional care prior to the cardiac arrest.

In this study, we defined caregiver as a partner, spouse or significant other who was closely related to the patient. There were no additional inclusion or exclusion criteria for the caregivers. If a patient had a partner or a spouse, that person was asked to participate in the trial together with the patient. If the patient did not have a partner or a spouse, we asked the patient to assign another person as the caregiver, but this was not obligatory.

### 2.4. Procedure

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

Baseline measurements were planned two weeks after the cardiac arrest, with follow-up at three and twelve months (main study end point). At baseline, we also assessed the patient's level of daily functioning and participation in society prior to the cardiac arrest. Research assistants visited the patients at their homes to perform the measurements. The Medical Ethics Committee of Maastricht University Medical Centre approved the study protocol.

### 2.5. Randomisation

Participants were randomly assigned to either the intervention group or the control group, with a 1:1 allocation ratio. Randomisation took place after the baseline measurements. The randomisation procedure was performed centrally by the project leader using a computerised block randomisation containing blocks of 15. The randomisation scheme included stratification on two variables: hospital site and location of the cardiac arrest (in-hospital versus out-of-hospital).

Research assistants administered the assessments and were blinded for group allocation. To check the success of the blinding, they were asked to indicate group allocation for all participants who completed the trial, choosing one of the following options: 'Intervention group', 'Control group' or 'I don't know'.

### 2.6. Intervention

In addition to usual health care, patients in the intervention group received an early intervention named 'Stand still ..., and move on'. This intervention is a short, individualised, semi-structured intervention for survivors of cardiac arrest and their caregivers. Table 1 describes the content and characteristics of the intervention. More details about the rationale and content of the intervention, as well as training of the nurses, have been published previously [11]. Furthermore, a process evaluation has found the intervention to be feasible [14].

### 2.7. Standard care

This new early intervention was set in the context of and added to standard care. All participating hospitals had general outpatient cardiac rehabilitation programmes in which patients could enrol at their cardiologists' discretion [20]. However, there were no specific programmes for cardiac arrest survivors and standard care did not include any specific attention to cognitive impairments.

### 2.8. Outcomes and follow-up

Table 2 describes the measurement instruments that were used. Primary outcome measures were the patient's participation in society and quality of life one year after the cardiac arrest. Secondary outcome measures were the patient's level of cognitive functioning, emotional state, extended daily activities and return to work, as well as the caregiver's quality of life, strain and the emotional state. We assessed all the outcome measures for the effect evaluation three times: at two weeks (baseline), three months and twelve months (endpoint) after the cardiac arrest. More details about the administered measurement instruments can be found in the study protocol [12].

'Work situation' was a socio-demographic variable in the protocol, but since return to work is an important variable reflecting societal participation, it is now reported as a secondary outcome measure. 'Return to work' was defined as partial or complete return to a paid job.

The EuroQol 6D was administered as a cost-effectiveness study parameter and is therefore not included in this effect evaluation.

At baseline, we recorded socio-demographic and medical variables together with some measures of functioning (left ventricular ejection

**Table 1**  
Content and characteristics of the intervention.

Target group	Survivors of cardiac arrest and their caregivers
Main elements	<ol style="list-style-type: none"> <li>1. Screening for cognitive and emotional problems</li> <li>2. Provision of support and information on cardiac arrest and possible neurological consequences</li> <li>3. Promotion of self-management strategies</li> <li>4. Referral to specialised care if indicated</li> </ol>
Obligatory topics – with examples	<ol style="list-style-type: none"> <li>1. Cognitive changes and challenges <ul style="list-style-type: none"> <li>– Consequences of hypoxic-ischaemic brain injury</li> <li>– Possible cognitive changes and fatigue</li> <li>– Advice on how to deal with cognitive problems</li> </ul> </li> <li>2. Emotional changes and challenges <ul style="list-style-type: none"> <li>– Possible emotional changes (e.g., anxiety, depression, fear of recurrence)</li> <li>– Social isolation, loneliness and loss</li> <li>– Caregiver strain</li> <li>– Advice on how to deal with emotional problems</li> </ul> </li> <li>3. Principles of self-management <ul style="list-style-type: none"> <li>– Explanation of the principles of self-management</li> <li>– Practising self-management techniques</li> </ul> </li> </ol>
Optional topics	<ul style="list-style-type: none"> <li>– Cardiac topics</li> <li>– Physical changes and challenges</li> <li>– Activities of daily living</li> <li>– Changes and challenges for the caregiver</li> <li>– Partner relationships and sexuality</li> <li>– Dealing with healthcare providers</li> <li>– Any other questions from patients or caregivers</li> </ul>
Written information	<ul style="list-style-type: none"> <li>– A special information booklet was provided to all participants<sup>a</sup></li> <li>– Pre-existing brochures about cardiac and neurological topics were offered as needed</li> </ul>
Available screening instruments (not obligatory)	<ol style="list-style-type: none"> <li>1. Cognitive screening <ul style="list-style-type: none"> <li>– Checklist Cognition and Emotion [15]</li> <li>– Cognitive Log [16]</li> </ul> </li> <li>2. Emotional screening <ul style="list-style-type: none"> <li>– Hospital Anxiety and Depression Scale [17]</li> <li>– Impact of Event Scale [18]</li> </ul> </li> <li>3. Screening for caregiver strain <ul style="list-style-type: none"> <li>– Caregiver Strain Index [19]</li> </ul> </li> </ol>
Providers of intervention	Specialised nurses with experience in the field of cardiology, neurology or rehabilitation medicine
Start intervention	Soon after discharge from the hospital, preferably within one month
Frequency	Between one and six face-to-face consultations
Duration of consultations	First session: 1 h Follow-up sessions: 30 min Telephone consultations are optional.
Location	Home visits or out-patient clinic

<sup>a</sup> Available as additional online file.

fraction, New York Heart Association Classification [21] and Barthel Index [22]).

### 2.9. Sample size and power calculation

Scores on the Community Integration Questionnaire (CIQ) were used to determine an optimal sample size. Since no studies on survivors of cardiac arrest using this outcome measure were available at the start of the study, we used the scores of patients with traumatic brain injury which were used as a reference value (mean 16.09 (SD 4.20)) [33]. Sample size calculation (independent-samples t-test, one-sided testing), with an assumed clinical relevant difference between groups of at

**Table 2**  
Primary and secondary outcome measures.

Outcome measures	Measurement instrument	Range questionnaire Min (poor)–max (good)
<i>Primary</i>		
Participation in society	Community Integration Questionnaire [23]	0–29
Quality of life	Short-Form-36 (SF-36), 8 subdomains [24] EuroQol VAS [25]	0–100 0–100
<i>Secondary</i>		
Cognitive functioning	Cognitive Log [16] Adult Memory and Information Processing Battery [26] Verbal fluency [27] Trail Making Test A + B [28] Paragraph recall direct + delayed [29] Cognitive Failures Questionnaire [30]	0–30 0– <sup>a</sup> 0– <sup>a</sup> 0–21 100–0
Emotional functioning	Hospital Anxiety and Depression Scale (HADS) Total [17] – Subscale Anxiety – Subscale Depression Impact of Event Scale [31]	42–0 21–0 21–0 75–0
Extended daily activities	Frenchay Activity Index [32]	0–45
Caregiver strain	Caregiver Strain Index [19]	13–0

<sup>a</sup> There is no formal end score.

least 10%, an alpha of 0.05 and a power ( $1 - \beta$ ) of 0.8, showed that each group needed 84 patients, resulting in a target sample size of 168 patients. With an estimated 15% loss to follow-up, we aimed to include 200 participants.

### 2.10. Statistical analysis

To check for selection bias, we compared baseline characteristics (age and gender) of compliant and non-compliant patients. To check for the selective dropout of participants, we examined the differences between participants who completed the trial and dropouts on the following baseline characteristics: age, gender, initial overall cognitive status, basic activities of daily living and caregiver strain. Group differences were studied using an independent-samples t-test (continuous variables with normal distribution), a Mann–Whitney U-test (continuous variables with non-normal distribution) or a Chi-square test (dichotomous variables).

To investigate effectiveness, we performed linear mixed model analyses according to the intention to treat principle, with the primary and secondary outcome measures as dependent variables. The following variables were entered as fixed terms: hospital, location of cardiac arrest, time and the interaction term group \* time. We assumed an unstructured covariance structure for the repeated measures, used a restricted maximum likelihood estimation and based significance on likelihood ratio tests. Linear mixed model analyses replaced multiple regression analysis (as was described in the protocol), as this is a more advanced statistical technique with the following advantages: it is more suitable for repeated measures as it considers baseline level and correlation between repeated measures, and patients who drop out are included in the analysis (assuming the data to be missing at random).

We separately analysed differences in the proportions of people who had returned to work at three and twelve months using a Chi-square test.

Additionally, we performed per protocol analyses, incorporating only those patients in the intervention group who had received the

intervention, and compared those results with the intention to treat analyses.

As we tested multiple primary and secondary outcome measures a  $p \leq 0.01$  (two-sided) was considered statistically significant. Effect sizes were reported as estimated mean differences. Effects were considered clinically relevant only if the estimated mean difference indicated an improvement of 10% or more compared with the observed mean in the control group. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0.

### 3. Results

#### 3.1. Participants

Fig. 1 presents the flow of participants through the study. Overall, 185 patients were included in the study, of whom 143 (77%) completed the trial. Patient recruitment took longer than expected, leading us to extend of the end of the recruitment period from April 2010 to December 2010.

The group of patients who refused to participate was significantly older (mean 67 (SD 12) years versus 60 (SD 12) years,  $p < 0.001$ ), and had a significantly lower percentage of males (69% versus 83%,  $p = 0.007$ ). There were no significant differences between participants who dropped out during the trial and those who completed it.

We performed baseline assessments at a median of 24 days after the cardiac arrest (range 9–70 days), with three- and twelve-month follow-

up assessments at a median of 96 days (range 74–162) and 369 days (range 353–471), respectively. Table 3 shows the patients' baseline characteristics.

In addition to the 185 patients, 155 caregivers participated in the study. They were related to the patients either as a spouse/partner ( $n = 138$ , 89%), child ( $n = 8$ , 5%), parent ( $n = 2$ , 1%), sibling ( $n = 4$ , 3%) or friend/other ( $n = 3$ , 2%). Caregivers had a mean age of 55 years (SD 12) and 134 (86%) were female.

#### 3.2. Effects of the intervention

Table 4 presents the effects of the intervention. At baseline, there were no significant differences between the intervention and control groups. At 12 months, there were no significant differences with regard to participation in society, but there were significant differences in estimated means at 12 months in favour of the intervention group on three domains of quality of life on the SF-36: Role Emotional ( $p = 0.006$ ), Mental Health ( $p = 0.003$ ) and General Health ( $p = 0.010$ ). Estimated mean differences improved by 24%, 9% and 13%, respectively, compared with observed means in the control group.

On the secondary outcome measures, we found significant improvements at 12 months on overall emotional state (HADS total score,  $p = 0.002$ ) and anxiety (HADS anxiety subscale,  $p = 0.001$ ), with estimated mean differences 40% and 43% higher, respectively, compared to observed means in the control group. Return to work at three months was significantly higher in the intervention group: 24 people (50%)

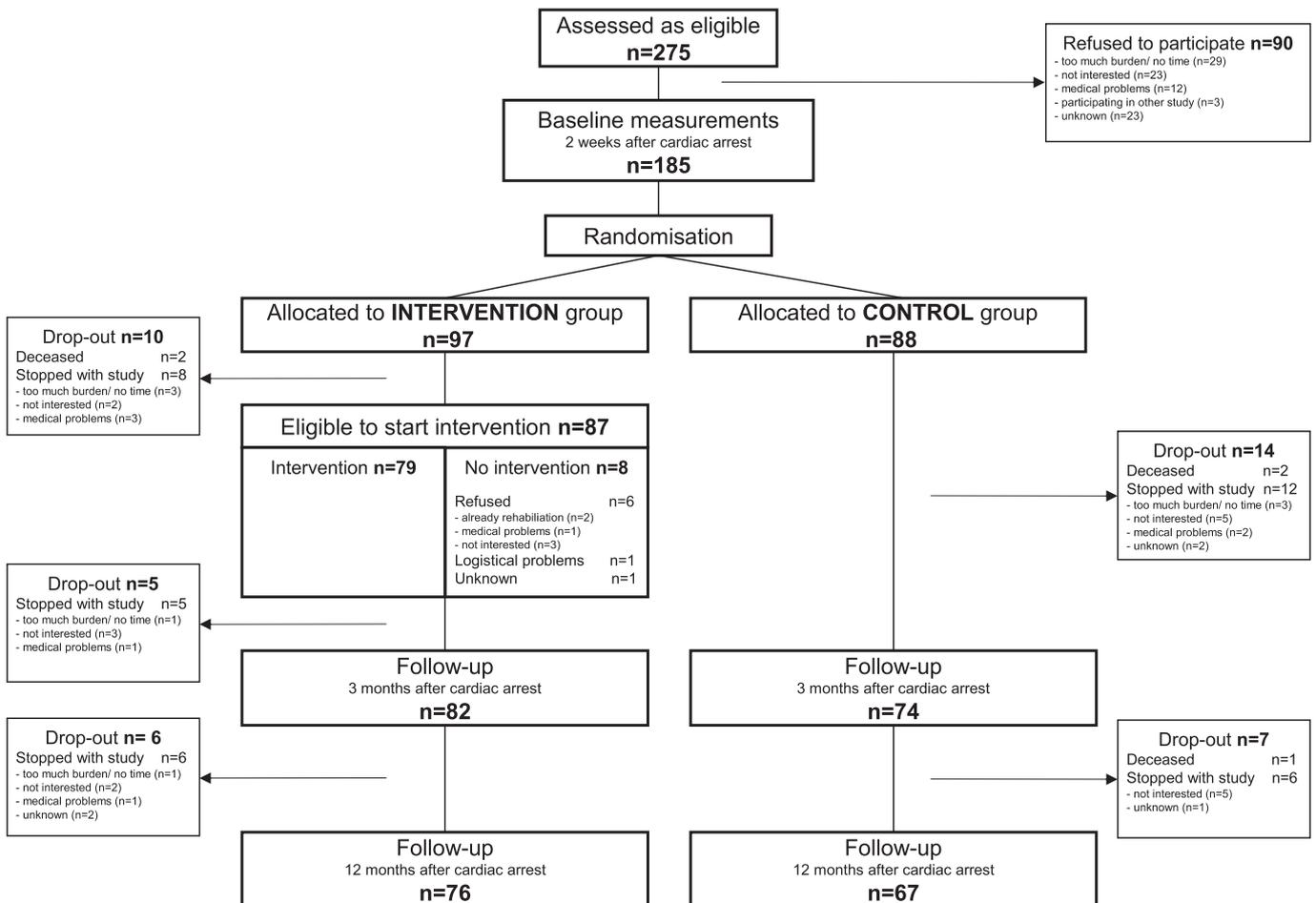


Fig. 1. Flow of participants through the study.

**Table 3**  
Baseline characteristics patients.

	Intervention n = 97		Control n = 88	
	n	n (%) or mean (SD) or median (range)	n	n (%) or mean (SD) or median (range)
<i>Socio-demographic variables</i>				
Male, n (%)	97	80 (83%)	88	74 (84%)
Age, at cardiac arrest, years	97	60 (12)	88	60 (12)
Marital status	90		88	
Married/living with partner		78 (87%)		71 (84%)
Single/divorced/widowed		12 (13%)		14 (16%)
Highest level of education	91		85	
Basic education		37 (41%)		35 (41%)
Further education		29 (32%)		29 (34%)
Higher education		25 (27%)		21 (25%)
Employment status, pre-morbid	91		84	
Paid job		44 (48%)		45 (54%)
Retired/disability pension		36 (40%)		32 (38%)
Sick leave		3 (3%)		1 (1%)
<i>Medical history</i>				
No cardiovascular history	91	37 (41%)	82	29 (35%)
Hypertension		27 (30%)		23 (28%)
Myocardial infarction		21 (23%)		28 (34%)
Heart failure		3 (3%)		7 (9%)
Cardiac arrest		1 (1%)		1 (1%)
CABG		8 (8%)		6 (7%)
Arrhythmia		8 (8%)		9 (10%)
Diabetes mellitus		14 (15%)		10 (12%)
Neurological history		8 (9%)		10 (12%)
<i>Characteristics cardiac arrest</i>				
Cardiac cause	79	77 (98%)	81	77 (95%)
Location out-of-hospital	97	77 (79%)	88	70 (80%)
Witnessed cardiac arrest	95	89 (94%)	86	83 (97%)
Bystander CPR	92	83 (90%)	85	76 (89%)
Initial cardiac rhythm VF/VT	82	80 (98%)	77	71 (92%)
Time collapse – ROSC, minutes	41	10 (0–70)	44	10 (0–60)
Duration coma, in days	63	1 (0–17)	58	2 (0–19)
<i>Medical interventions</i>				
Therapeutic hypothermia	92	44 (48%)	85	38 (45%)
Catheterisation with PCI		41 (44%)		37 (44%)
CABG		10 (11%)		13 (15%)
ICD/pacemaker		21 (23%)		24 (22%)
<i>Location of discharge</i>				
Home	92	80 (87%)	80	71 (89%)
Rehabilitation centre		7 (8%)		8 (10%)
Nursing home		5 (5%)		1 (1%)
<i>Baseline functioning at 2 weeks</i>				
LVEF at discharge, %	31	44 (10–67)	32	44 (20–60)
NYHA classification	83		84	
1		35 (42%)		34 (41%)
2		31 (37%)		38 (45%)
3		9 (11%)		7 (8%)
4		8 (10%)		5 (6%)
Barthel Index	84	18.12 (3.61)	82	18.63 (3.02)

CABG = coronary artery bypass graft; CPR = cardiopulmonary resuscitation; VF = ventricular fibrillation; VT = ventricular tachycardia; ROSC = return of spontaneous circulation; PCI = percutaneous coronary intervention; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

had already returned to work, compared with 8 people (21%) in the control group ( $p = 0.006$ ). But there was no significant difference in employment status at 12 months: 32 people (74%) in the intervention group and 27 people (71%) in the control group ( $p = 0.734$ ) had returned to work.

We did not find any significant effects on the outcome measures for the caregivers (Table 5). Per protocol analyses found similar results as intention to treat analyses.

### 3.3. Success of blinding

Research assistants answered the question about group allocation for 134 of the 143 patients who completed the trial. They answered correctly in 71 cases (53%), incorrectly in 33 cases (25%) and 'I don't know' in 29 cases (22%).

## 4. Discussion

Cardiac arrest survivors who received our new early intervention had an improved quality of life, a better overall emotional state and less anxiety compared with those who only received the usual care. Additionally, people in the intervention group seemed to return to work more rapidly, a finding which could also have socio-economic importance. Improvements were both statistically significant and clinically relevant, indicating that our compact intervention does indeed have the potential to increase functional outcome and quality of life for survivors of a cardiac arrest. To the best of our knowledge, this is the first study to report such results.

What distinguishes our intervention from existing interventions is the specific attention given to potential cognitive impairments. Although cognitive impairments are common after a cardiac arrest, patients are often unaware of these brain-injury-related consequences, and health care professionals also may not recognise these so-called 'invisible' problems [10]. To our knowledge, this is the first intervention to integrate active screening for possible cognitive problems into a psychosocial and evidence-based intervention for survivors of a cardiac arrest and their caregivers. The effectiveness of the intervention can probably not be attributed to self-management as our process evaluation found that this was rarely taught [14].

This study had several strengths. First, it had a broad population, including patients of all ages who suffered both out-of-hospital and in-hospital cardiac arrests, and who did or did not have an ICD. This increases the generalisability of our results. Secondly, since we have already shown that this intervention is feasible, implementation in regular health care is therefore possible [14]. The fact that our intervention is brief makes it attractive for future implementation, as costs will probably be low.

This study had some issues related to sample size. First, we did not reach the target sample size of 168 participants, as only 143 of the 185 participants who enrolled in the trial completed it. Second, we adapted the level of significance from 0.05 (one-sided), as mentioned in the original protocol, to 0.01 (two-sided) in order to account for multiple testing [12]. As a consequence, the original sample size calculation is not in accordance with our actual statistical analysis. Therefore, we have now checked the effect sizes that can be detected with our actual sample size and used the adapted significance level. With the current number of participants (intervention group  $n = 76$ , control group  $n = 67$ ), using an alpha of 0.01 and a power ( $1 - \beta$ ) of 0.8, a standardised effect size (Cohen's  $d$ ) of 0.58 can be detected with the independent-samples  $t$ -test. This indicates that medium effect sizes can be detected with our current sample.

We used linear mixed models for the final analyses, which resulted in power gain over the independent-samples  $t$ -test. This occurred because it takes differences in baseline scores into account and uses all available data, which means that data from patients who drop out are also used in the analysis. The fact that clinically relevant improvements on several important outcome measures were also found to be statistically significant indicates that the study was sufficiently powered.

This study also had some limitations. First, the patients who refused to participate were somewhat older and more often female. Elderly people may be more hesitant to participate in a study because of fears that it will be burdensome. The greater number of females who refused participation may be related to this age difference as women, on average, live longer than men. However, since the distribution of gender and age was

**Table 4**  
Patient outcomes and effect of the intervention.

	Intervention	Control	Estimated mean difference	Standard error	p-Value
	Observed mean (SD)	Observed mean (SD)			
<i>Primary outcomes</i>					
<i>Participation</i>					
Community Integration Questionnaire					
– Premorbid	15.59 (4.77)	16.17 (4.34)			
– 3 months	13.99 (4.79)	13.70 (5.47)	0.21	0.73	0.770
– 12 months	16.16 (4.68)	14.60 (5.16)	1.19	0.63	0.062
<i>Quality of life</i>					
SF-36 Physical Functioning					
– Baseline	59.16 (28.44)	54.11 (26.00)			
– 3 months	73.44 (25.69)	69.71 (25.46)	1.87	3.24	0.565
– 12 months	78.47 (25.03)	73.05 (27.37)	4.59	3.71	0.218
SF-36 Social Functioning					
– Baseline	54.55 (28.31)	52.56 (28.37)			
– 3 months	71.05 (25.18)	70.96 (24.67)	–0.58	3.99	0.885
– 12 months	81.77 (21.08)	79.88 (23.21)	2.95	3.61	0.416
SF-36 Role Physical					
– Baseline	23.46 (33.85)	23.77 (34.21)			
– 3 months	42.67 (41.26)	33.09 (40.39)	9.76	6.49	0.135
– 12 months	66.90 (41.36)	59.61 (43.23)	7.95	6.93	0.253
SF-36 Role Emotional					
– Baseline	52.19 (44.00)	56.91 (42.39)			
– 3 months	69.66 (42.02)	62.75 (44.06)	8.26	6.73	0.221
– 12 months	84.04 (32.30)	69.27 (41.70)	16.38	5.84	<b>0.006</b>
SF-36 Mental Health					
– Baseline	71.51 (22.13)	73.90 (19.29)			
– 3 months	76.21 (19.26)	76.81 (18.68)	0.59	2.38	0.805
– 12 months	81.35 (14.78)	76.06 (17.27)	6.87	2.25	<b>0.003</b>
SF-36 Vitality					
– Baseline	56.65 (24.48)	56.95 (23.08)			
– 3 months	64.04 (19.87)	64.42 (19.66)	0.54	2.55	0.831
– 12 months	65.83 (19.41)	62.23 (19.94)	5.07	2.70	0.063
SF-36 Bodily Pain					
– Baseline	58.55 (27.74)	57.77 (29.97)			
– 3 months	76.45 (24.38)	71.13 (26.46)	6.58	3.78	0.084
– 12 months	86.03 (21.29)	76.69 (26.16)	9.46	3.86	0.016
SF-36 General Health					
– Baseline	56.95 (20.93)	61.22 (19.68)			
– 3 months	60.06 (23.36)	61.32 (20.44)	2.63	2.56	0.305
– 12 months	64.79 (22.35)	60.00 (22.04)	8.07	3.08	<b>0.010</b>
EuroQol VAS					
– Baseline	61.01 (18.91)	61.18 (18.62)			
– 3 months	70.95 (17.06)	71.30 (15.95)	–0.25	2.33	0.915
– 12 months	75.90 (16.50)	74.32 (14.45)	1.76	2.31	0.447
<i>Secondary outcomes</i>					
<i>Cognitive functioning</i>					
Cognitive Log					
– Baseline	26.39 (3.43)	26.04 (3.28)			
– 3 months	26.81 (3.06)	27.18 (2.43)	–0.53	0.38	0.167
– 12 months	27.24 (2.58)	27.27 (2.64)	–0.08	0.37	0.833
AMIPB task A					
– Baseline	27.44 (10.70)	28.30 (9.65)			
– 3 months	30.47 (9.84)	30.97 (9.49)	–0.15	0.91	0.874
– 12 months	31.61 (10.07)	32.48 (9.84)	0.05	1.05	0.961
Verbal fluency					
– Baseline	19.41 (6.56)	18.86 (6.35)			
– 3 months	21.05 (7.67)	21.81 (6.34)	–1.40	0.80	0.082
– 12 months	22.50 (7.49)	23.33 (6.99)	–1.28	0.94	0.175
Trail Making Test A <sup>a</sup>					
– Baseline	46.51 (32.63)	47.23 (21.60)			
– 3 months	41.89 (24.60)	45.75 (26.38)	0.38	2.36	0.873
– 12 months	44.96 (32.75)	41.97 (24.84)	5.13	3.21	0.113
Trail Making Test B <sup>b</sup>					
– Baseline	123.83 (104.52)	129.48 (93.49)			
– 3 months	112.71 (89.62)	111.11 (65.56)	0.35	7.29	0.962
– 12 months	103.26 (92.75)	109.08 (73.28)	–10.53	6.79	0.124
Paragraph recall direct					
– Baseline	6.61 (3.37)	6.34 (2.72)			
– 3 months	7.01 (3.46)	7.49 (2.95)	–0.64	0.42	0.132
– 12 months	6.84 (3.02)	7.03 (2.96)	–0.19	0.41	0.633
Paragraph recall delayed					
– Baseline	4.88 (3.14)	4.39 (2.56)			
– 3 months	5.99 (3.79)	6.41 (3.10)	–0.82	0.45	0.069

(continued on next page)

Table 4 (continued)

	Intervention	Control	Estimated mean difference	Standard error	p-Value
	Observed mean (SD)	Observed mean (SD)			
- 12 months	5.27 (3.17)	5.70 (2.81)	-0.61	0.40	0.130
<i>Secondary outcomes</i>					
<i>Cognitive functioning</i>					
<i>Cognitive Failures Questionnaire<sup>a</sup></i>					
- Baseline	24.70 (15.38)	22.55 (13.94)			
- 3 months	26.25 (16.32)	22.66 (14.68)	2.28	1.79	0.205
- 12 months	25.20 (15.14)	26.48 (15.57)	-1.31	1.99	0.513
<i>Emotional state</i>					
<i>HADS Total<sup>a</sup></i>					
- Baseline	10.13 (8.79)	9.27 (7.87)			
- 3 months	8.32 (7.11)	7.42 (6.73)	0.20	0.92	0.827
- 12 months	5.74 (6.02)	8.22 (7.50)	-3.25	1.02	<b>0.002</b>
<i>HADS Anxiety<sup>a</sup></i>					
- Baseline	5.33 (5.09)	4.62 (4.14)			
- 3 months	3.99 (3.53)	4.25 (3.80)	-0.69	0.49	0.157
- 12 months	2.83 (3.06)	4.18 (4.06)	-1.79	0.54	<b>0.001</b>
<i>HADS Depression<sup>a</sup></i>					
- Baseline	4.83 (4.34)	4.64 (4.45)			
- 3 months	4.33 (4.13)	3.27 (3.40)	0.87	0.53	0.103
- 12 months	2.90 (3.46)	4.03 (4.07)	-1.36	0.58	0.020
<i>Impact of Event Scale<sup>a</sup></i>					
- Baseline	18.39 (18.07)	19.11 (15.28)			
- 3 months	19.21 (18.39)	15.17 (15.40)	3.83	2.07	0.066
- 12 months	11.81 (14.56)	16.78 (16.31)	-4.18	2.27	0.068
<i>Extended daily activities</i>					
<i>Frenchay Activity Index</i>					
- Premorbid	26.48 (7.51)	26.35 (7.44)			
- 3 months	23.15 (9.63)	22.71 (9.70)	0.32	1.22	0.794
- 12 months	26.02 (8.60)	25.89 (8.47)	-0.76	1.05	0.472

AMIPB = Adult Memory and Information Processing Battery; HADS = Hospital Anxiety and Depression Scale.

The bold-faced values indicate values which have a significant p-value ( $p \leq 0.01$ )

<sup>a</sup> Outcome measures on which lower scores indicate better functioning.

equal between the intervention and control groups, we do not think this affected the results.

A second limitation is that the research assistants were not successfully blinded in all cases. Although we instructed the research assistants to do their best to ensure participants did not reveal their group assignment, this was sometimes spontaneously disclosed during home visits. However, as the research assistants were not involved in the data analyses and did not have any other conflicts of interest, we do not expect this have biased the study's results.

Some other points are worth discussing. Anxiety and depression are acknowledged risk factors for new cardiac events and mortality in patients after myocardial infarction [34,35]. The finding that this intervention improved overall emotional state and lowered anxiety may therefore have an additional positive effect on cardiovascular prognosis. To investigate this, long-term follow-up would be required.

Another important finding was that caregivers showed even more symptoms of anxiety, depression and posttraumatic stress than the patients did, which confirms that caregivers are at high risk for emotional problems. However, this intervention did not result in significant improvements for the caregivers. A review of the literature on family members of patients who had been admitted to intensive care units also found that further research is needed to determine how to reduce the negative consequences for the family members [36]. Therefore, it is essential to investigate what additional needs caregivers have and to identify risk factors [37].

The costs of this intervention are relatively low. Societal gain is expected, as it seems to improve long-term quality of life and accelerate the patient's return to work. However, cost-effectiveness analyses will be subject of a separate analysis (to be reported).

To conclude, this study described an effective and feasible early intervention that improved patient's quality of life and emotional state after cardiac arrest, and resulted in a more rapid return to

work. Our findings indicate that health care professionals should not only address the cardiac consequences of a cardiac arrest, but must also consider brain-related consequences. Future efforts should therefore focus on making this additional care available to all cardiac arrest survivors.

#### Author contributions

VM was the principle investigator on this project, working under supervision of CH, JV and DW. VM, CH, WB, MK, TG, DW and JV were involved in the design of the intervention. VM performed data analyses, with help from BW, who acted as statistical consultant. All authors take responsibility for the integrity of the data and the accuracy of the data analysis. VM wrote the drafts of the manuscript. All authors read, critically reviewed and approved the final manuscript. JV is the guarantor.

#### Competing interests

No authors have any competing interests.

#### Ethical approval

This study was approved by the Medical Ethics Committee of Maastricht University Medical Centre, The Netherlands. All participants gave written informed consent.

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**Table 5**  
Caregiver outcomes and effect of the intervention.

	Intervention	Control	Estimated mean difference	Standard error	p-Value
	Observed mean (SD)	Observed mean (SD)			
<b>Quality of life</b>					
<b>SF-36 Physical Functioning</b>					
– Baseline	82.63 (23.06)	81.11 (21.55)			
– 3 months	84.39 (22.27)	84.91 (18.67)	– 2.45	1.97	0.216
– 12 months	85.00 (19.46)	82.84 (21.27)	1.96	2.19	0.372
<b>SF-36 Social Functioning</b>					
– Baseline	64.10 (28.37)	64.29 (28.50)			
– 3 months	78.86 (23.88)	79.09 (21.79)	– 0.33	3.82	0.932
– 12 months	87.30 (17.60)	83.00 (21.69)	2.81	3.44	0.416
<b>SF-36 Role Physical</b>					
– Baseline	63.61 (40.79)	60.21 (44.03)			
– 3 months	72.79 (40.23)	76.79 (34.99)	– 8.33	5.78	0.152
– 12 months	79.84 (35.60)	77.55 (36.17)	1.48	6.13	0.809
<b>SF-36 Role Emotional</b>					
– Baseline	52.50 (44.93)	50.00 (47.14)			
– 3 months	67.65 (42.70)	67.86 (41.18)	– 3.38	6.95	0.628
– 12 months	86.02 (31.68)	79.74 (33.39)	3.28	5.70	0.567
<b>SF-36 Mental Health</b>					
– Baseline	60.68 (19.42)	57.63 (24.77)			
– 3 months	72.46 (17.92)	74.57 (19.79)	– 2.59	2.80	0.357
– 12 months	80.06 (14.48)	75.92 (17.50)	2.16	2.60	0.406
<b>SF-36 Vitality</b>					
– Baseline	54.81 (21.92)	53.59 (22.57)			
– 3 months	65.80 (19.19)	63.30 (22.79)	2.03	2.96	0.493
– 12 months	70.97 (17.10)	64.61 (21.70)	4.66	2.98	0.121
<b>SF-36 Bodily Pain</b>					
– Baseline	79.46 (23.14)	77.13 (23.94)			
– 3 months	77.23 (22.17)	77.69 (20.93)	– 1.89	3.07	0.539
– 12 months	82.19 (21.20)	79.67 (24.07)	2.06	3.77	0.585
<b>SF-36 General Health</b>					
– Baseline	64.81 (18.66)	67.07 (20.95)			
– 3 months	69.93 (17.85)	68.48 (20.04)	3.76	2.33	0.110
– 12 months	69.35 (18.34)	68.27 (22.40)	2.91	2.90	0.317
<b>EuroQol VAS</b>					
– Baseline	76.03 (15.22)	75.83 (16.01)			
– 3 months	78.76 (13.39)	76.70 (18.19)	2.59	2.29	0.261
– 12 months	81.69 (15.02)	77.12 (16.70)	4.56	2.60	0.082
<b>Caregiver strain</b>					
<b>Caregiver Strain Index<sup>a</sup></b>					
– Baseline	5.15 (3.55)	4.87 (3.37)			
– 3 months	3.32 (2.85)	4.21 (3.53)	– 0.43	0.45	0.348
– 12 months	2.74 (3.01)	3.25 (2.97)	– 0.12	0.45	0.786
<b>Emotional state</b>					
<b>HADS Total<sup>a</sup></b>					
– Baseline	14.99 (9.57)	15.26 (10.49)			
– 3 months	10.25 (8.80)	9.79 (8.70)	0.56	1.28	0.664
– 12 months	8.11 (7.18)	7.59 (6.62)	0.98	1.09	0.372
<b>HADS Anxiety<sup>a</sup></b>					
– Baseline	8.55 (5.05)	8.79 (5.48)			
– 3 months	6.29 (4.84)	5.86 (4.47)	0.43	0.69	0.530
– 12 months	5.02 (4.05)	4.83 (4.20)	0.68	0.62	0.280
<b>HADS Depression<sup>a</sup></b>					
– Baseline	6.50 (4.97)	6.43 (5.45)			
– 3 months	3.91 (4.32)	3.89 (4.74)	0.12	0.66	0.860
– 12 months	3.10 (3.62)	3.04 (3.30)	0.20	0.58	0.723
<b>Impact of Event Scale<sup>a</sup></b>					
– Baseline	32.39 (15.62)	32.59 (16.14)			
– 3 months	24.92 (17.55)	22.08 (16.19)	2.49	2.34	0.288
– 12 months	21.20 (17.07)	19.87 (17.82)	2.42	2.23	0.279

HADS = Hospital Anxiety and Depression Scale.

<sup>a</sup> Outcome measures on which lower scores indicate better functioning.

were not involved in the design, performance or interpretation of the study.

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## References

- [1] V.R. Moolaert, J.A. Verbunt, C.M. van Heugten, D.T. Wade, Cognitive impairments in survivors of out-of-hospital cardiac arrest: a systematic review, *Resuscitation* 80 (2009) 297–305.
- [2] R. de Vos, H.C. de Haes, R.W. Koster, R.J. de Haan, Quality of survival after cardiopulmonary resuscitation, *Arch. Intern. Med.* 159 (1999) 249–254.

- [3] H. Saner, E. Borner Rodriguez, A. Kummer Bangerter, R. Schuppel, M. von Planta, Quality of life in long-term survivors of out-of-hospital cardiac arrest, *Resuscitation* 53 (2002) 7–13.
- [4] K.M. Busl, D.M. Greer, Hypoxic–ischemic brain injury: pathophysiology, neuropathology and mechanisms, *NeuroRehabilitation* 26 (2010) 5–13.
- [5] R.O. Roine, S. Kajaste, M. Kaste, Neuropsychological sequelae of cardiac arrest, *JAMA* 269 (1993) 237–242.
- [6] A. Lundgren-Nilsson, H. Rosen, C. Hofgren, K.S. Sunnerhagen, The first year after successful cardiac resuscitation: function, activity, participation and quality of life, *Resuscitation* 66 (2005) 285–289.
- [7] G. Pusswald, E. Fertl, M. Faltl, E. Auff, Neurological rehabilitation of severely disabled cardiac arrest survivors. Part II. Life situation of patients and families after treatment, *Resuscitation* 47 (2000) 241–248.
- [8] E.M. Wachelder, V.R. Moolaert, C. van Heugten, J.A. Verbunt, S.C. Bekkers, D.T. Wade, Life after survival: long-term daily functioning and quality of life after an out-of-hospital cardiac arrest, *Resuscitation* 80 (2009) 517–522.
- [9] V.R. Moolaert, E.M. Wachelder, J.A. Verbunt, D.T. Wade, C.M. van Heugten, Determinants of quality of life in survivors of cardiac arrest, *J. Rehabil. Med.* 42 (2010) 553–558.
- [10] S.M. Cobbe, K. Dalziel, I. Ford, A.K. Marsden, Survival of 1476 patients initially resuscitated from out of hospital cardiac arrest, *BMJ* 312 (1996) 1633–1637.
- [11] V.R. Moolaert, J.A. Verbunt, W.G. Bakx, A.P. Gorgels, M.C. de Krom, P.H. Heuts, et al., 'Stand still ... and move on', a new early intervention service for cardiac arrest survivors and their caregivers: rationale and description of the intervention, *Clin. Rehabil.* 25 (2011) 867–879.
- [12] V.R. Moolaert, J.A. Verbunt, C.M. van Heugten, W.G. Bakx, A.P. Gorgels, S.C. Bekkers, et al., Activity and Life After Survival of a Cardiac Arrest (ALASCA) and the effectiveness of an early intervention service: design of a randomised controlled trial, *BMC Cardiovasc. Disord.* 7 (2007) 26.
- [13] J.P. Nolan, C.D. Deakin, J. Soar, B.W. Bottiger, G. Smith, European Resuscitation Council guidelines for resuscitation 2005. Section 4. Adult advanced life support, *Resuscitation* 67 (Suppl. 1) (2005) S39–S86.
- [14] V.R. Moolaert, J.C. van Haastregt, D.T. Wade, C.M. van Heugten, J.A. Verbunt, 'Stand still ... and move on', an early neurologically-focused follow-up for cardiac arrest survivors and their caregivers: a process evaluation, *BMC Health Serv. Res.* 14 (2014) 34.
- [15] C. van Heugten, S. Rasquin, I. Winkens, G. Beusmans, F. Verhey, Checklist for cognitive and emotional consequences following stroke (CLCE-24): development, usability and quality of the self-report version, *Clin. Neurol. Neurosurg.* 109 (2007) 257–262.
- [16] A.L. Alderson, T.A. Novack, Reliable serial measurement of cognitive processes in rehabilitation: the cognitive log, *Arch. Phys. Med. Rehabil.* 84 (2003) 668–672.
- [17] P. Spinhoven, J. Ormel, P.P. Sloekers, G.I. Kempen, A.E. Speckens, A.M. Van Hemert, A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects, *Psychol. Med.* 27 (1997) 363–370.
- [18] E.C. Sundin, M.J. Horowitz, Impact of event scale: psychometric properties, *Br. J. Psychiatry* 180 (2002) 205–209.
- [19] M. Thornton, S.S. Travis, Analysis of the reliability of the modified caregiver strain index, *J. Gerontol. B Psychol. Sci. Soc. Sci.* 58 (2003) S127–S132.
- [20] NHS/NVVC, Richtlijn Hartrevalidatie 2004, Nederlandse Hartstichting, Den Haag, 2004.
- [21] J.A. Bennett, B. Riegel, V. Bittner, J. Nichols, Validity and reliability of the NYHA classes for measuring research outcomes in patients with cardiac disease, *Heart Lung* 31 (2002) 262–270.
- [22] R. de Haan, M. Limburg, J. Schuling, J. Broeshart, L. Jonkers, P. van Zuylen, Clinimetric evaluation of the Barthel Index, a measure of limitations in daily activities, *Ned. Tijdschr. Geneesk.* 137 (1993) 917–921.
- [23] A.M. Sander, K.L. Fuchs, W.M. High Jr., K.M. Hall, J.S. Kreutzer, M. Rosenthal, The Community Integration Questionnaire revisited: an assessment of factor structure and validity, *Arch. Phys. Med. Rehabil.* 80 (1999) 1303–1308.
- [24] N.K. Aaronson, M. Muller, P.D. Cohen, M.L. Essink-Bot, M. Fekkes, R. Sanderman, et al., Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations, *J. Clin. Epidemiol.* 51 (1998) 1055–1068.
- [25] B. Schweikert, H. Hahmann, R. Leidl, Validation of the EuroQol questionnaire in cardiac rehabilitation, *Heart* 92 (2006) 62–67.
- [26] A.M. Vlaar, D.T. Wade, The Adult Memory and Information Processing Battery (AMIPB) test of information-processing speed: a study of its reliability and feasibility in patients with multiple sclerosis, *Clin. Rehabil.* 17 (2003) 386–393.
- [27] A.M. Vlaar, D.T. Wade, Verbal fluency assessment of patients with multiple sclerosis: test–retest and inter-observer reliability, *Clin. Rehabil.* 17 (2003) 756–764.
- [28] W.E. O'Donnell, D.M. Reynolds, C.B. De Soto, Neuropsychological impairment scale (NIS): initial validation study using trailmaking test (A & B) and WAIS digit symbol (scaled score) in a mixed grouping of psychiatric, neurological, and normal patients, *J. Clin. Psychol.* 39 (1983) 746–748.
- [29] A. Sunderland, K. Watts, A.D. Baddeley, J.E. Harris, Subjective memory assessment and test performance in elderly adults, *J. Gerontol.* 41 (1986) 376–384.
- [30] D.E. Broadbent, P.F. Cooper, P. FitzGerald, K.R. Parkes, The Cognitive Failures Questionnaire (CFQ) and its correlates, *Br. J. Clin. Psychol.* 21 (Pt 1) (1982) 1–16.
- [31] E. van der Ploeg, T.T. Mooren, R.J. Kleber, P.G. van der Velden, D. Brom, Construct validation of the Dutch version of the impact of event scale, *Psychol. Assess.* 16 (2004) 16–26.
- [32] J.C. Turnbull, P. Kersten, M. Habib, L. McLellan, M.A. Mullee, S. George, Validation of the Frenchay Activities Index in a general population aged 16 years and older, *Arch. Phys. Med. Rehabil.* 81 (2000) 1034–1038.
- [33] J.D. Corrigan, K. Smith-Knapp, C.V. Granger, Outcomes in the first 5 years after traumatic brain injury, *Arch. Phys. Med. Rehabil.* 79 (1998) 298–305.
- [34] A.M. Roest, E.J. Martens, J. Denollet, P. de Jonge, Prognostic association of anxiety post myocardial infarction with mortality and new cardiac events: a meta-analysis, *Psychosom. Med.* 72 (2010) 563–569.
- [35] J.P. van Melle, P. de Jonge, T.A. Spijkerman, J.G. Tijssen, J. Ormel, D.J. van Veldhuisen, et al., Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis, *Psychosom. Med.* 66 (2004) 814–822.
- [36] J.E. Davidson, C. Jones, O.J. Bienvenu, Family response to critical illness: postintensive care syndrome-family, *Crit. Care Med.* 40 (2012) 618–624.
- [37] M. Zimmerli, K. Tislar, G.M. Balestra, W. Langewitz, S. Marsch, S. Hunziker, Prevalence and risk factors for post-traumatic stress disorder in relatives of out-of-hospital cardiac arrest patients, *Resuscitation* 85 (2014) 801–808.