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A one year longitudinal study of psychological distress and self-assessed health in survivors of out-of-hospital cardiac arrest.

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3 **Running headline:** A one year longitudinal study of psychological distress and self-assessed
4 health in survivors of out-of-hospital cardiac arrest.
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Abstract

Objectives: Few studies have investigated the emotional and health-related outcome after out-of-hospital cardiac arrest (OHCA) over time. This longitudinal study aims to evaluate psychological distress, self-assessed health, and predictors of these outcomes in survivors of OHCA, three and 12 months after resuscitation.

Methods: Recruitment took place from 2008 to 2011 and survivors of OHCA were identified through the national Swedish Cardiopulmonary Resuscitation Registry. Inclusion criteria were age ≥ 18 years, survival ≥ 12 months and a Cerebral Performance Category score ≤ 2 . Questionnaires containing the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L) were administered at three and 12 months after the OHCA. Participants were also asked to report treatment-requiring comorbidities.

Results: Overall, survivors reported significantly less psychological distress and better self-assessed health at the 12-month follow-up compared to three months, although one-third of the study participants reported an increase in psychological distress over time. Comorbidity was associated with higher levels of anxiety at three months after OHCA, while being female was linked to more psychological distress at 12 months and poor self-assessed health at three months. Young age was associated with poor self-assessed health at both time points.

Conclusion: The level of psychological distress and health improve among survivors of OHCA between three and 12 months after resuscitation. Higher levels of psychological distress can be expected among female survivors and those with treatment-requiring comorbidity, while survivors of young age and who are female are at risk of poor self-assessed health.

Strengths and limitations of this study

- Data were collected from virtually every out-of-hospital cardiac arrest survivor within the course of 4 years in a large region of Sweden.
- A nurse responsible for data collection was placed at each hospital in the region to match survivors with data from the Swedish Cardiopulmonary Resuscitation Registry.
- Only survivors with a cerebral performance category score of ≤ 2 were included.
- The use of generic measures of health has a limited ability to capture the complexity of the health state in survivors of cardiac arrest.

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3 **Key words:** Cardiac arrest; Follow-up; Outcome; Anxiety; Depression; Quality of life.
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6 **Introduction**

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8 Out-of-hospital cardiac arrest (OHCA) is a deadly condition that affects approximately 5000
9 inhabitants in Sweden each year (1). The survival rate of OHCA is low, although great efforts
10 have been made to raise the number of survivors in recent years; consequently, the 30-day
11 survival rate in Sweden has increased from 4.5% in 1992 to 11.4% in 2017 (2). When the
12 heart stops anoxic brain injury occurs within minutes and is the most critical factor in
13 determining the chance of survival and level of functioning, if resuscitation is successful (3).
14 Following cerebral anoxia, cardiac arrest survivors are known to be at risk of cognitive and
15 emotional deficits (4-7). Although most survivors with a good neurological outcome return to
16 high function and quality of life (8, 9), long-term emotional problems have been reported by
17 up to one-third in Swedish-samples (10, 11). Furthermore, the ability to pinpoint survivors
18 who need psychiatric rehabilitation will become more important as survival rates continue to
19 increase.
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29 There is already an extensive body of knowledge regarding the outcome after cardiac arrest
30 in different patient populations and time points. However, few studies have investigated the
31 emotional and health-related outcome in the same sample over time, and little is known about
32 factors associated with post cardiac arrest improvement in these aspects (9, 10, 12, 13). The
33 interpretation of the available literature is complicated by high heterogeneity in study
34 outcomes, and knowledge regarding psychological distress and self-assessed health after
35 OHCA in relation to the average population in Sweden is lacking (7, 14).
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41 We have previously reported that reduced well-being is experienced by half of OHCA
42 survivors at three months, and that female survivors report significantly more anxiety and
43 worse health compared to males (15). In this study, we will investigate how the emotional and
44 health-related outcomes change in survivors of OHCA with good neurological functioning
45 between three and 12 months after resuscitation. Further, we will also evaluate predictors of
46 psychological distress and poor self-assessed health at these time points.
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Methods

Design and setting

This was a longitudinal study with self-administered postal questionnaires sent to survivors three and 12 months after the OHCA. The setting was a region in Sweden with 1.6 million inhabitants and nine hospitals that treat cardiac arrest. The frequency of OHCA was 850 cases annually and the survival rate approximately 10%.

Study population

The study population was identified through the national Swedish Cardiopulmonary Resuscitation Registry (SCRR). Every person who suffered from an OHCA and for whom resuscitation was initiated should be included in the SCRR. To ensure complete coverage, there was a specially-trained nurse at each hospital who could identify missing cases and match patients treated for OHCA with data from the SCRR.

Recruitment took place from 1st January 2008 to 31st December 2011 and every adult survivor of OHCA in the region was assessed for inclusion. The study inclusion criteria were age ≥ 18 years, survival ≥ 12 months, and a Cerebral Performance Category (CPC) score ≤ 2 at discharge, denoting good neurological functioning (16). Exclusion criteria were cardiac arrest due to trauma, attempted suicide, intoxication, or abuse. Survivors with other severe illness and survivors treated but not residing in the region were also excluded.

Procedure and questionnaire

Eligible survivors received a postal questionnaire in Swedish three months after the OHCA. Respondents at three months then received a second questionnaire at 12 months. A reminder was sent if no response was received after three weeks. The questionnaire consisted of the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L). Study participants were also asked to report treatment-requiring comorbidity.

The HADS is a 14-item screening instrument developed to detect psychological distress in terms of anxiety and/or depression (17). It is divided into two subscales, seven items regarding anxiety (HADS-anxiety) and seven items regarding symptoms of depression (HADS-depression). Each item has four levels, scored 0-3, with a maximum score of 21 in each subscale. Scoring >7 in one subscale indicates mild to moderate problems and a score >10 indicates severe problems. Although the HADS has never been thoroughly evaluated in a

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3 cardiac arrest population, it is considered a reliable measurement for depression and anxiety
4 in patients with somatic illness (18) and is frequently used in cardiovascular research (7).

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6 EQ-5D-3L is designed to measure health and includes the EQ-5D-3L descriptive system
7 and a visual analogue scale (EQ VAS) (19). The descriptive system
8
9 comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and
10 anxiety/depression); each dimension has three levels (no problems, moderate problems and
11 severe problems) denoting a score of 1-3. The total score in the EQ-5D-3L descriptive system
12 can be converted to an index-value which ranges between -0.594 and 1.00 , calculated with
13 the UK EQ-5D index tariff (20). An index value of 1.00 indicates full health, while negative
14 values represents health states worse than death (19). EQ VAS is a thermometer where the
15 patient assesses his or her current health on a scale from zero to 100, with endpoints labelled
16 'best imaginable health state' and 'worst imaginable health state'. EQ-5D-3L is commonly
17 used in cardiovascular research (21). However, the use of EQ-5D-3L in OHCA populations
18 has been questioned as the instrument has shown a limited ability to differentiate between
19 survivors of good health (22).

29 30 31 *Statistics and data analysis*

32 Statistical analyses were executed with IBM SPSS Statistics 24.0 (Armonk, NY: IBM Corp).
33 All p-values were two-sided and interpreted at a 0.05 significance level. Nonparametric tests
34 were used for all comparisons as all dependent variables were non-normally distributed. The
35 χ^2 test was applied for nominal values and the Mann-Whitney U-test for ordinal values.
36 Wilcoxon signed ranks test was used to explore the change between three and 12 months.
37 Predictors of psychological distress (HADS) and poor self-assessed health (EQ-5D-3L index
38 values) were investigated using multivariate binary logistic regression models. The outcome
39 was dichotomised as good or bad with regard to the mean scores in two Swedish reference
40 populations, matched to gender and age-group. Reference values regarding the HADS were
41 drawn from a random sample gathered 1997 in Jämtland County, Sweden ($n=624$) (23);
42 similarly, reference values regarding the EQ-5D-3L index values were drawn from a random
43 sample gathered 2001 in Stockholm County, Sweden ($n=3069$) (24). The predictors were
44 included based on clinical reasoning and are presented in Table 1; correlations between them
45 were examined using Spearman's rank correlation and only variables with a Spearman's $\rho \pm$
46 ≤ 0.7 were accepted. Univariate analysis was conducted separately between each individual
47 predictor. The significant level of the univariate analysis was 0.25 and predictors with a p-
48 value > 0.25 were excluded from further analysis. Hosmer and Lemeshow tests and Receiver
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3 Operating Characteristics curves (ROC-curves) were performed to ensure the reliability of the
4 logistic regression models.
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8 *Patient and public involvement*

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10 None of the included patients were involved in the design or conduction of this study. The
11 results will be reported to the Health & Medical Care Committee of the Regional Executive
12 Board, Region Västra Götaland, Sweden.
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16 *Ethics*

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18 Ethical permission was granted by the Regional Ethics Review board, Western Sweden (No.
19 465-07). Written consent was obtained from all participants.
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23 **Results**

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25 There were 3082 cases of OHCA in the region during the study period, of which 298 were
26 alive at 30 days. One-hundred-fifty survivors fulfilled the inclusion criteria for a three-month
27 follow-up and 94 responded. Of the respondents at three months, 85 were included at 12
28 months and 74 responded again (87% response rate); in the group that did not receive a
29 second questionnaire, five had died and four were lost due to logistical errors (Figure 1).
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34 The representativeness of the study population has been investigated in a prior study (25),
35 and there were no significant differences regarding age, gender, cardiac arrest circumstances,
36 or in-hospital interventions between respondents and non-respondents. However, there were
37 differences between participants and the survivors that only responded once. Double
38 respondents were significantly younger ($Z=2.316$, $p=0.021$), had a lower frequency of cardiac
39 arrest at home ($\chi^2=6.249$, $p=0.014$), and a higher frequency of ventricular fibrillation or
40 ventricular tachycardia as initial rhythm ($\chi^2=5.067$, $p=0.032$). Background characteristics and
41 self-reported comorbidity of the participants are presented in Table 1.
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48 Overall, survivors of OHCA reported a significantly improved emotional and health-related
49 outcome over time (Table 2). About half of the survivors reported less psychological distress
50 in the HADS at 12 months (51% decrease in anxiety and 46% in symptoms of depression);
51 although one-third reported an increase in psychological distress (30% increase in anxiety and
52 28% in symptoms of depression). Two-thirds of female survivors reported more
53 psychological distress at the 12-month follow up, corresponding to one-fifth among male
54 survivors. Comparably, half of the survivors reported better self-assessed health at 12 months
55 in EQ-5D-3L, whereas 41% reported the same health state at three and 12 months. Among the
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3 survivors who remained unchanged, 73% reported an EQ-5D-3L index value of 1.00,
4 denoting full health at both time points. However, only one survivor entered full health at
5 both times in EQ VAS (Figure 2).
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8 Binary logistic regression analyses were performed to find predictors of psychological
9 distress and poor self-assessed health (Table 3). The presence of treatment-requiring
10 comorbidity was found to predict more anxiety at three months after resuscitation (OR 4.07,
11 $p=0.04$), but there was no significant correlation regarding comorbidity at the 12-month
12 follow-up; instead, being female was found to predict more anxiety (OR 9.23, $p=0.01$) and
13 more symptoms of depression (OR 14.78, $p=0.002$) at this time. Being female was also found
14 to predict poor self-assessed health at three months (OR 6.33, $p=0.04$), and there was a
15 negative correlation between older age and poor self-assessed health at three and 12 months,
16 respectively (OR 0.91, $p=0.002$; OR 0.93, $p=0.003$).
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26 Discussion

27 One objective of this study was to investigate how the emotional and health-related outcomes
28 change between three and 12 months in survivors of OHCA with good neurological
29 functioning. We found an encouraging progression as survivors at large showed less
30 psychological distress and better self-assessed health over time. In comparison, participants in
31 this study even surpassed the average level of depression and self-assessed health in the
32 Swedish population at their 12-month follow-up (23, 24). However, we also found that even
33 though about half of OHCA survivors report a decrease in psychological distress between
34 three and 12 months, almost one-third report increased psychological distress; hence, our
35 results indicate that the emotional outcome after OHCA may differ considerably on an
36 individual level.
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44 As stated earlier, few prior longitudinal studies have investigated the emotional and health-
45 related outcomes after cardiac arrest. In accordance with our results, two small sample studies
46 have previously reported a decrease of anxiety and depressive symptoms in cardiac arrest
47 survivors over time (13, 26). In contrast, a rather large prospective study found no change in
48 anxiety or depressive symptoms between one and 12 months (12). It is possible that the
49 heterogeneity in emotional outcomes observed in this study could explain a part of the
50 discrepancies in the available literature. As regards self-assessed health, the improvements
51 seen in this study confirm the results of two previous longitudinal studies (9, 10). However,
52 these previous studies found that the greatest health-related improvements occurred in the
53 early stages of recovery, within three months after cardiac arrest (9, 10). Moreover, although
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3 the 'minimal clinically important difference' in the HADS and EQ-5D-3L among survivors of
4 cardiac arrest is unknown, estimates from other patient populations indicate that the
5 improvements seen in this study might not be clinically noticeable (27, 28).
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8 A second objective was to evaluate predictors of psychological distress and poor self-
9 assessed health after OHCA. Since it is already known that cardiac arrest survivors generally
10 report few emotional problems and good health, it is difficult to define a threshold for a bad
11 outcome among those who perform well neurologically. In this study, the outcome was
12 dichotomised as good or bad in comparison to mean scores from the average Swedish
13 population. Prior studies have concluded that many survivors reach an emotional state and
14 health comparable to the average population, although no study has previously investigated
15 predictors of this outcome (9, 10, 29). In addition, there is also a lack of knowledge regarding
16 factors associated with post cardiac arrest improvement over time (13, 30). We found that
17 comorbidity is associated with higher levels of anxiety compared to the average population at
18 three months after OHCA. However, we did not find a significant correlation between
19 comorbidity and anxiety or depression at the 12-month follow-up. In contrast, being female
20 was strongly associated with psychological distress at one year after resuscitation, but this
21 was not significant at three months. We also found a significant correlation between being
22 female and poor self-assessed health at three months, while young age was associated with
23 poor self-assessed health at both three and 12 months.
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36 Studies investigating prognostic factors regarding the emotional or health-related outcomes
37 after cardiac arrest are scarce. However, receiving an ICD has been linked to higher levels
38 psychological distress (31), but this effect has not been shown in a cardiac arrest population
39 (12). We did not find any significant correlation regarding ICD in our regression models
40 either. Young age and being female have previously been associated with anxiety among
41 cardiac arrest survivors (29), but there were no significant correlation between psychological
42 distress and age in our study population. Nevertheless, we did find a considerably higher
43 likelihood of depression among female survivors of OHCA at 12 months, which has not
44 previously been reported. Also novel is the likelihood of a better self-assessed health among
45 survivors of higher age.
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53 The European Resuscitation Council has provided guidelines for post cardiac arrest
54 rehabilitation since 2015 and has pointed out the need of structured follow-up care, including
55 physical, neurological, and emotional screening (32). Still, far from all cardiac arrest
56 survivors in Sweden are offered rehabilitation or neuropsychological evaluation, despite
57 recommendations from the Swedish Resuscitation Council (33, 34). Instead, survivors in
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3 Sweden are often followed based on the aetiology of the cardiac arrest with little to no focus
4 on emotional sequelae (34, 35). Our results indicate that even if the majority of OHCA
5 survivors live without psychological distress and with good self-assessed health, there are
6 individuals that experience major problems. Consequently, it should be expected that some
7 survivors will benefit from psychiatric rehabilitation, and survivors of young age, who are
8 female, and those with treatment-requiring comorbidity should be screened early on.
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15 *Strengths and limitations*

16 This study has several strengths. During the study period of four years, a specially-trained
17 nurse was placed at every hospital in a large region of Sweden. With this approach, we were
18 able to collect data from virtually every case of OHCA. The study design also allowed us to
19 match non-respondents with data collected from the SCRR at the time of their hospitalisation,
20 thus enabling comparisons between respondents and non-respondents. Consequently, we were
21 able to confirm that the study population represents the group at large in these aspects.
22 Another strength is that the outcomes in this study could be compared with the average
23 Swedish population. Knowledge regarding factors of importance for an emotional state and
24 self-assessed health in line with the normal population after OHCA in Sweden is missing.
25 This information will help to generalise the overall picture of OHCA survival and provide
26 guidance regarding which survivors that need psychiatric rehabilitation. Furthermore, the
27 response rate was very high at 12 months.
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38 The main limitations of this study are the retrospective design and the restrictive inclusion
39 of survivors with good neurological functioning, which limits the applicability on OHCA
40 survivors more broadly. However, we made the assessment that inclusion of survivors with a
41 severe cerebral dysfunction would complicate the interpretability of the results. Another
42 methodical limitation in this study is the use of EQ-5D-3L to measure self-assessed health. A
43 recent study concluded that EQ-5D-3L might underestimate the health in OHCA survivors,
44 yielding high ceiling effects, which was apparent in the EQ-5D-3L descriptive system in this
45 study as well (22). Although EQ VAS showed higher interpretability with a more varied
46 outcome in our study population, it is known that generic measures of health often fail to
47 capture the true complexity of the health state in survivors of cardiac arrest (36). Finally,
48 some survivors were excluded due to severe illness and a few non-respondents mentioned
49 poor health as the reason for not participating. Therefore, it is possible that the participants in
50 this study had a better outcome than survivors more generally.
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Conclusions

On a group level, there is a significant improvement in the emotional and health-related outcomes among survivors of OHCA between three and 12 months after resuscitation. Higher levels of psychological distress can be expected among female survivors and those with treatment-requiring comorbidity, while young and female survivors are at risk of a poor self-assessed health. These findings should be considered in the follow-up after OHCA, although future research is required to identify further predictors regarding the long-term outcome and chance of improvement post cardiac arrest.

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Competing interests

The authors declare no conflict of interest.

Contributors

All authors have made a substantial contribution to the conception and design of the study. AV analysed the data and wrote the manuscript with input from all authors. KSS and ÅÅ initiated and planned the study, collected the data, assisted in the interpretation of the data and took part in drafting the manuscript. JH took part in the planning of the study, contributed with external expertise and have continuously revised the manuscript. DJ helped analyze the data and have continuously revised the manuscript.

Data sharing statement

Due to ethical restrictions, data are available on request. Interested researchers may submit a request for data to the authors (adam.viktorisson@gu.se). According to Swedish regulation: <http://www.epn.se/en/start/regulations/>, the permission to use data is only for what has been

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applied for and then approved by the Ethical board. To not follow the regulations is seen as scientific misconduct.

For peer review only

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3 **Figure legends**
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6 **Figure 1.** Flowchart of study participants.
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10 **Figure 2.** Reported outcomes in the HADS and EQ-5D-3L at three and 12 months (n=74).
11 Diagonal lines divide the participants with regard to what time they reported the highest
12 score. Scores from 7 participants are missing in EQ VAS.
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Table 1. Background characteristics and self-reported comorbidity of participants.

<i>n (%) unless otherwise stated</i>	Participants n=74	Missing data*
Age. Median (min-max) ^a	63 (25-89)	
Female ^a	13 (18)	
Time to EMS in minutes. Median (min-max)	7 (1-61)	11
Cardiac arrest circumstances		
Cardiac aetiology ^a	62 (86)	2
Cardiac arrest at home	22 (30)	
CPR before arrival of EMS	41 (55)	
Initial rhythm: VF or VT	61 (86)	3
Witnessed cardiac arrest	69 (95)	1
In-hospital interventions		
CABG	5 (7)	2
ICD ^a	19 (27)	4
Induced hypothermia (33°C) ^a	35 (49)	2
PCI	39 (54)	2
Comorbidity**^a		
Anaemia or other blood disease	0	
Back pain	3 (4)	
Cancer	1 (1)	
Diabetes mellitus	2 (3)	
Gastrointestinal disease	5 (7)	
Heart disease	54 (73)	
Hypertension	27 (36)	

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3	Liver disease	1 (1)
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5	Osteoarthritis	2 (3)
6		
7	Pulmonary disease	3 (4)
8		
9	Renal disease	0
10		
11	Rheumatoid arthritis	1 (1)
12		
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14 * Number of participants where information is missing

15 ** Number of participants with self-reported treatment-requiring comorbidity

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17 ^a Variables included as predictors in the univariate regression analyses

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20 Abbreviations: VF, ventricular fibrillation; VT ventricular tachycardia; CRP,
21 cardiopulmonary resuscitation; EMS, emergency medical service; PCI,
22 percutaneous coronary intervention; CABG, coronary artery bypass grafting; ICD,
23 implantable cardioverter defibrillator
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Table 2. Comparison of mean scores at three and 12 months in the HADS and EQ-5D-3L (n=74).

	3 months	12 months	<i>Z</i> -value	<i>p</i>
	Observed mean (SD)	Observed mean (SD)		
HADS				
HADS-Anxiety	5.6 (±4.8)	4.7 (±4.3)	2.337	0.02*
HADS-Depression	3.4 (±3.5)	2.6 (±2.6)	2.199	0.03*
Total score	9.0 (±7.8)	7.3 (±6.5)	2.579	0.01*
EQ-5D-3L				
EQ VAS (n=67)	73 (±18)	77 (±19)	2.292	0.02*
Index value	0.82 (±0.26)	0.88 (±0.15)	2.966	0.003*

* $p < 0.05$ indicates statistical significance

Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; SD, standard deviation; VAS, visual analogue scale

Table 3. Predictors of psychological distress and poor self-assessed health (n=70).

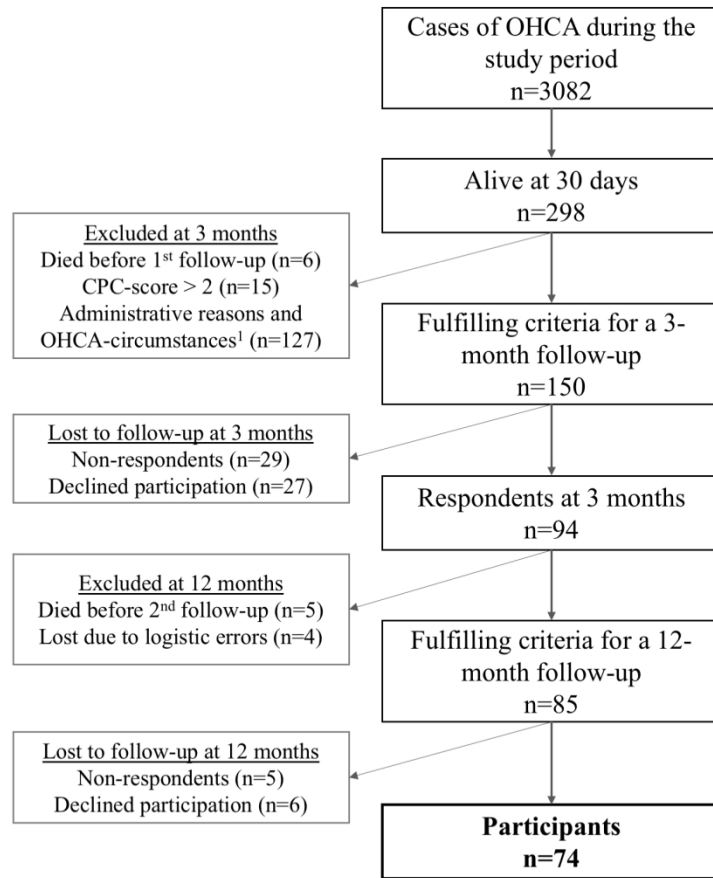
Predictors	3 months				12 months			
	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²
HADS-Anxiety								
Age	0.99 (0.95-1.03)	0.02	0.63	0.195	0.98 (0.93-1.03)	0.02	0.40	0.276
Comorbidity	4.07 (1.07-17.00)	0.73	0.04*		3.79 (0.70-20.42)	0.86	0.12	
Being female	4.94 (0.91-26.83)	0.86	0.06		9.23 (1.68-50.61)	0.78	0.01*	
Hypothermia	1.25 (0.43-3.62)	0.54	0.68		1.20 (0.38-3.76)	0.58	0.75	
HADS-Depression								
Age	0.99 (0.94-1.04)	0.03	0.57	0.136	0.99 (0.94-1.05)	0.03	0.81	0.300
Comorbidity	1.45 (0.33-6.44)	0.76	0.62		1.20 (0.25-5.85)	0.81	0.82	
Being female	3.71 (0.90-15.37)	0.78	0.07		14.78 (2.60-83.87)	0.87	0.002*	
Hypothermia	1.16 (0.37-3.61)	0.58	0.81		2.75 (0.82-9.28)	0.62	0.10	
ICD	1.52 (0.40-5.69)	0.68	0.54		0.55 (0.11-2.77)	0.82	0.47	
EQ-5D-3L index value								
Age	0.91 (0.86-0.97)	0.03	0.002*	0.362	0.93 (0.89-0.98)	0.02	0.003*	0.288
Comorbidity	1.19 (0.28-5.01)	0.73	0.81		2.53 (0.51-12.69)	0.82	0.26	
Being female	6.33 (1.03-38.81)	0.93	0.04*		2.09 (0.46-9.40)	0.77	0.34	

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4 * $p < 0.05$ indicates statistical significance
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7 Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; OR,
8 odds ratio; SE, standard error; CI, confidence interval; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary
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¹⁾ Administrative reasons include survivors documented with an incorrect social security number, not able to be identified within 3 months or not residing in the region. OHCA-circumstances include trauma, attempted suicide, drowning and intoxication as cause of the cardiac arrest or severe illness afterwards.

Figure 1. Flowchart of study participants.

249x299mm (190 x 190 DPI)

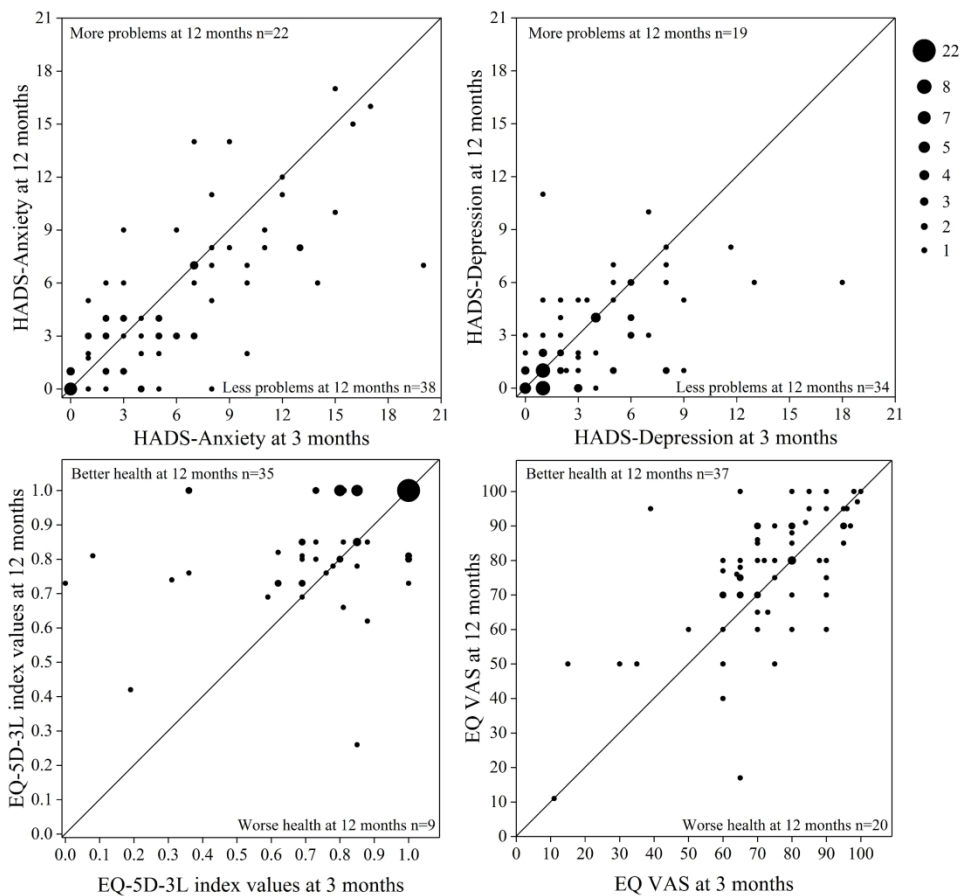


Figure 2. Reported outcomes in the HADS and EQ-5D-3L at three and 12 months (n=74). Diagonal lines divide the participants with regard to what time they reported the highest score. Scores from 7 participants are missing in EQ VAS.

245x245mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	See tables and figures
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Not applicable
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(b) Report category boundaries when continuous variables were categorized	7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A one year longitudinal study of psychological distress and self-assessed health in survivors of out-of-hospital cardiac arrest.

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Cardiac arrest, Follow-up, Outcome, Anxiety, Depression, Quality of life

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3 **Running headline:** A one year longitudinal study of psychological distress and self-assessed
4 health in survivors of out-of-hospital cardiac arrest.
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Abstract

Objectives: Few studies have investigated the psychological and health-related outcome after out-of-hospital cardiac arrest (OHCA) over time. This longitudinal study aims to evaluate psychological distress in terms of anxiety and depression, self-assessed health, and predictors of these outcomes in survivors of OHCA, three and 12 months after resuscitation.

Methods: Recruitment took place from 2008 to 2011 and survivors of OHCA were identified through the national Swedish Cardiopulmonary Resuscitation Registry. Inclusion criteria were age ≥ 18 years, survival ≥ 12 months and a Cerebral Performance Category score ≤ 2 . Questionnaires containing the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L) were administered at three and 12 months after the OHCA. Participants were also asked to report treatment-requiring comorbidities.

Results: Of 298 survivors, 85 were eligible for this study and 74 responded. Anxiety was reported by 22 survivors at three months and by 17 at 12 months, while depression was reported by 10 at three months and 4 at 12 months. The mean EQ-5D-3L index value increased from 0.82 (± 0.26) to 0.88 (± 0.15) over time. There were significantly less symptoms of psychological distress ($p=0.01$) and better self-assessed health ($p=0.003$) at 12-months. Treatment-requiring comorbidity predicted anxiety (OR 4.07, $p=0.04$), while being female and young age predicted poor health (OR 6.33, $p=0.04$; OR 0.91, $p=0.002$) at three months. At 12 months, being female was linked to anxiety (OR 9.23, $p=0.01$) and depression (OR 14.78, $p=0.002$), while young age predicted poor health (OR 0.93, $p=0.003$).

Conclusion: The level of psychological distress and self-assessed health improve among survivors of OHCA between three and 12 months after resuscitation. Higher levels of psychological distress can be expected among female survivors and those with comorbidity, while survivors of young age and who are female are at greater risk of poor health.

Strengths and limitations of this study

- Data were collected from virtually every out-of-hospital cardiac arrest survivor within the course of 4 years in a large region of Sweden.
- A nurse responsible for data collection was placed at each hospital in the region to match survivors with data from the Swedish Cardiopulmonary Resuscitation Registry.
- Only survivors with a cerebral performance category score of ≤ 2 were included.

- The use of generic measures of health has a limited ability to capture the complexity of the health state in survivors of cardiac arrest.

Key words: Cardiac arrest; Follow-up; Outcome; Anxiety; Depression; Quality of life.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a deadly condition that affects approximately 5000 inhabitants in Sweden each year (1). The survival rate of OHCA is low, although great efforts have been made to raise the number of survivors in recent years; consequently, the 30-day survival rate in Sweden has increased from 4.5% in 1992 to 11.4% in 2017 (2). When the heart stops hypoxic brain injury occurs within minutes and is the most critical factor in determining the chance of survival and level of functioning, if resuscitation is successful (3). Following cerebral hypoxia, cardiac arrest survivors are known to be at risk of cognitive and emotional deficits (4-7). Although most survivors with a good neurological outcome return to high function and quality of life (8, 9), long-term psychological problems have been reported by up to one-third in Swedish-samples (10, 11). Furthermore, the ability to pinpoint survivors who need psychiatric rehabilitation will become more important as survival rates continue to increase.

There is already an extensive body of knowledge regarding the outcome after cardiac arrest in different patient populations and time points. Time to awakening, gender, age, role of bystander, use of hypothermia and percutaneous coronary intervention (PCI) have previously been related to the outcome after cardiac arrest (6, 12, 13). However, few studies have investigated the psychological and health-related outcome in the same sample over time (9, 10, 14), and little is known about factors associated with post cardiac arrest improvement in these aspects. The interpretation of the available literature is complicated by high heterogeneity in study outcomes, and knowledge regarding psychological distress and self-assessed health after OHCA in relation to the average population is lacking (7, 15).

We have previously reported that reduced well-being is experienced by half of OHCA survivors at three months, and that female survivors report significantly more anxiety and worse health compared to males (16). In this study, we will investigate how the psychological and health-related outcomes change in survivors of OHCA with good neurological functioning between three and 12 months after resuscitation. Further, we will also evaluate predictors of psychological distress and self-assessed poor health at these time points.

Methods

Design and setting

This was a longitudinal study with self-administered postal questionnaires sent to survivors three and 12 months after the OHCA. The setting was a region in Sweden with 1.6 million inhabitants and nine hospitals that treat cardiac arrest. The frequency of OHCA was 850 cases annually and the survival rate approximately 10%.

Study population

The study population was identified through the national Swedish Cardiopulmonary Resuscitation Registry (SCRR). Every person who suffered from an OHCA and for whom resuscitation was initiated should be included in the SCRR. To ensure complete coverage, there was a specially-trained nurse at each hospital who could identify missing cases and match patients treated for OHCA with data from the SCRR.

Recruitment took place from 1st January 2008 to 31st December 2011 and every adult survivor of OHCA in the region was assessed for inclusion. The study inclusion criteria were age ≥ 18 years, survival ≥ 12 months, and a Cerebral Performance Category (CPC) score ≤ 2 at discharge, denoting good neurological functioning (17). Exclusion criteria were cardiac arrest due to trauma, attempted suicide, intoxication, or abuse. Survivors with other severe illness and survivors treated but not residing in the region were also excluded.

Procedure and questionnaire

Eligible survivors received a postal questionnaire in Swedish three months after the OHCA. Survivors who responded to the questionnaires and gave a written consent were included. Participants at three months then received a second questionnaire at 12 months. A reminder was sent if no response was received after three weeks. The questionnaire consisted of the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L). Study participants were also asked to report treatment-requiring comorbidity.

The HADS is a 14-item screening instrument developed to detect psychological distress in terms of clinically significant anxiety and/or depression (18). It is divided into two subscales, seven items regarding anxiety (HADS-anxiety) and seven items regarding symptoms of depression (HADS-depression). Each item has four levels, scored 0-3, with a maximum score of 21 in each subscale. Scoring >7 in one subscale indicates mild to moderate problems and a score >10 indicates severe problems. Although the HADS has never been thoroughly

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3 evaluated in a cardiac arrest population, it is considered a reliable measurement for depression
4 and anxiety in patients with somatic illness (19) and is frequently used in cardiovascular
5 research (7).
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8 EQ-5D-3L is designed to measure subjective health and includes the EQ-5D-3L descriptive
9 system and a visual analogue scale (EQ VAS) (20). The descriptive system
10 comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and
11 anxiety/depression); each dimension has three levels (no problems, moderate problems and
12 severe problems) denoting a score of 1-3. The total score in the EQ-5D-3L descriptive system
13 can be converted to an index-value which ranges between -0.594 and 1.00 , calculated with
14 the UK EQ-5D index tariff (21). An index value of 1.00 indicates full health, while negative
15 values represents health states worse than death (20). EQ VAS is visualized as a continuum
16 of value scale where the patient assesses his or her current health on a scale from zero to 100,
17 with endpoints labelled 'best imaginable health state' and 'worst imaginable health state'.
18 EQ-5D-3L is commonly used in cardiovascular research (22). However, the use of EQ-5D-3L
19 in OHCA populations has been questioned as the instrument has shown a limited ability to
20 differentiate between survivors of good health (23).
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32 *Statistics and data analysis*

34 Statistical analyses were executed with IBM SPSS Statistics 24.0 (Armonk, NY: IBM Corp).
35 All p-values were two-sided and interpreted at a 0.05 significance level. Nonparametric tests
36 were used for all comparisons as all dependent variables were non-normally distributed. The
37 χ^2 test was applied for nominal values and the Mann-Whitney U-test for ordinal values.
38 Wilcoxon signed ranks test was used to explore the change between three and 12 months.
39 Predictors of psychological distress (HADS) and self-assessed poor health (EQ-5D-3L index
40 values) were investigated using multivariate binary logistic regression models. The outcome
41 was dichotomised as good or bad with regard to the mean scores in two Swedish reference
42 populations, matched to gender and age-group. A bad outcome was considered a score two
43 standard deviations below the mean of the reference population. Reference values regarding
44 the HADS were drawn from a random sample gathered 1997 in Jämtland County, Sweden
45 (n=624) (24); similarly, reference values regarding the EQ-5D-3L index values were drawn
46 from a random sample gathered 2001 in Stockholm County, Sweden (n=3069) (25). The
47 predictors were included based on clinical reasoning and are presented in Table 1. With
48 regard to the sample size, only six variables were evaluated and correlations between them
49 were examined using Spearman's rank correlation; only variables with a Spearman's rho \pm
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3 ≤ 0.7 were accepted. Univariate analysis was conducted separately between each individual
4 predictor. The significant level of the univariate analysis was 0.25 and predictors with a p-
5 value > 0.25 were excluded from further analysis. Hosmer and Lemeshow tests and Receiver
6 Operating Characteristics curves (ROC-curves) were performed to ensure the reliability of the
7 logistic regression models.
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10 11 12 13 *Patient and public involvement*

14 None of the included patients were involved in the design or conduction of this study and no
15 patient opinion regarding the subject has been obtained. The results will be reported to the
16 Health & Medical Care Committee of the Regional Executive Board, Region Västra
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Göteborg, Sweden.

Ethics

Ethical permission was granted by the Regional Ethics Review board, Western Sweden (No.
465-07). Written consent was obtained from all participants.

Results

There were 3082 cases of OHCA in the region during the study period, of which 298 were
alive at 30 days. One-hundred-fifty survivors fulfilled the inclusion criteria for a three-month
follow-up and 94 responded. Of the respondents at three months, 85 were included at 12
months and 74 responded again (87% response rate); in the group that did not receive a
second questionnaire, five had died and four were lost due to logistical errors (Figure 1).

The representativeness of the study population has been investigated in a prior study (26),
and there were no significant differences regarding age, gender, cardiac arrest circumstances,
or in-hospital interventions between respondents and non-respondents. However, there were
differences between participants and the survivors that only responded once. Double
respondents were significantly younger ($Z=2.316$, $p=0.021$), had a lower frequency of cardiac
arrest at home ($\chi^2=6.249$, $p=0.014$), and a higher frequency of ventricular fibrillation or
ventricular tachycardia as initial rhythm ($\chi^2=5.067$, $p=0.032$). Background characteristics and
self-reported comorbidity of the participants are presented in Table 1.

Mild to moderate anxiety (>7 in HADS-A) was reported by 22 survivors at the three months
follow-up and by 17 at 12 months. Mild to moderate depression (>7 in HADS-D) was
reported by 10 survivors at three months and by four at 12 months. A score indicating severe
anxiety (>10 in HADS-A) was reported by 12 survivors at three months and by eight at 12

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3 months, while severe depression (>10 in HADS-D) was reported by three at three months and
4 one at 12 months. Overall, survivors of OHCA reported a significantly improved
5 psychological and health-related outcome over time (Table 2). About half of the survivors
6 reported less psychological distress in the HADS at 12 months (51% decrease in anxiety and
7 46% in symptoms of depression); although one-third reported an increase in psychological
8 distress (30% increase in anxiety and 28% in symptoms of depression). Two-thirds of female
9 survivors reported more psychological distress at the 12-month follow up, corresponding to
10 one-fifth among male survivors. Comparably, half of the survivors reported better self-
11 assessed health at 12 months in EQ-5D-3L, whereas 41% reported the same health state at
12 three and 12 months. Among the survivors who remained unchanged, 73% reported an EQ-
13 5D-3L index value of 1.00, denoting full health at both time points. However, only one
14 survivor entered full health at both times in EQ VAS (Figure 2).

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16 Binary logistic regression analyses were performed to find predictors of psychological
17 distress and self-assessed poor health (Table 3). The presence of treatment-requiring
18 comorbidity was found to predict more anxiety at three months after resuscitation (OR 4.07,
19 $p=0.04$), but there was no significant odds ratio regarding comorbidity at 12 months; instead,
20 being female was found to predict more anxiety (OR 9.23, $p=0.01$) and more symptoms of
21 depression (OR 14.78, $p=0.002$) at this time. Being female was also found to predict self-
22 assessed poor health at three months (OR 6.33, $p=0.04$), while young age was found to predict
23 poor health at three and 12 months, respectively (OR 0.91, $p=0.002$; OR 0.93, $p=0.003$).

39 Discussion

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41 One objective of this study was to investigate how the psychological and health-related
42 outcomes change between three and 12 months in survivors of OHCA with good neurological
43 functioning. We found an encouraging progression as survivors at large showed less
44 psychological distress and better self-assessed health over time. In comparison, participants in
45 this study even surpassed the average level of depression and self-assessed health in the
46 Swedish population at their 12-month follow-up (24, 25). However, we also found that even
47 though about half of OHCA survivors report a decrease in psychological distress between
48 three and 12 months, almost one-third report increased psychological distress; hence, our
49 results indicate that the psychological outcome after OHCA may differ considerably on an
50 individual level.

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52 As stated earlier, few prior longitudinal studies have investigated the psychological and
53 health-related outcomes after cardiac arrest. In accordance with our results, two small sample
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3 studies have previously reported a decrease of anxiety and depressive symptoms in cardiac
4 arrest survivors over time (13, 27). In contrast, a rather large prospective study found no
5 change in anxiety or depressive symptoms between one and 12 months (14). It is possible that
6 the heterogeneity in psychological outcomes observed in this study could explain a part of the
7 discrepancies in the available literature. As regards self-assessed health, the improvements
8 seen in this study confirm the results of two previous longitudinal studies (9, 10). However,
9 these previous studies found that the greatest health-related improvements occurred in the
10 early stages of recovery, within three months after cardiac arrest (9, 10). Moreover, although
11 the 'minimal clinically important difference' in the HADS and EQ-5D-3L among survivors of
12 cardiac arrest is unknown, estimates from other patient populations indicate that the
13 improvements seen in this study might not be clinically noticeable (28, 29).

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22 A second objective was to evaluate predictors of psychological distress self-assessed poor
23 health after OHCA. Since it is already known that cardiac arrest survivors generally report
24 few psychological problems and good health, it is difficult to define a threshold for a bad
25 outcome among those who perform well neurologically. In this study, the outcome was
26 dichotomised as good or bad in comparison to mean scores from the average Swedish
27 population. Prior studies have concluded that many survivors reach an psychological state and
28 health comparable to the average population, although no study has previously investigated
29 predictors of this outcome (9, 10, 30). In addition, there is also a lack of knowledge regarding
30 factors associated with post cardiac arrest improvement over time (13, 31). We found that
31 comorbidity is associated with higher levels of anxiety compared to the average population at
32 three months after OHCA. However, we did not find a significant correlation between
33 comorbidity and anxiety or depression at the 12-month follow-up. In contrast, being female
34 was strongly associated with psychological distress at one year after resuscitation, but this
35 was not significant at three months. We also found a significant correlation between being
36 female and self-assessed poor health at three months, while young age was associated with
37 self-assessed poor health at both three and 12 months.

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Studies investigating prognostic factors regarding the psychological or health-related outcomes after cardiac arrest are scarce. However, receiving an ICD has been linked to higher levels of psychological distress (32), but this effect has not been shown in a cardiac arrest population (14). We did not find any significant correlation regarding ICD in our regression models either. Young age and being female have previously been associated with anxiety among cardiac arrest survivors (30), but there were no significant correlation between psychological distress and age in our study population. Nevertheless, we did find a

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3 considerably higher likelihood of depression among female survivors of OHCA at 12 months,
4 which has not previously been reported. Also novel is the likelihood of a better self-assessed
5 health among survivors of higher age.
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8 The European Resuscitation Council has provided guidelines for post cardiac arrest
9 rehabilitation since 2015 and has pointed out the need of a structured follow-up care,
10 including physical, neurological, and emotional screening (33). Still, far from all cardiac
11 arrest survivors in Sweden are offered rehabilitation or neuropsychological evaluation, despite
12 recommendations from the Swedish Resuscitation Council (34, 35). Instead, survivors in
13 Sweden are often followed based on the aetiology of the cardiac arrest with little to no focus
14 on emotional sequelae (35, 36). Our results indicate that even if the majority of OHCA
15 survivors live without psychological distress and with good self-assessed health, there are
16 individuals that experience major problems. Consequently, it should be expected that some
17 survivors will benefit from psychiatric rehabilitation, and survivors of young age, who are
18 female, and those with treatment-requiring comorbidity should be screened early on.
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29 *Strengths and limitations*

30 This study has several strengths. During the study period of four years, a specially-trained
31 nurse was placed at every hospital in a large region of Sweden. With this approach, we were
32 able to collect data from virtually every case of OHCA. The study design also allowed us to
33 match non-respondents with data collected from the SCRR at the time of their hospitalisation,
34 thus enabling comparisons between respondents and non-respondents. Consequently, we were
35 able to confirm that the study population represents the group at large in these aspects.
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40 Another strength is that the outcomes in this study could be compared with the average
41 Swedish population. Knowledge regarding factors of importance for a psychological state and
42 self-assessed health in line with the normal population after OHCA in Sweden is missing.
43 This information will help to generalise the overall picture of OHCA survival and provide
44 guidance regarding which survivors who need psychiatric rehabilitation. Furthermore, the
45 response rate was very high at 12 months.
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50 The main limitations of this study are the retrospective design and the restrictive inclusion
51 of survivors with good neurological functioning (CPC-score ≤ 2), which limits the
52 applicability on OHCA survivors more broadly. However, we made the assessment that
53 inclusion of survivors with a severe cerebral dysfunction would complicate the interpretability
54 of the results. Furthermore, it is not possible to differentiate between patients with a CPC-
55 score of one and two. However, as mentioned above, we lack knowledge of the minimal
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3 clinically important difference regarding the HADS and EQ-5D-3L in this population. The
4 strict inclusion is also reflected by the relatively small sample size which further limits the
5 generalisability of the results. Another methodical limitation in this study is the use of EQ-
6 5D-3L to measure self-assessed health. A recent study concluded that EQ-5D-3L might
7 underestimate the health in OHCA survivors, yielding high ceiling effects, which was
8 apparent in the EQ-5D-3L descriptive system in this study as well (23). Although EQ VAS
9 showed higher interpretability with a more varied outcome in our study population, it is
10 known that generic measures of health often fail to capture the true complexity of the health
11 state in survivors of cardiac arrest (37). Finally, some survivors were excluded due to severe
12 illness and a few non-respondents mentioned poor health as the reason for not participating.
13 Therefore, it is possible that the participants in this study had a better outcome than survivors
14 more generally.
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24 25 **Conclusions**

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27 On a group level, there is a significant improvement in the psychological and health-related
28 outcomes among survivors of OHCA between three and 12 months after resuscitation. Higher
29 levels of psychological distress can be expected among female survivors and those with
30 treatment-requiring comorbidity, while young and female survivors are at risk of a self-
31 assessed poor health. These findings should be considered in the follow-up after OHCA,
32 although future research is required to identify further predictors regarding the long-term
33 outcome and chance of improvement post cardiac arrest.
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43 Executive Board (VGFOUREG-78031), Region Västra Götaland, Sweden. The guarantor had
44 no role in the design or execution of this study.
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52 would also like to thank Dr. Kate Bramley-Moore for English language editing assistance.
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56 **Competing interests**

57 The authors declare no conflict of interest.
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Contributors

All authors have made a substantial contribution to the conception and design of the study. AV analysed the data and wrote the manuscript with input from all authors. KSS and ÅA initiated and planned the study, collected the data, assisted in the interpretation of the data and took part in drafting the manuscript. JH took part in the planning of the study, contributed with external expertise and have continuously revised the manuscript. DJ helped analyze the data and have continuously revised the manuscript.

Data sharing statement

Due to ethical restrictions, data are available on request. Interested researchers may submit a request for data to the authors (adam.viktorisson@gu.se). According to Swedish regulation: <http://www.epn.se/en/start/regulations/>, the permission to use data is only for what has been applied for and then approved by the Ethical board. To not follow the regulations is seen as scientific misconduct.

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3 **Figure legends**
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6 **Figure 1.** Flowchart of study participants.
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10 **Figure 2.** Scatter plot with individual reported outcomes in the HADS and EQ-5D-3L at three
11 months (x-axis) and 12 months (y-axis). Dots above the diagonal lines indicate a higher score
12 at the 12-month follow-up. Scores from 7 participants are missing in EQ VAS.
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Table 1. Background characteristics and self-reported comorbidity of participants.

<i>n (%) unless otherwise stated</i>	Participants n=74	Missing data*
Age. Median (min-max) ^a	63 (25-89)	
Female ^a	13 (18)	
Time to EMS in minutes. Median (min-max)	7 (1-61)	11
Cardiac arrest circumstances		
Cardiac aetiology ^a	62 (86)	2
Cardiac arrest at home	22 (30)	
CPR before arrival of EMS	41 (55)	
Initial rhythm: VF or VT	61 (86)	3
Witnessed cardiac arrest	69 (95)	1
In-hospital interventions		
CABG	5 (7)	2
ICD ^a	19 (27)	4
Induced hypothermia (33°C) ^a	35 (49)	2
PCI	39 (54)	2
Comorbidity**^a		
Anaemia or other blood disease	0	
Back pain	3 (4)	
Cancer	1 (1)	
Diabetes mellitus	2 (3)	
Gastrointestinal disease	5 (7)	
Heart disease	54 (73)	
Hypertension	27 (36)	

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3	Liver disease	1 (1)
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5	Osteoarthritis	2 (3)
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7	Pulmonary disease	3 (4)
8		
9	Renal disease	0
10		
11	Rheumatoid arthritis	1 (1)
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14 * Number of participants where information is missing

15 ** Number of participants with self-reported treatment-requiring comorbidity

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17 ^a Variables included as predictors in the univariate regression analyses

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20 Abbreviations: VF, ventricular fibrillation; VT ventricular tachycardia; CRP,
21 cardiopulmonary resuscitation; EMS, emergency medical service; PCI,
22 percutaneous coronary intervention; CABG, coronary artery bypass grafting; ICD,
23 implantable cardioverter defibrillator
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Table 2. Comparison of mean scores at three and 12 months in the HADS and EQ-5D-3L (n=74).

	3 months	12 months	<i>Z</i> -value	<i>p</i>
	Observed mean (SD)	Observed mean (SD)		
HADS				
HADS-Anxiety	5.6 (±4.8)	4.7 (±4.3)	2.337	0.02*
HADS-Depression	3.4 (±3.5)	2.6 (±2.6)	2.199	0.03*
Total score	9.0 (±7.8)	7.3 (±6.5)	2.579	0.01*
EQ-5D-3L				
EQ VAS (n=67)	73 (±18)	77 (±19)	2.292	0.02*
Index value	0.82 (±0.26)	0.88 (±0.15)	2.966	0.003*

* $p < 0.05$ indicates statistical significance

Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; SD, standard deviation; VAS, visual analogue scale

Table 3. Predictors of psychological distress and self-assessed poor health (n=70).

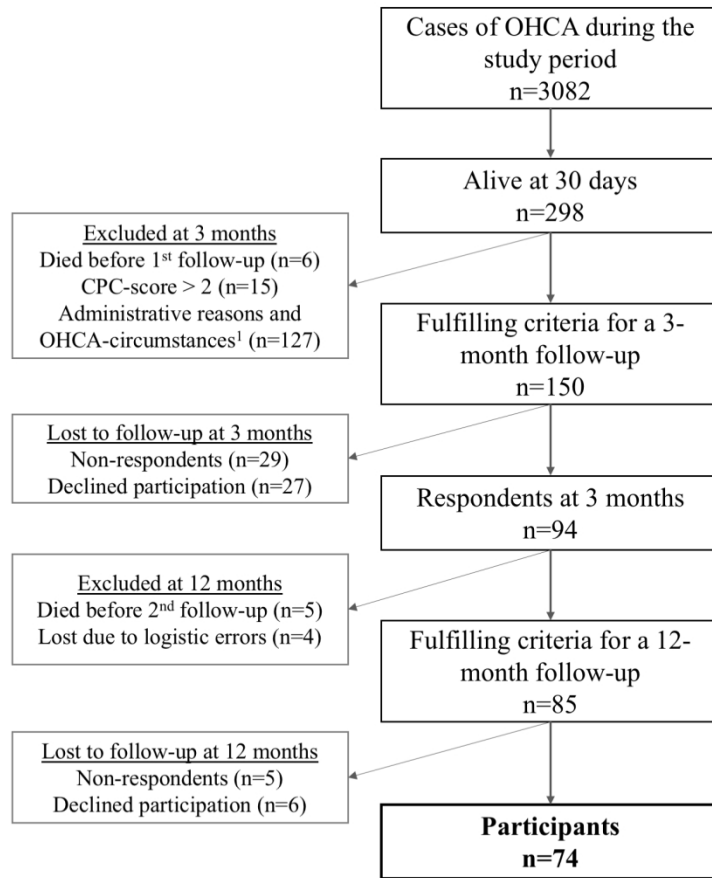
Predictors	3 months				12 months			
	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²
HADS-Anxiety								
Age	0.99 (0.95-1.03)	0.02	0.63	0.195	0.98 (0.93-1.03)	0.02	0.40	0.276
Comorbidity	4.07 (1.07-17.00)	0.73	0.04*		3.79 (0.70-20.42)	0.86	0.12	
Being female	4.94 (0.91-26.83)	0.86	0.06		9.23 (1.68-50.61)	0.78	0.01*	
Hypothermia	1.25 (0.43-3.62)	0.54	0.68		1.20 (0.38-3.76)	0.58	0.75	
HADS-Depression								
Age	0.99 (0.94-1.04)	0.03	0.57	0.136	0.99 (0.94-1.05)	0.03	0.81	0.300
Comorbidity	1.45 (0.33-6.44)	0.76	0.62		1.20 (0.25-5.85)	0.81	0.82	
Being female	3.71 (0.90-15.37)	0.78	0.07		14.78 (2.60-83.87)	0.87	0.002*	
Hypothermia	1.16 (0.37-3.61)	0.58	0.81		2.75 (0.82-9.28)	0.62	0.10	
ICD	1.52 (0.40-5.69)	0.68	0.54		0.55 (0.11-2.77)	0.82	0.47	
EQ-5D-3L index value								
Age	0.91 (0.86-0.97)	0.03	0.002*	0.362	0.93 (0.89-0.98)	0.02	0.003*	0.288
Comorbidity	1.19 (0.28-5.01)	0.73	0.81		2.53 (0.51-12.69)	0.82	0.26	
Being female	6.33 (1.03-38.81)	0.93	0.04*		2.09 (0.46-9.40)	0.77	0.34	

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4 * $p < 0.05$ indicates statistical significance
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7 Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; OR,
8 odds ratio; SE, standard error; CI, confidence interval; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary
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¹⁾ Administrative reasons include survivors documented with an incorrect social security number, not able to be identified within 3 months or not residing in the region. OHCA-circumstances include trauma, attempted suicide, drowning and intoxication as cause of the cardiac arrest or severe illness afterwards.

Figure 1. Flowchart of study participants.

249x299mm (190 x 190 DPI)

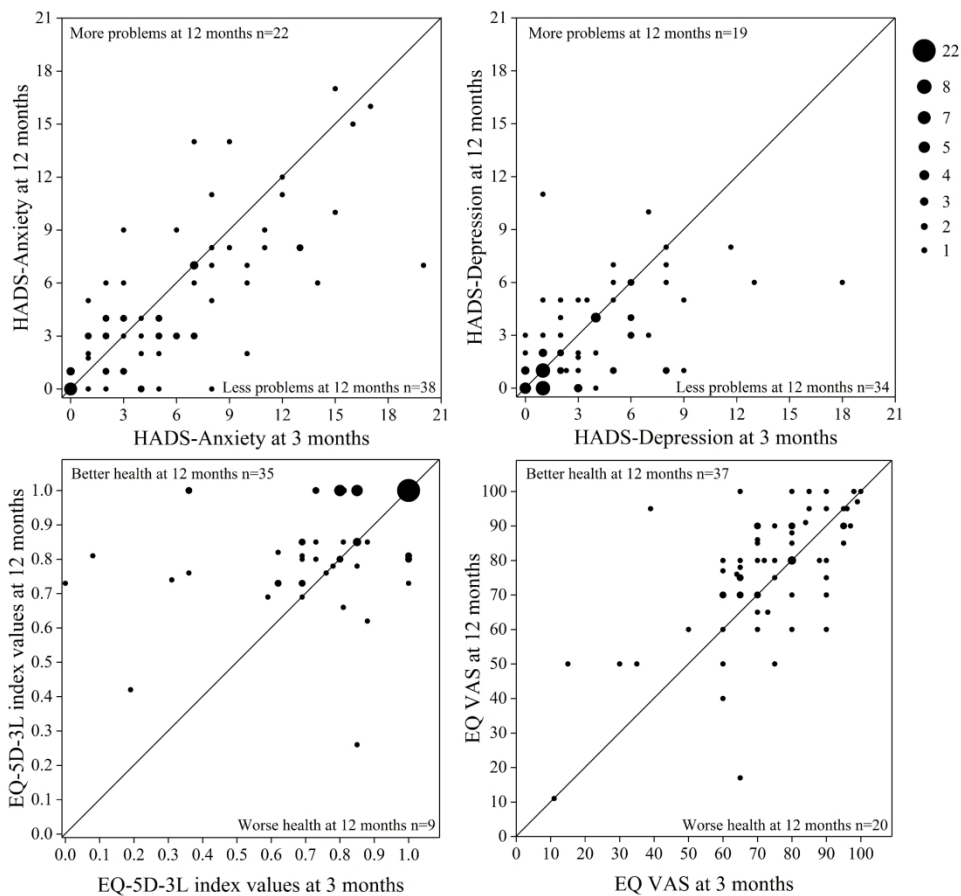


Figure 2. Reported outcomes in the HADS and EQ-5D-3L at three and 12 months (n=74). Diagonal lines divide the participants with regard to what time they reported the highest score. Scores from 7 participants are missing in EQ VAS.

245x245mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	See tables and figures
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Not applicable
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(b) Report category boundaries when continuous variables were categorized	7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A one year longitudinal study of psychological distress and self-assessed health in survivors of out-of-hospital cardiac arrest.

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Cardiac arrest, Follow-up, Outcome, Anxiety, Depression, Quality of life

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3 **Running headline:** A one year longitudinal study of psychological distress and self-assessed
4 health in survivors of out-of-hospital cardiac arrest.
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Abstract

Objectives: Few studies have investigated the psychological and health-related outcome after out-of-hospital cardiac arrest (OHCA) over time. This longitudinal study aims to evaluate psychological distress in terms of anxiety and depression, self-assessed health, and predictors of these outcomes in survivors of OHCA, three and 12 months after resuscitation.

Methods: Recruitment took place from 2008 to 2011 and survivors of OHCA were identified through the national Swedish Cardiopulmonary Resuscitation Registry. Inclusion criteria were age ≥ 18 years, survival ≥ 12 months and a Cerebral Performance Category score ≤ 2 . Questionnaires containing the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L) were administered at three and 12 months after the OHCA. Participants were also asked to report treatment-requiring comorbidities.

Results: Of 298 survivors, 85 were eligible for this study and 74 responded. Anxiety was reported by 22 survivors at three months and by 17 at 12 months, while depression was reported by 10 at three months and 4 at 12 months. The mean EQ-5D-3L index value increased from 0.82 (± 0.26) to 0.88 (± 0.15) over time. There were significantly less symptoms of psychological distress ($p=0.01$) and better self-assessed health ($p=0.003$) at 12-months. Treatment-requiring comorbidity predicted anxiety (OR 4.07, $p=0.04$), while being female and young age predicted poor health (OR 6.33, $p=0.04$; OR 0.91, $p=0.002$) at three months. At 12 months, being female was linked to anxiety (OR 9.23, $p=0.01$) and depression (OR 14.78, $p=0.002$), while young age predicted poor health (OR 0.93, $p=0.003$).

Conclusion: The level of psychological distress and self-assessed health improve among survivors of OHCA between three and 12 months after resuscitation. Higher levels of psychological distress can be expected among female survivors and those with comorbidity, while survivors of young age and who are female are at greater risk of poor health.

Strengths and limitations of this study

- Data were collected from virtually every out-of-hospital cardiac arrest survivor within the course of 4 years in a large region of Sweden.
- A nurse responsible for data collection was placed at each hospital in the region to match survivors with data from the Swedish Cardiopulmonary Resuscitation Registry.
- Only survivors with a cerebral performance category score of ≤ 2 were included.

- The use of generic measures of health has a limited ability to capture the complexity of the health state in survivors of cardiac arrest.

Key words: Cardiac arrest; Follow-up; Outcome; Anxiety; Depression; Quality of life.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a deadly condition that affects approximately 5000 inhabitants in Sweden each year (1). The survival rate of OHCA is low, although great efforts have been made to raise the number of survivors in recent years; consequently, the 30-day survival rate in Sweden has increased from 4.5% in 1992 to 11.4% in 2017 (2). When the heart stops hypoxic brain injury occurs within minutes and is the most critical factor in determining the chance of survival and level of functioning, if resuscitation is successful (3). Following cerebral hypoxia, cardiac arrest survivors are known to be at risk of cognitive and emotional deficits (4-7). Although most survivors with a good neurological outcome return to high function and quality of life (8, 9), long-term psychological problems have been reported by up to one-third in Swedish-samples (10, 11). Furthermore, the ability to pinpoint survivors who need psychiatric rehabilitation will become more important as survival rates continue to increase.

There is already an extensive body of knowledge regarding the outcome after cardiac arrest in different patient populations and time points. Time to awakening, gender, age, role of bystander, use of hypothermia and percutaneous coronary intervention (PCI) have previously been related to the outcome after cardiac arrest (6, 12, 13). However, few studies have investigated the psychological and health-related outcome in the same sample over time (9, 10, 14), and little is known about factors associated with post cardiac arrest improvement in these aspects. The interpretation of the available literature is complicated by high heterogeneity in study outcomes, and knowledge regarding psychological distress and self-assessed health after OHCA in relation to the average population is lacking (7, 15).

We have previously reported that reduced well-being is experienced by half of OHCA survivors at three months, and that female survivors report significantly more anxiety and worse health compared to males (16). In this study, we will investigate how the psychological and health-related outcomes change in survivors of OHCA with good neurological functioning between three and 12 months after resuscitation. Further, we will also evaluate gender differences as well as predictors of psychological distress and self-assessed poor health at these time points.

Methods

Design and setting

This was a longitudinal study with self-administered postal questionnaires sent to survivors three and 12 months after the OHCA. The setting was a region in Sweden with 1.6 million inhabitants and nine hospitals that treat cardiac arrest. The frequency of OHCA was 850 cases annually and the survival rate approximately 10%.

Study population

The study population was identified through the national Swedish Cardiopulmonary Resuscitation Registry (SCRR). Every person who suffered from an OHCA and for whom resuscitation was initiated should be included in the SCRR. To ensure complete coverage, there was a specially-trained nurse at each hospital who could identify missing cases and match patients treated for OHCA with data from the SCRR.

Recruitment took place from 1st January 2008 to 31st December 2011 and every adult survivor of OHCA in the region was assessed for inclusion. The study inclusion criteria were age ≥ 18 years, survival ≥ 12 months, and a Cerebral Performance Category (CPC) score ≤ 2 at discharge, denoting good neurological functioning (17). Exclusion criteria were cardiac arrest due to trauma, attempted suicide, intoxication, or abuse. Survivors with other severe illness and survivors treated but not residing in the region were also excluded.

Procedure and questionnaire

Eligible survivors received a postal questionnaire in Swedish three months after the OHCA. Survivors who responded to the questionnaires and gave a written consent were included. Participants at three months then received a second questionnaire at 12 months. A reminder was sent if no response was received after three weeks. The questionnaire consisted of the Hospital Anxiety and Depression scale (HADS) and European Quality of Life 5 Dimensions 3 Level (EQ-5D-3L). Study participants were also asked to report treatment-requiring comorbidity.

The HADS is a 14-item screening instrument developed to detect psychological distress in terms of clinically significant anxiety and/or depression (18). It is divided into two subscales, seven items regarding anxiety (HADS-anxiety) and seven items regarding symptoms of depression (HADS-depression). Each item has four levels, scored 0-3, with a maximum score of 21 in each subscale. Scoring >7 in one subscale indicates mild to moderate problems and a

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3 score >10 indicates severe problems. Although the HADS has never been thoroughly
4 evaluated in a cardiac arrest population, it is considered a reliable measurement for depression
5 and anxiety in patients with somatic illness (19) and is frequently used in cardiovascular
6 research (7).
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10 EQ-5D-3L is designed to measure subjective health and includes the EQ-5D-3L descriptive
11 system and a visual analogue scale (EQ VAS) (20). The descriptive system
12 comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and
13 anxiety/depression); each dimension has three levels (no problems, moderate problems and
14 severe problems) denoting a score of 1-3. The total score in the EQ-5D-3L descriptive system
15 can be converted to an index-value which ranges between -0.594 and 1.00, calculated with
16 the UK EQ-5D index tariff (21). An index value of 1.00 indicates full health, while negative
17 values represents health states worse than death (20). EQ VAS is visualized as a continuum
18 of value scale where the patient assesses his or her current health on a scale from zero to 100,
19 with endpoints labelled 'best imaginable health state' and 'worst imaginable health state'.
20 EQ-5D-3L is commonly used in cardiovascular research (22). However, the use of EQ-5D-3L
21 in OHCA populations has been questioned as the instrument has shown a limited ability to
22 differentiate between survivors of good health (23).
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34 *Statistics and data analysis*

35 Statistical analyses were executed with IBM SPSS Statistics 24.0 (Armonk, NY: IBM Corp).
36 All p-values were two-sided and interpreted at a 0.05 significance level. Nonparametric tests
37 were used for all comparisons as all dependent variables were non-normally distributed. The
38 χ^2 test was applied for nominal values and the Mann-Whitney U-test for ordinal values.
39 Wilcoxon signed ranks test was used to explore the change between three and 12 months.
40 Predictors of psychological distress (HADS) and self-assessed poor health (EQ-5D-3L index
41 values) were investigated using multivariate binary logistic regression models. The outcome
42 was dichotomised as good or bad with regard to the mean scores in two Swedish reference
43 populations, matched to gender and age-group. A bad outcome was considered a score two
44 standard deviations below the mean of the reference population. Reference values regarding
45 the HADS were drawn from a random sample gathered 1997 in Jämtland County, Sweden
46 (n=624) (24); similarly, reference values regarding the EQ-5D-3L index values were drawn
47 from a random sample gathered 2001 in Stockholm County, Sweden (n=3069) (25). The
48 predictors were included based on clinical reasoning and are presented in Table 1. With
49 regard to the sample size, only six variables were evaluated and correlations between them
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3 were examined using Spearman's rank correlation; only variables with a Spearman's rho \pm
4 ≤ 0.7 were accepted. Univariate analysis was conducted separately between each individual
5 predictor. The significant level of the univariate analysis was 0.25 and predictors with a p-
6 value > 0.25 were excluded from further analysis. Hosmer and Lemeshow tests and Receiver
7 Operating Characteristics curves (ROC-curves) were performed to ensure the reliability of the
8 logistic regression models.
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15 *Patient and public involvement*

16 None of the included patients were involved in the design or conduction of this study and no
17 patient opinion regarding the subject has been obtained. The results will be reported to the
18 Health & Medical Care Committee of the Regional Executive Board, Region Västra
19 Götaland, Sweden.
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25 *Ethics*

26 Ethical permission was granted by the Regional Ethics Review board, Western Sweden (No.
27 465-07). Written consent was obtained from all participants.
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32 **Results**

33 There were 3082 cases of OHCA in the region during the study period, of which 298 were
34 alive at 30 days. One-hundred-fifty survivors fulfilled the inclusion criteria for a three-month
35 follow-up and 94 responded. Of the respondents at three months, 85 were included at 12
36 months and 74 responded again (87% response rate); in the group that did not receive a
37 second questionnaire, five had died and four were lost due to logistical errors (Figure 1).
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42 The representativeness of the study population has been investigated in a prior study (26),
43 and there were no significant differences regarding age, gender, cardiac arrest circumstances,
44 or in-hospital interventions between respondents and non-respondents. However, there were
45 differences between participants and the survivors that only responded once. Double
46 respondents were significantly younger ($Z=2.316$, $p=0.021$), had a lower frequency of cardiac
47 arrest at home ($\chi^2=6.249$, $p=0.014$), and a higher frequency of ventricular fibrillation or
48 ventricular tachycardia as initial rhythm ($\chi^2=5.067$, $p=0.032$). Background characteristics and
49 self-reported comorbidity of the participants are presented in Table 1.
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56 Mild to moderate anxiety (>7 in HADS-A) was reported by 22 (30%) survivors at the three
57 months follow-up and by 17 (23%) at 12 months. Mild to moderate depression (>7 in HADS-
58 D) was reported by 10 (14%) survivors at three months and by four (5%) at 12 months. A
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3 score indicating severe anxiety (>10 in HADS-A) was reported by 12 survivors at three
4 months and by eight at 12 months, while severe depression (>10 in HADS-D) was reported
5 by three at three months and one at 12 months. Overall, survivors of OHCA reported a
6 significantly improved psychological and health-related outcome over time (Table 2). About
7 half of the survivors reported less psychological distress in the HADS at 12 months (51%
8 decrease in anxiety and 46% in symptoms of depression); although one-third reported an
9 increase in psychological distress (30% increase in anxiety and 28% in symptoms of
10 depression). Two-thirds of female survivors reported more psychological distress at the 12-
11 month follow up, corresponding to one-fifth among male survivors. Comparably, half of the
12 survivors reported better self-assessed health at 12 months in EQ-5D-3L, whereas 41%
13 reported the same health state at three and 12 months. Among the survivors who remained
14 unchanged, 73% reported an EQ-5D-3L index value of 1.00, denoting full health at both time
15 points. However, only one survivor entered full health at both times in EQ VAS (Figure 2).

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17 Binary logistic regression analyses were performed to find predictors of psychological
18 distress and self-assessed poor health (Table 3). The presence of treatment-requiring
19 comorbidity was found to predict more anxiety at three months after resuscitation (OR 4.07,
20 $p=0.04$), but there was no significant odds ratio regarding comorbidity at 12 months; instead,
21 being female was found to predict more anxiety (OR 9.23, $p=0.01$) and more symptoms of
22 depression (OR 14.78, $p=0.002$) at this time. Being female was also found to predict self-
23 assessed poor health at three months (OR 6.33, $p=0.04$), while young age was found to predict
24 poor health at three and 12 months, respectively (OR 0.91, $p=0.002$; OR 0.93, $p=0.003$).

40 41 **Discussion**

42 One objective of this study was to investigate how the psychological and health-related
43 outcomes change between three and 12 months in survivors of OHCA with good neurological
44 functioning. We found an encouraging progression as survivors at large showed less
45 psychological distress and better self-assessed health over time. In comparison, participants in
46 this study even surpassed the average level of depression and self-assessed health in the
47 Swedish population at their 12-month follow-up (24, 25). However, we also found that even
48 though about half of OHCA survivors report a decrease in psychological distress between
49 three and 12 months, almost one-third report increased psychological distress; hence, our
50 results indicate that the psychological outcome after OHCA may differ considerably on an
51 individual level.
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3 As stated earlier, few prior longitudinal studies have investigated the psychological and
4 health-related outcomes after cardiac arrest. In accordance with our results, two small sample
5 studies have previously reported a decrease of anxiety and depressive symptoms in cardiac
6 arrest survivors over time (13, 27). In contrast, a rather large prospective study found no
7 change in anxiety or depressive symptoms between one and 12 months (14). It is possible that
8 the heterogeneity in psychological outcomes observed in this study could explain a part of the
9 discrepancies in the available literature. As regards self-assessed health, the improvements
10 seen in this study confirm the results of two previous longitudinal studies (9, 10). However,
11 these previous studies found that the greatest health-related improvements occurred in the
12 early stages of recovery, within three months after cardiac arrest (9, 10). Moreover, although
13 the 'minimal clinically important difference' in the HADS and EQ-5D-3L among survivors of
14 cardiac arrest is unknown, estimates from other patient populations indicate that the
15 improvements seen in this study might not be clinically noticeable (28, 29).

16
17 A second objective was to evaluate predictors of psychological distress self-assessed poor
18 health after OHCA. Since it is already known that cardiac arrest survivors generally report
19 few psychological problems and good health, it is difficult to define a threshold for a bad
20 outcome among those who perform well neurologically. In this study, the outcome was
21 dichotomised as good or bad in comparison to mean scores from the average Swedish
22 population. Prior studies have concluded that many survivors reach an psychological state and
23 health comparable to the average population, although no study has previously investigated
24 predictors of this outcome (9, 10, 30). In addition, there is also a lack of knowledge regarding
25 factors associated with post cardiac arrest improvement over time (13, 31). We found that
26 comorbidity is associated with higher levels of anxiety compared to the average population at
27 three months after OHCA. However, we did not find a significant association between
28 comorbidity and anxiety or depression at the 12-month follow-up. In contrast, being female
29 was strongly associated with psychological distress at one year after resuscitation, but this
30 was not significant at three months. We also found a significant association between being
31 female and self-assessed poor health at three months, while young age was associated with
32 self-assessed poor health at both three and 12 months.

33
34 Studies investigating prognostic factors regarding the psychological or health-related
35 outcomes after cardiac arrest are scarce. However, receiving an ICD has been linked to higher
36 levels of psychological distress (32), but this effect has not been shown in a cardiac arrest
37 population (14). We did not find any significant association regarding ICD in our regression
38 models either. Young age and being female have previously been associated with anxiety
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3 among cardiac arrest survivors (30), but there were no significant association between
4 psychological distress and age in our study population. Nevertheless, we did find a
5 considerably higher likelihood of depression among female survivors of OHCA at 12 months,
6 which has not previously been reported. Also novel is the likelihood of a better self-assessed
7 health among survivors of higher age.
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11 The European Resuscitation Council has provided guidelines for post cardiac arrest
12 rehabilitation since 2015 and has pointed out the need of a structured follow-up care,
13 including physical, neurological, and emotional screening (33). Still, far from all cardiac
14 arrest survivors in Sweden are offered rehabilitation or neuropsychological evaluation, despite
15 recommendations from the Swedish Resuscitation Council (34, 35). Instead, survivors in
16 Sweden are often followed based on the aetiology of the cardiac arrest with little to no focus
17 on emotional sequelae (35, 36). Our results indicate that even if the majority of OHCA
18 survivors live without psychological distress and with good self-assessed health, there are
19 individuals that experience major problems. Consequently, it should be expected that some
20 survivors will benefit from psychiatric rehabilitation, and survivors of young age, who are
21 female, and those with treatment-requiring comorbidity should be screened early on.
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32 *Strengths and limitations*

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34 This study has several strengths. During the study period of four years, a specially-trained
35 nurse was placed at every hospital in a large region of Sweden. With this approach, we were
36 able to collect data from virtually every case of OHCA. The study design also allowed us to
37 match non-respondents with data collected from the SCRR at the time of their hospitalisation,
38 thus enabling comparisons between respondents and non-respondents. Consequently, we were
39 able to confirm that the study population represents the group at large in these aspects.
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41 Another strength is that the outcomes in this study could be compared with the average
42 Swedish population. Knowledge regarding factors of importance for a psychological state and
43 self-assessed health in line with the normal population after OHCA in Sweden is missing.
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45 This information will help to generalise the overall picture of OHCA survival and provide
46 guidance regarding which survivors who need psychiatric rehabilitation. Furthermore, the
47 response rate was very high at 12 months.
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55 The main limitations of this study are the retrospective design and the restrictive inclusion
56 of survivors with good neurological functioning (CPC-score ≤ 2), which limits the
57 applicability on OHCA survivors more broadly. However, we made the assessment that
58 inclusion of survivors with a severe cerebral dysfunction would complicate the interpretability
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3 of the results. Furthermore, it is not possible to differentiate between patients with a CPC-
4 score of one and two. However, as mentioned above, we lack knowledge of the minimal
5 clinically important difference regarding the HADS and EQ-5D-3L in this population. The
6 strict inclusion is also reflected by the relatively small sample size, resulting in a low count of
7 events per variable in the logistic regression (five variables were evaluated in 70 participants),
8 why the significance of these results should be interpreted with caution. Another methodical
9 limitation in this study is the use of EQ-5D-3L to measure self-assessed health. A recent study
10 concluded that EQ-5D-3L might underestimate the health in OHCA survivors, yielding high
11 ceiling effects, which was apparent in the EQ-5D-3L descriptive system in this study as well
12 (23). Although EQ VAS showed higher interpretability with a more varied outcome in our
13 study population, it is known that generic measures of health often fail to capture the true
14 complexity of the health state in survivors of cardiac arrest (37). Finally, some survivors were
15 excluded due to severe illness and a few non-respondents mentioned poor health as the reason
16 for not participating. Therefore, it is possible that the participants in this study had a better
17 outcome than survivors more generally.
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30 **Conclusions**

31 On a group level, there is a significant improvement in the psychological and health-related
32 outcomes among survivors of OHCA between three and 12 months after resuscitation. Higher
33 levels of psychological distress can be expected among female survivors and those with
34 treatment-requiring comorbidity, while young and female survivors are at risk of a self-
35 assessed poor health. These findings should be considered in the follow-up after OHCA,
36 although future research is required to identify further predictors regarding the long-term
37 outcome and chance of improvement post cardiac arrest.
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49 no role in the design or execution of this study.
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Competing interests

The authors declare no conflict of interest.

Contributors

All authors have made a substantial contribution to the conception and design of the study. AV analysed the data and wrote the manuscript with input from all authors. KSS and ÅA initiated and planned the study, collected the data, assisted in the interpretation of the data and took part in drafting the manuscript. JH took part in the planning of the study, contributed with external expertise and have continuously revised the manuscript. DJ helped analyze the data and have continuously revised the manuscript.

Data sharing statement

Due to ethical restrictions, data are available on request. Interested researchers may submit a request for data to the authors (adam.viktorisson@gu.se). According to Swedish regulation: <http://www.epn.se/en/start/regulations/>, the permission to use data is only for what has been applied for and then approved by the Ethical board. To not follow the regulations is seen as scientific misconduct.

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55 **Figure legends**

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58 **Figure 1.** Flowchart of study participants.
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5 **Figure 2.** Scatter plot with individual reported outcomes in the HADS and EQ-5D-3L at three
6 months (x-axis) and 12 months (y-axis). Dots above the diagonal lines indicate a higher score
7 at the 12-month follow-up. Scores from 7 participants are missing in EQ VAS.
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56 **Table 1.** Background characteristics and self-reported comorbidity of participants.
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<i>n (%) unless otherwise stated</i>	Participants n=74	Missing data*
Age. Median (min-max) ^a	63 (25-89)	
Female ^a	13 (18)	
Time to EMS in minutes. Median (min-max)	7 (1-61)	11
Cardiac arrest circumstances		
Cardiac aetiology ^a	62 (86)	2
Cardiac arrest at home	22 (30)	
CPR before arrival of EMS	41 (55)	
Initial rhythm: VF or VT	61 (86)	3
Witnessed cardiac arrest	69 (95)	1
In-hospital interventions		
CABG	5 (7)	2
ICD ^a	19 (27)	4
Induced hypothermia (33°C) ^a	35 (49)	2
PCI	39 (54)	2
Comorbidity**^a	60 (81)	
Anaemia or other blood disease	0	
Back pain	3 (4)	
Cancer	1 (1)	
Diabetes mellitus	2 (3)	
Gastrointestinal disease	5 (7)	
Heart disease	54 (73)	
Hypertension	27 (36)	
Liver disease	1 (1)	
Osteoarthritis	2 (3)	

Pulmonary disease	3 (4)
Renal disease	0
Rheumatoid arthritis	1 (1)

* Number of participants where information is missing

** Number of participants with self-reported treatment-requiring comorbidity

^a Variables included as predictors in the univariate regression analyses

Abbreviations: VF, ventricular fibrillation; VT ventricular tachycardia; CRP, cardiopulmonary resuscitation; EMS, emergency medical service; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ICD, implantable cardioverter defibrillator

Table 2. Comparison of mean scores at three and 12 months in the HADS and EQ-5D-3L (n=74).

	3 months	12 months	Z-value	p
	Observed mean (SD)	Observed mean (SD)		
HADS				
HADS-Anxiety	5.6 (±4.8)	4.7 (±4.3)	2.337	0.02*
HADS-Depression	3.4 (±3.5)	2.6 (±2.6)	2.199	0.03*
Total score	9.0 (±7.8)	7.3 (±6.5)	2.579	0.01*
EQ-5D-3L				
EQ VAS (n=67)	73 (±18)	77 (±19)	2.292	0.02*
Index value	0.82 (±0.26)	0.88 (±0.15)	2.966	0.003*

* $p < 0.05$ indicates statistical significance

Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; SD, standard deviation; VAS, visual analogue scale

Table 3. Predictors of psychological distress and self-assessed poor health (n=70).

Predictors	3 months				12 months			
	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²	OR (95% CI)	SE	<i>p</i>	<i>R</i> ²
HADS-Anxiety								
Age	0.99 (0.95-1.03)	0.02	0.63	0.195	0.98 (0.93-1.03)	0.02	0.40	0.276
Comorbidity	4.07 (1.07-17.00)	0.73	0.04*		3.79 (0.70-20.42)	0.86	0.12	
Being female	4.94 (0.91-26.83)	0.86	0.06		9.23 (1.68-50.61)	0.78	0.01*	
Hypothermia	1.25 (0.43-3.62)	0.54	0.68		1.20 (0.38-3.76)	0.58	0.75	
HADS-Depression								
Age	0.99 (0.94-1.04)	0.03	0.57	0.136	0.99 (0.94-1.05)	0.03	0.81	0.300
Comorbidity	1.45 (0.33-6.44)	0.76	0.62		1.20 (0.25-5.85)	0.81	0.82	
Being female	3.71 (0.90-15.37)	0.78	0.07		14.78 (2.60-83.87)	0.87	0.002*	
Hypothermia	1.16 (0.37-3.61)	0.58	0.81		2.75 (0.82-9.28)	0.62	0.10	
ICD	1.52 (0.40-5.69)	0.68	0.54		0.55 (0.11-2.77)	0.82	0.47	
EQ-5D-3L index value								
Age	0.91 (0.86-0.97)	0.03	0.002*	0.362	0.93 (0.89-0.98)	0.02	0.003*	0.288
Comorbidity	1.19 (0.28-5.01)	0.73	0.81		2.53 (0.51-12.69)	0.82	0.26	
Being female	6.33 (1.03-38.81)	0.93	0.04*		2.09 (0.46-9.40)	0.77	0.34	

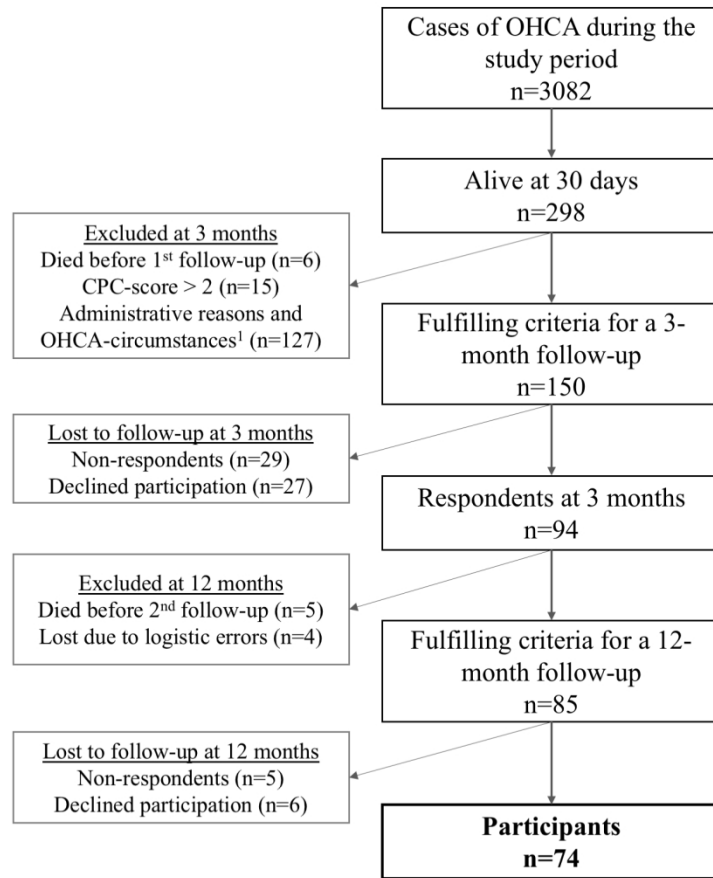
* *p* < 0.05 indicates statistical significance

Abbreviations: HADS, hospital anxiety and depression scale; EQ-5D-3L, European quality of life 5 dimensions 3 level; OR, odds ratio; SE, standard error; CI, confidence interval; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary

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intervention

For peer review only



¹⁾ Administrative reasons include survivors documented with an incorrect social security number, not able to be identified within 3 months or not residing in the region. OHCA-circumstances include trauma, attempted suicide, drowning and intoxication as cause of the cardiac arrest or severe illness afterwards.

Figure 1. Flowchart of study participants.

249x299mm (190 x 190 DPI)

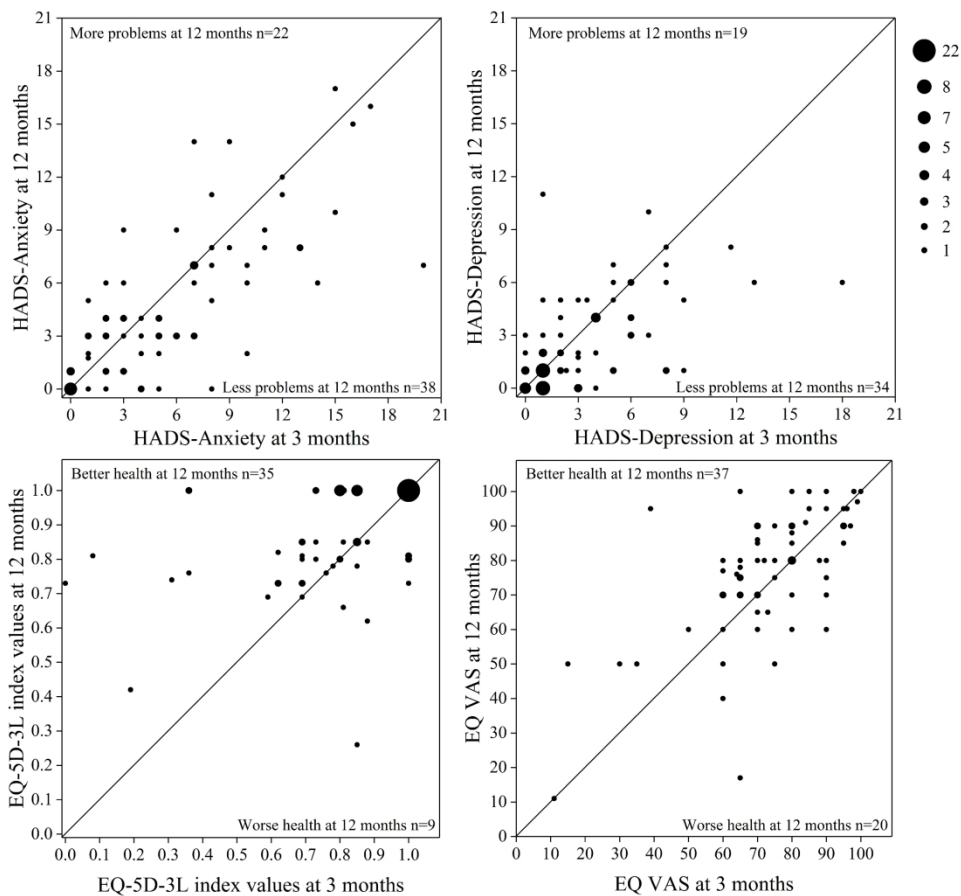


Figure 2. Reported outcomes in the HADS and EQ-5D-3L at three and 12 months (n=74). Diagonal lines divide the participants with regard to what time they reported the highest score. Scores from 7 participants are missing in EQ VAS.

245x245mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5-6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	See tables and figures
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	Not applicable
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	Not applicable
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	Not applicable
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
		(b) Report category boundaries when continuous variables were categorized	7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.