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Long-term physical and mental outcomes after out-of-hospital cardiac arrest– Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS survey)

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Long-term physical and mental outcomes after out-of-hospital cardiac arrest– Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS survey)

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Word count abstract: 298

Word count manuscript: 3842

Key words: Out-of-hospital cardiac arrest survivor, relatives of out-of-hospital cardiac arrest survivors, cross-sectional survey, self-report.

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ABSTRACT

Introduction

The number of out-of-hospital cardiac arrest (OHCA) survivors is increasing. However, there remains limited knowledge on the long-term physical and mental problems suffered by survivors and their relatives. The aims of the DANCAS (DANish cardiac arrest survivorship) survey are to describe the prevalence of physical and mental problems, identify predictors associated with suffering them and to determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions.

Methods and analysis

The DANCAS survey has a cross-sectional design involving a survey of OHCA survivors and their relatives. OHCA survivors will be identified through the Danish Cardiac Arrest Registry as having suffered an OHCA between 1st January 2016 and 31st December 2019. Each survivor will be asked to identify their closest relative to complete the relatives' survey. Contents of survivor survey: EQ-5D-5L, Hospital Anxiety and Depression Scale, Two Simple Questions, Modified Fatigue Impact Scale, 12-item World Health Organisation Disability Assessment Scale 2.0, Nordic Physical Activity Questionnaire Short, plus questions on unmet rehabilitation and information needs. Contents of relatives' survey: World Health Organisation-Five Well-Being Index, Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest and the Modified Carer Strain Index. Self-report outcome data collected through the surveys will be enriched by data from Danish national registries including: demographic characteristics, circumstances of cardiac arrest and co-morbidities. The survey will be completed either electronically or by post December 2020-February 2021.

Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences.

Article Summary

Strengths and limitations of this study:

-Denmark has markedly improved the survival rate among OHCA survivors during the last five years.

-This will be one of the largest nationwide surveys of OHCA survivors to date with data collected from survivors and relatives up to five-years after cardiac arrest.

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-Data will be derived from both self-report measures and national registries providing a comprehensive picture of the problems experienced by OHCA survivors and the risk factors associated with suffering them.

-The response rate from OHCA survivors suffering from cognitive problems and/or fatigue may be lower due to difficulties completing the survey compared to those without these problems to counter this the survey will be available both electronically and on paper.

-The change in physical and mental problems over time may be influenced by a treatment cohort effect and other unknown time-dependent modifying factors.

INTRODUCTION

The number of people surviving an out-of-hospital cardiac arrest (OHCA) is increasing every year due to advances in pre-hospital and acute medical care.[1][2] In Denmark, thirty-day survival after OHCA improved from 4-16% between 2001 and 2018.[3] This amounts to at least 800 new survivors every year.[3] Still, after the acute phase ends, the physical and mental impact of OHCA may continue.[4] Most OHCA survivors will have a new or ongoing cardiac condition.[5][6] They may suffer from mental trauma due to surviving a near-death experience.[7] Further, reduced oxygen levels to the brain during an OHCA can cause cognitive deficits in up to 50% of survivors.[8-10] Due to this combination of factors, OHCA survivors have been shown to suffer anxiety and depression, fatigue and reduced participation in society.[7][8][11][12] General health, return-to-work rates and quality of life do, however, appear to improve over time[13-15] but data regarding: health measures, return-to-work patterns and unmet rehabilitation needs beyond 12-months after OHCA are limited.[7][11][14][16][17]

As most OHCA occur in private homes, relatives are likely to witness the event.[18] Combined with the changes in both physical and mental status of many OHCA survivors, quality of life and mental health among relatives might be influenced. It has previously been described how relatives of OHCA survivors suffer from emotional problems including anxiety, depression and post-traumatic stress, due to becoming a carer for their loved one or fear of the cardiac arrest reoccurring.[19][20] Likewise, lack of control, feelings of insecurity, mood and sleep disturbances have been reported among relatives.[21][22] Yet, very few research studies have investigated the consequences of OHCA for relatives in the longer term,[23][24] or how these are associated with witnessing the event or with the physical, mental problems suffered by the OCHA survivor.

Rehabilitation for OHCA survivors is recommended in international guidelines[4][25] but the specific content and timing of these interventions has not been established. Survivors will commonly be

offered cardiac rehabilitation related to their new or ongoing cardiac condition,[4 26] but it has been suggested that the psychological and neurological rehabilitation needs of OHCA are not met to the same degree.[27] Hence, the aims of this national cross-sectional study are to 1) describe the long-term prevalence of physical and mental problems for OHCA survivors and their relatives 2) identify predictors associated with increased risk of suffering these problems and 3) determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions. Specific objectives for each aim will be defined in future publications.

METHODS AND ANALYSIS

Study design

The DANCAS (DANish Cardiac Arrest Survivorship) survey aims will be achieved through a cross-sectional study design.

Setting and participants

In Denmark, pre-hospital care, hospital care and all cardiac treatment and rehabilitation are funded via the tax system and are free of charge for patients. The Danish Out-of-Hospital Cardiac Arrest (DHRCA) registry will be used to identify the Danish personal identification numbers of people who have suffered an OHCA from 1st January 2016 to 31st December 2019 and were alive 30-days after their cardiac arrest (figure 1). All patients in Denmark who have suffered an OHCA, where bystanders or paramedics attempted treatment are included in the DHRCA registry. Data is recorded electronically immediately after the OHCA in the pre-hospital patient record by paramedics from one of the five regional ambulance services and collected in the DHRCA.

The DHRCA started collecting data in 2001, however, before 2016, this was recorded by hand on paper and hence significant gaps in the data exist[3]. In addition, pre-hospital and medical management of OHCA has changed significantly in the period 2001-2015.[28] Consequently, the proposed timeframe of 1-5 years since OHCA provides both a long-term perspective and ensures data is relevant to the contemporary OHCA survivor population.

The extracted Danish personal identification numbers will be matched by the Danish National Health Digital Board to data in the Danish National Patient Registry to remove any people who have died, and to retrieve names, and addresses.

The information letter received by the OHCA survivors will ask them to identify their closest relative and ask them to complete the relatives' survey. This method of recruitment has been tested in the development of the survey and is feasible. Closest relative is defined as a partner, spouse, sibling, or parent that is closest to the survivor.

Eligibility criteria

OHCA survivor participants included in the survey will have a Danish personal identification number, be alive at least ten-months post-cardiac arrest, resident in Denmark, over 18-years of age and able to read and write in Danish and not protected from receiving inquiries during scientific surveys.

Relative participants must have a relative who has survived an OHCA, be over 18 years of age and be able to read and write in Danish. The relatives do not need to have a Danish personal identification number, as they will be invited to complete their survey via the information letter to the OHCA survivor participants. However, they will be asked to provide their Danish personal identification number to allow linkage with Danish national registries.

Data collection

All OHCA survivor participants that meet the eligibility criteria will receive an invitation to participate in the survey via REDCap (Research Electronic Data Capture) software to their E-boks (government electronic mail account) or via post if they do not have an E-boks address. Based on the age profile of OHCA survivors over the last 5-years and the age-profile of Danes with E-boks addresses it is estimated that 20% of participants will require a postal survey.

The invitation to participate will include a link for the relatives of the survivor to complete the separate relatives' survey. Invitations via post will include a paper copy of both surveys, two stamped addressed envelopes (for survivor and relative) and information on how to complete the surveys online rather than by post if they wish. A participant information sheet will be included with all invitations to participate in the survey. This will detail the purpose of the research study, how data will be used and will explain that by returning the survey, they are consenting to take part. The information sheet will include a telephone number to call a member of the research team if participants have any questions. Participants who receive the E-boks survey will have the option to request a paper survey by post. A reminder invitation will be sent via E-boks/post after two-weeks.

Additional data from the DHRCA will provide information on circumstances of the OHCA (Table 1).

Table. 1 Data on circumstances of OHCA from DHRCA

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Table. 1 Data on circumstances of OHCA from DHRCA

Location of cardiac arrest (Private/public)

First observed heart rhythm (shockable/not shockable)

Cardiopulmonary resuscitation was given before the arrival of the ambulance (Yes/No)

Defibrillated before the arrival of the ambulance (Yes/No)

Time to return of spontaneous circulation (minutes:second)

Development of the DANCAS surveys

The outcome domains for the two DANCAS surveys were developed from a public and patient involvement (PPI) event held in Denmark[29] (see PPI section below) and from the outcomes identified as important by participants in the COSCA (core outcome set for cardiac arrest) initiative.[30] For each of these outcome domains, appropriate existing self-report outcome measures were chosen. For domains where no outcome measure existed, questions from other patient groups were adapted for OHCA survivors or new questions were developed.

The PPI group participants tested individual outcome measures for acceptability and face validity where there was more than one outcome measure available (for example, in the domain 'function and disability'). The PPI group also gave feedback on draft versions of the whole DANCAS surveys, and the participant information sheet. Feedback was received from eight survivors, three relatives, and three clinicians with experience of treating OHCA survivors and relatives. Based on this feedback, we reduced the number of questions, removed any outcome measures where the item content overlapped and improved the clarity of the participation information sheet.

Self-report outcome measures in the DANCAS surveys

Full details on the self-report outcome measures, scoring, and Danish translations can be found in the Supplementary data.

The following self-report outcome measures will be completed by OHCA survivors:
EQ-5D-5L: This is a six-item standardised instrument for measuring current health status.[31] The questionnaire covers five-dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into five-levels: no problems, slight, moderate, severe or extreme problems. The sixth-item, a Visual Analogue Scale, 0-100, allows the respondent to provide a self-rating of his or her health. A higher score signifies a better health status.

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Hospital Anxiety and Depression Scale (HADS): The HADS consists of a seven-item subscale measuring symptoms of anxiety (HADS-A) and a seven-item subscale measuring symptoms of depression (HADS-D).[32] Each item has a four-choice response, with scores ranging from 0 (no symptoms) to 3 (maximum number of symptoms). The total scores on each subscale range from 0 to 21. A score of less than 8 indicates no psychological distress, 8 to 10 mild psychological distress and over 10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[33]

Two Simple Questions (TSQ): Consists of three-items. Developed to assess the survivor's own perception of mental recovery and dependency in daily activities after cardiac arrest.[34 35]

Modified Fatigue Impact Scale (MFIS): The MFIS assesses impact of fatigue on performance of functional activities and consists of 21-items in three-sub-scales (physical, cognitive and psychosocial). Total scores range from 0 to 84 with a score of 30 or more signifying a fatigued individual. It has been validated in people with multiple sclerosis and traumatic brain injury.[36 37]

12-item World Health Organisation Disability Assessment Schedule 2.0 (12-item WHO DAS 2.0): This assesses disability and functioning in the prior month on six adult life tasks. There are twelve-items scored from 0=no difficulty to 4=extreme difficulty, total score 0 to 48 with higher scores indicating greater difficulty. Used extensively to research rehabilitation and disability in a wide range of disease populations[38] and validated in patients with chronic diseases[39] including traumatic brain injury.[40]

The Nordic Physical Activity Questionnaire Short (NPAQ-Short):
The NPAQ-short assesses whether WHO recommendations on weekly exercise are met[41]. Participants under 65 years of age are asked if they are physically active at a moderate-to-high intensity (≥ 30 minutes a day) and at physically active at a high-level for ≥ 20 minutes twice a week. Participants over 65 years of age are asked about being physically active ≥ 30 minutes a day, and if they undertake strength or balance training. It has been found to be sufficiently reliable and valid to monitor physical activity levels in a Danish population.[41]

REHPA scale: A linear analogue self-assessment scale, where participants indicate how close they are to living the life they desire after their OHCA, indicating rehabilitation need. The scale is rated between 0 (goal reached) to 9 (infinitely far from).

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Questions on unmet rehabilitation needs have been adapted from the Danish Cancer Society questionnaire 'The experiences of cancer patients during diagnosis and treatment'.[42 43]. Participants are asked if they received the help they needed after their cardiac arrest in 6 areas: emotional reactions, cognitive problems, physical activity, peer-support and family (supplementary data). Questions on unmet information needs after cardiac arrest were adapted from a questionnaire evaluating experiences of healthcare quality in Denmark among patients with heart disease.[44] Participants are asked if they felt informed after their cardiac arrest on seven subjects: treatment of heart condition, medication for heart condition, emotional reaction, cognitive problems, physical activity, return-to-work and impact on family.

In addition to the HADS, the relatives' survey includes:

World Health Organisation Five Well-Being Index: The WHO-5 is a self-report measure of current mental well-being[45] that has been shown to be a valid tool across a wide range of study fields.[46] The tool consists of five statements with six responses on a scale from 'At no time' to 'All of the time' scoring 0-5. Scores are totaled and multiplied by 4 with 0 representing the worst imaginable well-being and 100 representing the best imaginable well-being. The WHO-5 was chosen as a generic global measure of health for the survey, as opposed to using the EQ-5D-5L as in the OHCA survivor survey. This choice was based on feedback from a PPI workshop asking relatives to fill-in and provide feedback on individual questionnaires. The relatives felt the EQ-5D-5L was about medical problems and was for their relative (who had suffered the OHCA) to complete and they were unsure how to answer the questions. Conversely, they understood why the WHO-5 might be relevant to their life situation and felt able to complete it.

The Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest (IQCODE-CA): This is a modified version of the observer-reported questionnaire designed to measure global cognitive decline in the dementia population.[47] Informants, defined as relatives or close friends are requested to compare current cognitive function with pre-cardiac arrest cognitive function. The tool contains 26-items scored on a five-point scale with higher scores indicating greater impairment. It has been shown to identify cardiac arrest survivors with possible cognitive problems.[47]

Modified carer strain index (MCSI): This is a self-reported questionnaire that screens for caregiver strain in long-term caregivers.[48] The tool has 13 questions scoring 2 points for 'yes', 1 point for 'sometimes' and 0 for 'no'. Scores range from 26-0 with higher scores indicating a higher level of caregiver strain. The MCSI has been found to be easily administered and a reliable test of strain in an informal caregiver population.[48]

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Further, one question derived from the Danish National Health Survey 2017[49] on loneliness and four questions on support received in the post-cardiac arrest period (created for this survey, supplementary data). Seven questions on educational level, labour market status and sick leave are also asked in the relatives section as their survey answers can only be connected to Danish labour market registry data if relatives choose to provide their Danish personal identification number in their survey response.

Data enrichment from registries

Following data collection via the two surveys, data enrichment will occur via Danish national registries for both survivors and relatives. The Danish Civil Registration System will provide gender, age and marital status. The Danish Education Register:[50] education level and the Danish Register on personal income[51]: income.

The Danish National Patient Register,[52] provides data on 19 selected somatic co-morbidities scored on a 3-point scale. This data will be used to calculate the Charlson Comorbidity Index,[53] based on the 10 years previous to the date of the surveys. The Charlson Comorbidity Index has three categories: 0, 1-2 and ≥3. This registry will also provide data on hospital admissions and healthcare use for the potential sub-study on societal costs after surviving OHCA.

Current and pre-OHCA employment status for the working-age population will be obtained from the Danish Register for Evaluation of Marginalization.(DREAM)[54] Participants who are not on any social benefits or participants who are on State Education Fund grants, maternity leave pay, or leave-of-absence schemes will be classified as being part of the workforce.[55] Accordingly, patients receiving unemployment benefits, being on paid sick leave, on early retirement payment or disability pension will be defined as being on social benefits. Pre-OHCA employment status will be assessed in a 5-week span before cardiac arrest to classify patients as either working or receiving social benefits.

Information from the DHRCA and other national registries will be collected for all eligible study participants both responders and non-responders to the survey (figure 1).

Data handling and record-keeping

The study has been registered on the Region of Southern Denmark's record of data processing activities (19/8559). A license agreement has been made with Odense Patient Data Explorative

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Network (OPEN) (OP_843) to establish the REDCap system, secure data storage, data analysis and data linkage with national registries. REDCap will be used to import Danish personal identification numbers for survey distribution via E-boks. Postal surveys received will be scanned, and the data imported into REDCap and destroyed.

Sample size considerations

Each year approximately 800 people are alive 30-days after surviving an OHCA in Denmark.[3] Hence, we estimate the survey will be sent to approximately n=3200 survivors. Based on similar studies in heart diseases,[17][56] we are assuming a 20% (n=640) loss due to a person having moved out of Denmark, being protected from inquiries or having died,[16] and a response rate of 60%. Hence, the estimated total study population would be approximately n= 1540 OHCA survivors with approximately n=380 in each of the four time interval groups. The response rate to the relatives' survey is likely to be less as not all survivors will have a relative able to complete the survey. Hence, estimated 50% (1200) of relatives will respond and 50% (600) of responders will provide CPR numbers.

Planned analysis

Continuous data will be checked for normality and described as mean and standard deviation (SD) or median with 25th and 75th quartiles [IQR, interquartile range], as appropriate. Categorical variables will be described as number and frequencies (n (%)). To investigate changes over time, participants will be stratified into four groups: those suffering an OHCA in 2016, 2017, 2018 and 2019 (figure 2). Differences in the prevalence of self-report problems between the groups will be determined by Chi-squared test or Fisher's Exact test as appropriate. The OHCA survivor and relatives' surveys will be linked via a unique identifying number to discover if associations exist between each groups' self-report outcomes.

Predictors of physical and mental problems will be identified from self-report outcomes, demographic characteristics, circumstances of OHCA and unmet rehabilitation/information needs using univariate binary logistic regression. All univariate predictors with $p < 0.10$ will be entered into a multivariate binary logistic regression, with description of odds ratios or β and 95% confidence intervals. In all regression analyses, both crude and adjusted models will be presented. Level of statistical significance will be set at $p < 0.05$.

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A potential sub-study is planned to calculate the total societal costs (healthcare costs and absenteeism from work) of surviving OHCA using the EQ-5D-5L data and registry data (National Prescription Registry,[57] and DREAM database).

Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Participants will be informed about the study via the participant information sheet. Consent to participate will be implied through the return of the completed survey.

Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences. The results of the proposed study will be reported with reference to the international statement in the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist for cross-sectional studies[58]. Health professionals will be informed of the study results through professional literature via new national clinical guidelines on rehabilitation after OHCA. Finally, the survey is part of a larger project on rehabilitation after surviving a cardiac arrest and all results, including the survey results, will be presented at a project-closing event to which all participants, stakeholders and interested parties will be invited.

Patient and public involvement

The themes for the survey were developed from a PPI event involving OHCA survivors, relatives and clinicians.[29] A further group of survivors and relatives have helped to develop the survey by testing individual questionnaires and by providing feedback on the whole survey. At the end of the study, the research advisory group and PPI group will discuss and comment on the findings and contribute to how the results will be disseminated and implemented in the next stage of the research.

Discussion

Recovery after OHCA can be complicated by a new or ongoing cardiac condition, mental trauma from surviving a near-death experience or possible anoxic brain injury. Small scale, short term studies suggest these complications can lead to an increased mental and physical burden for both survivors and their relatives. However, little is known about the long-term prevalence of physical and mental problems or who is at most risk of developing them. Rehabilitation has been

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recommended to meet the secondary physical and mental consequences of OHCA but more knowledge is needed including establishing the perceived unmet rehabilitation and information needs from OHCA survivors and their relatives themselves.

The results from this study will be used to identify the most prevalent problems suffered by OHCA survivors and their families and those at most risk of suffering them. This will allow researchers and managers within the Danish healthcare system to design assessment tools to ensure problems are detected early after OHCA, and survivors and relatives are offered rehabilitation plans tailored to their needs. Further, currently there are few high quality studies investigating the effectiveness of rehabilitation interventions for OHCA survivors. Results from the DANCAS survey will provide researchers with specific information to design the content and timing of new rehabilitation interventions for OHCA survivors and their relatives.

Although this study will be one of the largest surveys involving OHCA survivors and one of the first to survey both survivors and relatives, with the ability to link between the two, there are several potential limitations. The majority of the self-report questionnaires have undergone some validation testing. However, not all these tools have been validated in Danish or in the OHCA survivor population and some questions have been written specifically for this survey (see supplementary data).

The survey uses questionnaires based on self-report. However, approximately 50% of OHCA survivors suffer from cognitive deficits and/or fatigue, leading to difficulties completing the survey and hence potentially a lower response rate from survivors with these problems. To counter this, the survey will available both electronically and on paper, survivors will be allowed to have help to complete the survey and asked to state if they had help. In addition, the relatives' section of the survey will include an observer-reported cognitive questionnaire and relatives will be asked to complete this even if the survivor questionnaire is not completed. However, it remains possible that those with cognitive deficits and/or fatigue will be underrepresented in the survey response group and this has to be accepted as a limitation of the self-report method chosen to gain data from as many OHCA survivors as possible. Surveys will only be received by OHCA survivors able to access Eboks or living at home, so we are very unlikely to receive responses from any survivor living in long-term residential care. Further, the DHRCA only records OHCA and therefore people who have suffered an in-hospital cardiac arrest will not be included in this study.

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One aim of the survey is to describe how the prevalence of physical and mental problems suffered by survivors and their relatives changes over time since OHCA. Ideally, this would be investigated using a prospective longitudinal study with data from the same population at multiple follow-up points. The disadvantage of this design is the results would not be available for five-years, and participants are asked to complete multiple surveys. The design of our survey groups participants dependent on time since OHCA to describe changes over time. However, as these are not the same participants in each time interval group, there is a risk of an unknown time-dependent confounding factor effecting one of the groups more than another. Further, the cross-sectional design, by definition, does not allow the formation of solid conclusions but the generation of hypotheses based on associations between variables.

Author contributions VJ, LHT and ADZ conceived the study; VJ and LHT designed the study with ADZ, BB, LZ, TMB, RS, SRC and JFN. VJ led the writing of the manuscript, which was revised by all authors. The final manuscript was approved by all authors.

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Competing interests None declared

Patient consent Not required

Data statement: Within the boundaries of Danish legislation, the anonymised data from the study will be available for other researchers upon reasonable request when the results have been published.

Figure legends:

Figure 1. Flow chart of Survey Population

Figure 2. Design of DANCAS survey and grouping according to time since OHCA

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Individuals registered in DHRCA with date of OHCA 11-59 months before date on which data will be extracted and alive 30 days after OHCA (n)

According to National Patient Registry:
-Dead (n)
-Not resident in Denmark (n)
-Incorrect Danish Identification number (n)
-Protected from enquiry (n)
Total excluded (n)

Individuals invited to participate via E-boks (n) or post (n)

Incorrect E-boks (n)
Incorrect postal address (n)
Dead (n)
Mistakenly registered in DHRCA as an OHCA (n)

Total OHCA survivor survey population (n)

-Total survivor survey respondents (n)
-Responded with first contact (n)
-Responded with first reminder (n)

-Total non-respondents to survivor survey (n)
-Non-respondents who gave a reason for declining to participate (n)

-Total relatives survey respondents (n)
-Relatives' survey respondents who gave Danish Identification number (n)

Figure 1. Flow chart of Survey Population

169x143mm (150 x 150 DPI)
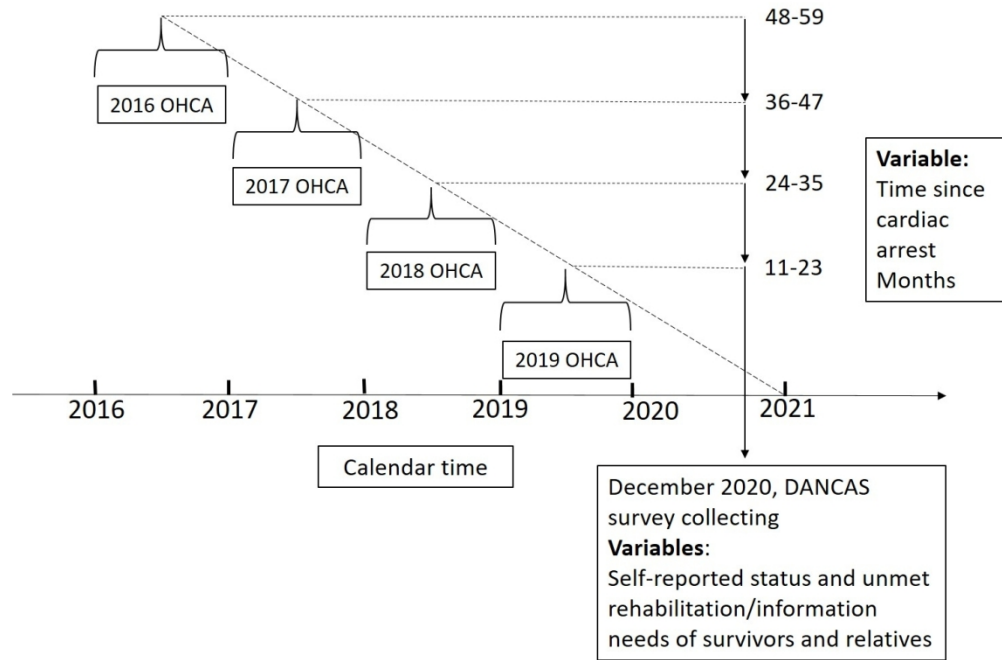
Figure 2. Design of DANCAS survey and grouping according to time since OHCA

250x169mm (150 x 150 DPI)

Supplementary data.

Table 1. Detailed content of DANCAS surveys

Outcome domain	Outcome measure	Items, scoring	Danish translation	Notes
Survivors				
Generic health	EQ-5D-5L	Five item health dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Divided into five levels: 1='No problems' to 5= 'Extreme problems', scores ≥ 2 signifies a problem. Sixth item: Self-rating of health. Visual Analogue Scale, 0-100. Higher scores signify better health status.[1]	Received from the EuroQoL group	
Anxiety and depression	HADS	Seven-item symptoms of anxiety subscale (HADS-A) Seven-item subscale symptoms of depression (HADS-D). Four responses: 0='No symptoms' to 3= 'maximum number of symptoms'. Total subscale scores range: 0-21. <8 = no psychological distress, 8-10 = mild psychological distress, >10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[2]	Received from DenHeart study group[3]	Valid measure of anxiety and depression in Danish cardiac disease population[3]

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Mental recovery/dependency	TSQ	Yes to Q1a + Yes to Q1b signify new problems with dependency after cardiac arrest. No to Q2 indicates problems with mental recovery after cardiac arrest.[4 5]	Received from TTM2 study group[4]	-
Fatigue impact on functional activities	MFIS	21 items in three sub-scales (physical, cognitive and psychosocial). Total scores range: 0-84. Total subscale scores: physical= 0 -36; cognitive=0=40; psychosocial= 0-8. ≥30 signify a fatigued individual (Antmann, 2012, Schiehser, 2015)	Translation received from e Provide, Mapi Research Trust.	Validated in people with multiple sclerosis.[6] and mild to moderate brain injury.[7]
Function and disability	12-item WHO DAS 2.0	12-item assessing 6 domains of functioning: 1) Understanding and communication; 2) Self-care; 3) Mobility; 4) Interpersonal relationships; 5) Work and household roles; and 6) Community and civic roles. Scored from 0= 'no difficulty' to 4= 'extreme difficulty or cannot do'. Total scores range: 0-48. Higher score indicating greater difficulty with activity and participation.	Available from:https://www.etf.dk/ergotera pi-og-politik/hverdagsr ehabilitering	Used extensively to research neurological conditions including traumatic brain injury and spinal cord injury,[8] and rehabilitation and disability in a wide range of disease populations.[9] Validated in patients with chronic diseases.[10]
Physical activity level	NPAQ	2-3 items depending on age: <65 years: 1) Physically active at a moderate-to-high intensity ≥ 30 minutes/day and 2) physically active at a high-level ≥ 20 minutes/day twice a week.	Available at: http://www.dans kernessundhed.d k/Spoergeskema	Tool determines whether WHO recommendations on weekly exercise are met.

		>65 years of age: 1) Physically active ≥ 30 minutes/day, and undertakes strength or balance training twice a week. Responses are Yes/No.[11]		Found to be sufficiently reliable and valid to monitor physical activity levels in a Danish population.[11]
Life satisfaction/rehabilitation need	REHPA scale	A linear analogue scale, participants indicate how close they are to living the life they desire after their OHCA. Scale ranges from 0= 'goal reached' to 9= 'infinitely far from'. Score of ≤3 will be considered as signifying having rehabilitation needs.	By DANCAS study authors	
Unmet rehabilitation needs		6-items asking if rehabilitation needs were met in different domains, for example, emotional reactions. Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[12]	Adapted by DANCAS authors from	Questions adapted from existing survey 'The Experience of Cancer Patients during Diagnosis and Treatment'.[12][13]
Unmet information needs	Adapted from Zinckernagel et al., 2017	7-items asking if information needs were met in different domains, for example, 'treatment of your heart condition' Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[14]	Adapted by DANCAS authors for OHCA survivors from a Danish survey of patients with heart disease.[14]	

Relatives				
Anxiety and depression	HADS	As above		
Mental well-being	WHO-5	Five items with 6 responses from 0='At no time' to 5='all of the time'. Scores are totaled and multiplied by 4 to give range 0-100. Score <50 signifies poor emotional well-being.[15]	Developed in Denmark.[16]	Valid in multiple patient populations.[17]
Cognitive problems in daily life	IQCODE-CA	26-items scored on a five-point scale, 1= 'much improved' to 5= 'much worse'. Scores are totaled, divided by the number of questions to give a total, range 1-5. Score ≥3.04 signifies cognitive decline after cardiac arrest.[18]	Received from TTM2 study group	Relatives or close friends compare current cognitive function with pre-cardiac arrest cognitive function. Has been shown to accurately identify cardiac arrest survivors with potential cognitive problems.[18]
Carer strain	MCSI	13-items, scored: 2= 'Yes, On a Regular Basis', 1= 'Yes, sometimes', 0= 'No'. Range: 0-26, higher scores signify a higher level of carer strain.[19]	Translated by DANCAS study authors[a]	Found to have high internal validity with a population of family caregivers.[19]
Witness to OHCA	Questions designed for this survey	1-item on whether they witnessed the OHCA	Created by DANCAS study authors	
Labour market	Questions designed for this survey	7-items on educational level completed, current labour market status, status in pre-OHCA period and details of any sick leave in post-OHCA period.	Created by DANCAS study authors	These questions are asked of the relatives as their survey answers cannot be connected to Danish

				labour market registry data unless they provide their Danish personal identification number.
Social isolation	Question from Danish national health survey	One item: Does it ever happen that you are alone even though you would prefer to be with other people?" Answers: "yes, often" and "yes, sometimes" signify loneliness. Other possible responses are "yes, but rarely" and "no.	Available at: http://www.dans kernessundhed.d k/Spoergeskema	
Support received post-OHCA	Questions designed for this survey	4-items on: whether relatives feel they have someone to talk to if they need support (yes, always/yes, mostly/yes, sometimes/no never or almost never); who have they received support from (multiple options); if they received the support they needed (Yes, No), and who would they have like to have received support from in the post-OHCA period (free text box).	Created by DANCAS study authors	

Abbreviations: HADS= Hospital Anxiety and Depression Scale; TSQ=Two Simple Questions; TTM2= Targeted Hypothermia versus Targeted Normothermia after OHCA trial 2; MFIS: Modified Fatigue Impact Scale, WHO DAS 2.0= World Health Organisation disability assessment schedule 2.0 Short; NPAQ= Nordic Physical activity questionnaire; REHPA= Danish Knowledge Center for Rehabilitation and Palliative Care; OHCA=Out-of-hospital Cardiac Arrest; DANCAS=DANish Cardiac Arrest Survivorship; WHO-5= World Health Organisation-Five Well-Being index; IQCODE-CA: Informant Questionnaire on Cognitive Decline in the Elderly, Cardiac Arrest Version; MCSI= Modified Carer Strain Index.

aTranslation, cultural adaption and psychometric testing performed by study authors, results are planned to be available in a future publication.

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Long-term physical and psychological outcomes after out-of-hospital cardiac arrest– Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS survey)

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**Long-term physical and psychological outcomes after out-of-hospital cardiac arrest–
Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS
survey)**

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Word count manuscript: 3837

Key words: Out-of-hospital cardiac arrest survivor, relatives of out-of-hospital cardiac arrest
survivors, cross-sectional survey, self-report.

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ABSTRACT

Introduction

The number of out-of-hospital cardiac arrest (OHCA) survivors is increasing. However, there remains limited knowledge on the long-term physical and psychological problems suffered by survivors and their relatives. The aims of the DANCAS (DANish cardiac arrest survivorship) survey are to describe the prevalence of physical and psychological problems, identify predictors associated with suffering them and to determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions.

Methods and analysis

The DANCAS survey has a cross-sectional design involving a survey of OHCA survivors and their relatives. OHCA survivors will be identified through the Danish Cardiac Arrest Registry as having suffered an OHCA between 1st January 2016 and 31st December 2019. Each survivor will be asked to identify their closest relative to complete the relatives' survey. Contents of survivor survey: EQ-5D-5L, Hospital Anxiety and Depression Scale, Two Simple Questions, Modified Fatigue Impact Scale, 12-item World Health Organisation Disability Assessment Scale 2.0, plus questions on unmet rehabilitation and information needs. Contents of relatives' survey: World Health Organisation-Five Well-Being Index, Hospital Anxiety and Depression Scale, Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest and the Modified Caregiver Strain Index. Self-report outcome data collected through the surveys will be enriched by data from Danish national registries including: demographic characteristics, circumstances of cardiac arrest and co-morbidities. The survey will be completed either electronically or by post December 2020-February 2021.

Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences.

Article Summary

Strengths and limitations of this study:

-Denmark has markedly improved the survival rate among OHCA survivors during the last five years.

-This will be one of the largest nationwide surveys of OHCA survivors to date with data collected from survivors and relatives up to five-years after cardiac arrest.

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-Data will be derived from both self-report measures and national registries providing a comprehensive picture of the problems experienced by OHCA survivors and the risk factors associated with suffering them.

-The response rate from OHCA survivors suffering from cognitive problems and/or fatigue may be lower due to difficulties completing the survey compared to those without these problems to counter this the survey will be available both electronically and on paper.

-The change in physical and psychological problems over time may be influenced by a treatment cohort effect and other unknown time-dependent modifying factors.

INTRODUCTION

The number of people surviving an out-of-hospital cardiac arrest (OHCA) is increasing every year due to advances in pre-hospital and acute medical care.[1][2] In Denmark, thirty-day survival after OHCA improved from 4% to 16% between 2001 and 2018.[3] This amounts to at least 800 new survivors every year.[3] Still, after the acute phase ends, the physical and psychological impact of OHCA may continue.[4] Most OHCA survivors will have a new or ongoing cardiac condition.[5][6] They may suffer from psychological trauma due to surviving a near-death experience.[7] Further, reduced oxygen levels to the brain during an OHCA can cause cognitive deficits in up to 50% of survivors.[8-10] Due to this combination of factors, OHCA survivors have been shown to suffer anxiety and depression, fatigue and reduced participation in society.[7][8][11][12] General health, return-to-work rates and quality of life do, however, appear to improve over time[13-15] but data regarding: health measures, return-to-work patterns and unmet rehabilitation needs beyond 12-months after OHCA are limited.[7][11][14][16][17]

As most OHCA occur in private homes, relatives are likely to witness the event.[18] Combined with the changes in both physical and psychological status of many OHCA survivors, quality of life and psychological health among relatives might be influenced. It has previously been described how relatives of OHCA survivors suffer from emotional problems including anxiety, depression and post-traumatic stress, due to becoming a carer for their loved one or fear of the cardiac arrest reoccurring.[19][20] Likewise, lack of control, feelings of insecurity, mood and sleep disturbances have been reported among relatives.[21][22] Yet, very few research studies have investigated the consequences of OHCA for relatives in the longer term,[23][24] or how these are associated with witnessing the event or with the physical, psychological problems suffered by the OCHA survivor.

Rehabilitation for OHCA survivors is recommended in international guidelines[4][25] but the specific content and timing of these interventions has not been established. Survivors will commonly be

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offered cardiac rehabilitation related to their new or ongoing cardiac condition,[4 26] but it has been suggested that the psychological and neurological rehabilitation needs of OHCA are not met to the same degree.[27] Hence, the aims of this national cross-sectional study are to 1) describe the long-term prevalence of physical and psychological problems for OHCA survivors and their relatives and how these change over time 2) identify predictors associated with increased risk of suffering these problems and 3) determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions. Specific objectives for each aim will be defined in future publications.

METHODS AND ANALYSIS

Study design

The DANCAS (DANish Cardiac Arrest Survivorship) survey aims will be achieved through a cross-sectional study design.

Setting and participants

In Denmark, pre-hospital care, hospital care and all cardiac treatment and rehabilitation are funded via the tax system and are free of charge for patients. The Danish Out-of-Hospital Cardiac Arrest (DHRCA) registry will be used to identify the Danish personal identification numbers of people who have suffered an OHCA from 1st January 2016 to 31st December 2019 and were alive 30-days after their cardiac arrest (figure 1). All patients in Denmark who have suffered an OHCA, where bystanders or paramedics attempted treatment are included in the DHRCA registry. Data is recorded electronically immediately after the OHCA in the pre-hospital patient record by paramedics from one of the five regional ambulance services and collected in the DHRCA.

The DHRCA started collecting data in 2001, however, before 2016, this was recorded by hand on paper and hence significant gaps in the data exist[3]. In addition, pre-hospital and medical management of OHCA has changed significantly in the period 2001-2015.[28] Consequently, the proposed timeframe of 1-5 years since OHCA provides both a long-term perspective and ensures data is relevant to the contemporary OHCA survivor population.

The extracted Danish personal identification numbers will be matched by the Danish National Health Digital Board to names, and addresses in the Danish National Patient Registry retrieve.

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The information letter received by the OHCA survivors will ask them to identify their closest relative and ask them to complete the relatives' survey. This method of recruitment has been tested in the development of the survey and is feasible. Closest relative is defined as a partner, spouse, sibling, or parent that is closest to the survivor.

Eligibility criteria

OHCA survivor participants included in the survey will have a Danish personal identification number, be alive at least 30-days post-cardiac arrest, resident in Denmark, over 18-years of age and able to read and write in Danish and not protected from receiving inquiries during scientific surveys.

Relative participants must have a relative who has survived an OHCA, be over 18 years of age and be able to read and write in Danish. The relatives do not need to have a Danish personal identification number, as they will be invited to complete their survey via the information letter to the OHCA survivor participants. However, they will be asked to provide their Danish personal identification number to allow linkage with Danish national registries.

Data collection

All OHCA survivor participants that meet the eligibility criteria will receive an invitation to participate in the survey via REDCap (Research Electronic Data Capture) software to their e-Boks (government electronic mail account) or via post if they do not have an E-boks address. Based on the age profile of OHCA survivors over the last 5-years and the age-profile of Danes with e-Boks addresses it is estimated that 20% of participants will require a postal survey.

The link to complete the separate relatives' survey will be included in the invitation sent to the OHCA survivors' eBoks. Invitations sent via post to the OHCA survivor will include a paper copy of both surveys, two stamped addressed envelopes (for survivor and relative) and information on how to complete the surveys online rather than by post if they wish. A participant information sheet will be included with all invitations to participate in the survey. This will detail the purpose of the research study, how data will be used and will explain that by returning the survey, they are consenting to take part. The information sheet will include a telephone number to call a member of the research team if participants have any questions. Participants who receive the E-boks survey will have the option to request a paper survey by post. A reminder invitation will be sent via E-boks/post after two-weeks.

Additional data from the DHRCA will provide information on circumstances of the OHCA (Table 1).

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Table. 1 Data on circumstances of OHCA from DHRCA

Table. 1 Data on circumstances of OHCA from DHRCA
Location of cardiac arrest (Private/public)
First observed heart rhythm (shockable/not shockable)
Cardiopulmonary resuscitation was given before the arrival of the ambulance (Yes/No)
Defibrillated before the arrival of the ambulance (Yes/No)
Time to return of spontaneous circulation (minutes: second)

Development of the DANCAS surveys

The outcome domains for the two DANCAS surveys were developed from a public and patient involvement (PPI) event held in Denmark[29] (see PPI section below) and from the outcomes identified as important by participants in the COSCA (core outcome set for cardiac arrest) initiative.[30] For each of these outcome domains, appropriate existing self-report outcome measures were chosen. For domains where no outcome measure existed, questions from other patient groups were adapted for OHCA survivors or new questions were developed.

The PPI group participants tested individual outcome measures for acceptability and face validity where there was more than one outcome measure available (for example, in the domain 'function and disability'). The PPI group also gave feedback on draft versions of the whole DANCAS surveys, and the participant information sheet. Feedback was received from eight survivors, three relatives, and three clinicians with experience of treating OHCA survivors and relatives. Based on this feedback, we reduced the number of questions, removed any outcome measures where the item content overlapped and improved the clarity of the participation information sheet.

Self-report outcome measures in the DANCAS surveys

Full details on the self-report outcome measures, scoring, and Danish translations can be found in the Supplementary data.

The following self-report outcome measures will be completed by OHCA survivors:
EQ-5D-5L: This is a six-item standardised instrument for measuring current health status.[31] The questionnaire covers five-dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into five-levels: no problems, slight, moderate,

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severe or extreme problems. The sixth-item, a Visual Analogue Scale, 0-100, allows the respondent to provide a self-rating of his or her health. A higher score signifies a better health status.

Hospital Anxiety and Depression Scale (HADS): The HADS consists of a seven-item subscale measuring symptoms of anxiety (HADS-A) and a seven-item subscale measuring symptoms of depression (HADS-D).[32] Each item has a four-choice response, with scores ranging from 0 (no symptoms) to 3 (maximum number of symptoms). The total scores on each subscale range from 0 to 21. A score of less than 8 indicates no psychological distress, 8 to 10 mild psychological distress and over 10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[33]

Two Simple Questions (TSQ): Consists of three-items. Developed to assess the survivor's own perception of mental recovery and dependency in daily activities after cardiac arrest.[34 35]

Modified Fatigue Impact Scale (MFIS): The MFIS assesses impact of fatigue on performance of functional activities and consists of 21-items in three-sub-scales (physical, cognitive and psychosocial). Total scores range from 0 to 84 with a score of 30 or more signifying a fatigued individual. It has been validated in people with multiple sclerosis and traumatic brain injury.[36 37]

12-item World Health Organisation Disability Assessment Schedule 2.0 (12-item WHO DAS 2.0): This assesses disability and functioning in the prior month on six adult life tasks. There are twelve-items scored from 0=no difficulty to 4=extreme difficulty, total score 0 to 48 with higher scores indicating greater difficulty. Used extensively to research rehabilitation and disability in a wide range of disease populations[38] and validated in patients with chronic diseases[39] including traumatic brain injury.[40]

REHPA scale: A linear analogue self-assessment scale, where participants indicate how close they are to living the life they desire after their OHCA, indicating rehabilitation need. The scale is rated between 0 (goal reached) to 9 (infinitely far from).

Questions on unmet rehabilitation needs have been adapted from the Danish Cancer Society questionnaire 'The experiences of cancer patients during diagnosis and treatment'.[41 42]. Participants are asked if they received the help they needed after their cardiac arrest in six areas: emotional reactions, cognitive problems, physical activity, peer-support and family (supplementary data). Questions on unmet information needs after cardiac arrest were adapted from a questionnaire evaluating experiences of healthcare quality in Denmark among patients with heart disease.[43]

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Participants are asked if they felt informed after their cardiac arrest on seven subjects: treatment of heart condition, medication for heart condition, emotional reaction, cognitive problems, physical activity, return-to-work and impact on family.

In addition to the HADS, the relatives' survey includes:

World Health Organisation Five Well-Being Index: The WHO-5 is a self-report measure of current mental well-being[44] that has been shown to be a valid tool across a wide range of study fields.[45] The tool consists of five statements with six responses on a scale from 'At no time' to 'All of the time' scoring 0-5. Scores are totaled and multiplied by 4 with 0 representing the worst imaginable well-being and 100 representing the best imaginable well-being. The WHO-5 was chosen as a generic global measure of health for the survey, as opposed to using the EQ-5D-5L as in the OHCA survivor survey. This choice was based on feedback from a PPI workshop asking relatives to fill-in and provide feedback on individual questionnaires. The relatives felt the EQ-5D-5L was about medical problems and was for their relative (who had suffered the OHCA) to complete and they were unsure how to answer the questions. Conversely, they understood why the WHO-5 might be relevant to their life situation and felt able to complete it.

The Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest (IQCODE-CA): This is a modified version of the observer-reported questionnaire designed to measure global cognitive decline in the dementia population.[46] Informants, defined as relatives or close friends are requested to compare current cognitive function of the survivor with pre-cardiac arrest cognitive function. The tool contains 26-items scored on a five-point scale with higher scores indicating greater impairment. It has been shown to identify cardiac arrest survivors with possible cognitive problems.[46]

Modified caregiver strain index (MCSI): This is a self-reported questionnaire that screens for caregiver strain in caregivers.[47] The tool has 13 questions scoring 2 points for 'yes', 1 point for 'sometimes' and 0 for 'no'. Scores range from 26-0 with higher scores indicating a higher level of caregiver strain. The MCSI has been found to be easily administered and a reliable test of strain in an informal caregiver population.[47]

Further, one question derived from the Danish National Health Survey 2017[48] on loneliness and four questions on support received in the post-cardiac arrest period (created for this survey, supplementary data). Seven questions on educational level, labour market status and sick leave are also asked in the relatives section as their survey answers can only be connected to Danish labour

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market registry data if relatives choose to provide their Danish personal identification number in their survey response.

Data enrichment from registries

Following data collection via the two surveys, data enrichment will occur via Danish national registries for both survivors and relatives. The Danish Civil Registration System will provide gender, age and marital status. The Danish Education Register:[49] education level and the Danish Register on personal income[50]: income.

The Danish National Patient Register,[51] provides data on 19 selected somatic co-morbidities scored on a 3-point scale. This data will be used to calculate the Charlson Comorbidity Index,[52] based on the 10 years previous to the date of the surveys. The Charlson Comorbidity Index has three categories: 0, 1-2 and ≥3. This registry will also provide data on hospital admissions and healthcare use for the potential sub-study on societal costs after surviving OHCA.

Current and pre-OHCA employment status for the working-age population will be obtained from the Danish Register for Evaluation of Marginalization.(DREAM)[53] Participants who are not on any social benefits or participants who are on State Education Fund grants, maternity leave pay, or leave-of-absence schemes will be classified as being part of the workforce.[54] Accordingly, patients receiving unemployment benefits, being on paid sick leave, on early retirement payment or disability pension will be defined as being on social benefits. Pre-OHCA employment status will be assessed in a 5-week span before cardiac arrest to classify patients as either working or receiving social benefits.

Information from the DHRCA and other national registries will be collected for all eligible study participants both responders and non-responders to the survey (figure 1).

Data handling and record-keeping

The study has been registered on the Region of Southern Denmark's record of data processing activities (19/8559). A license agreement has been made with Odense Patient Data Explorative Network (OPEN) (OP_843) to establish the REDCap system, secure data storage, data analysis and data linkage with national registries. REDCap will be used to import Danish personal identification numbers for survey distribution via E-boks. Postal surveys received will be scanned, and the data imported into REDCap and destroyed.

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Sample size considerations

Each year approximately 800 people are alive 30-days after surviving an OHCA in Denmark.[3] Hence, we estimate the survey could be sent to approximately n=3200 survivors. Based on similar studies in heart diseases,[17 55] we are assuming a 20% (n=640) loss due to a person having moved out of Denmark, being protected from inquiries or having died,[16] and a response rate of 60%. Hence, the estimated total study population would be approximately n= 1540 OHCA survivors. The response rate to the relatives' survey is likely to be less as not all survivors will have a relative able to complete the survey. Hence, estimated 50% (1200) of relatives will respond and 50% (600) of responders will provide Danish personal identification numbers.

Planned analysis

Continuous data will be checked for normality and described as mean and standard deviation (SD) or median with 25th and 75th quartiles [IQR, interquartile range], as appropriate. Categorical variables will be described as numbers and percentages (n (%)). To investigate changes in physical and psychological outcomes over time, participants will be stratified into four groups: those suffering an OHCA in 2016, 2017, 2018 and 2019 (figure 2). Differences in the prevalence of self-report problems between the groups will be determined by Chi-squared test or Fisher's Exact test as appropriate and time-trend analyses will be performed. The OHCA survivor and relatives' surveys will be linked via a unique identifying number to discover if associations exist between each groups' self-report outcomes.

Predictors of physical and psychological problems will be identified from self-report outcomes, demographic characteristics, circumstances of OHCA and unmet rehabilitation/information needs using univariate binary logistic regression. All univariate predictors with p<0.10 will be entered into a multivariate binary logistic regression, with description of odds ratios or β and 95% confidence intervals. In all regression analyses, both crude and adjusted models will be presented. Level of statistical significance will be set at p<0.05.

A potential sub-study is planned to calculate the total societal costs (healthcare costs and absenteeism from work) of surviving OHCA using the EQ-5D-5L data and registry data (National Prescription Registry,[56] and DREAM database).

Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been

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confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Participants will be informed about the study via the participant information sheet. Consent to participate will be implied through the return of the completed survey.

Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences. The results of the proposed study will be reported with reference to the international statement in the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist for cross-sectional studies[57]. Health professionals will be informed of the study results through professional literature via new national clinical guidelines on rehabilitation after OHCA. Finally, the survey is part of a larger project on rehabilitation after surviving a cardiac arrest and all results, including the survey results, will be presented at a project-closing event to which all participants, stakeholders and interested parties will be invited.

Patient and public involvement

The themes for the survey were developed from a PPI event involving OHCA survivors, relatives and clinicians.[29] A further group of survivors and relatives have helped to develop the survey by testing individual questionnaires and by providing feedback on the whole survey. At the end of the study, the research advisory group and PPI group will discuss and comment on the findings and contribute to how the results will be disseminated and implemented in the next stage of the research.

Discussion

Recovery after OHCA can be complicated by a new or ongoing cardiac condition, mental trauma from surviving a near-death experience or possible anoxic brain injury. Small scale, short term studies suggest these complications can lead to an increased physical and psychological burden for both survivors and their relatives. However, little is known about the long-term prevalence of physical and psychological problems or who is at most risk of developing them. Rehabilitation has been recommended to meet the secondary physical and psychological consequences of OHCA but more knowledge is needed including establishing the perceived unmet rehabilitation and information needs from OHCA survivors and their relatives themselves.

The results from this study will be used to identify the most prevalent problems suffered by OHCA survivors and their families and those at most risk of suffering them. This will allow researchers and managers within the Danish healthcare system to design assessment tools to ensure problems are detected early after OHCA, and survivors and relatives are offered rehabilitation plans tailored to

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their needs. Further, currently there are few high quality studies investigating the effectiveness of rehabilitation interventions for OHCA survivors. Results from the DANCAS survey will provide researchers with specific information to design the content and timing of new rehabilitation interventions for OHCA survivors and their relatives.

Although this study will be one of the largest surveys involving OHCA survivors and one of the first to survey both survivors and relatives, with the ability to link between the two, there are several potential limitations. The majority of the self-report questionnaires have undergone some validation testing. However, not all these tools have been validated in Danish or in the OHCA survivor population and some questions have been written specifically for this survey (see supplementary data).

The survey uses questionnaires based on self-report. However, approximately 50% of OHCA survivors suffer from cognitive deficits and/or fatigue, leading to difficulties completing the survey and hence potentially a lower response rate from survivors with these problems. To counter this, the survey will available both electronically and on paper, survivors will be allowed to have help to complete the survey and asked to state if they had help. In addition, the relatives' section of the survey will include an observer-reported cognitive questionnaire and relatives will be asked to complete this even if the survivor questionnaire is not completed. However, it remains possible that those with cognitive deficits and/or fatigue will be underrepresented in the survey response group and this has to be accepted as a limitation of the self-report method chosen to gain data from as many OHCA survivors as possible. Surveys will only be received by OHCA survivors able to access e-Boks or living at home, so we are very unlikely to receive responses from any survivor living in long-term residential care. Further, the DHRCA only records OHCA and therefore people who have suffered an in-hospital cardiac arrest will not be included in this study. To ensure the characteristics of the survey population are clear, baseline characteristics of non-responders will also be presented.

One aim of the survey is to describe how the prevalence of physical and psychological problems suffered by survivors and their relatives changes over time since OHCA. Ideally, this would be investigated using a prospective longitudinal study with data from the same population at multiple follow-up points. The disadvantage of this design is the results would not be available for five-years, and participants are asked to complete multiple surveys. The design of our survey groups participants dependent on time since OHCA to describe changes over time. However, as these are not the same participants in each time interval group, there is a risk of an unknown time-dependent confounding factor effecting one of the groups more than another. Further, the cross-sectional

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design, by definition, does not allow the formation of solid conclusions but the generation of hypotheses based on associations between variables.

Author contributions VJ, LHT and ADZ conceived the study; VJ and LHT designed the study with ADZ, BB, LZ, TMB, RS, SRC and JFN. VJ led the writing of the manuscript, which was revised by all authors. The final manuscript was approved by all authors.

Competing interests None declared

Patient consent Not required

Data statement: Within the boundaries of Danish legislation, the anonymised data from the study will be available for other researchers upon reasonable request when the results have been published.

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Figure legends:

Figure 1. Flow chart of Survey Population

Figure 2. Design of DANCAS survey and grouping according to time since OHCA

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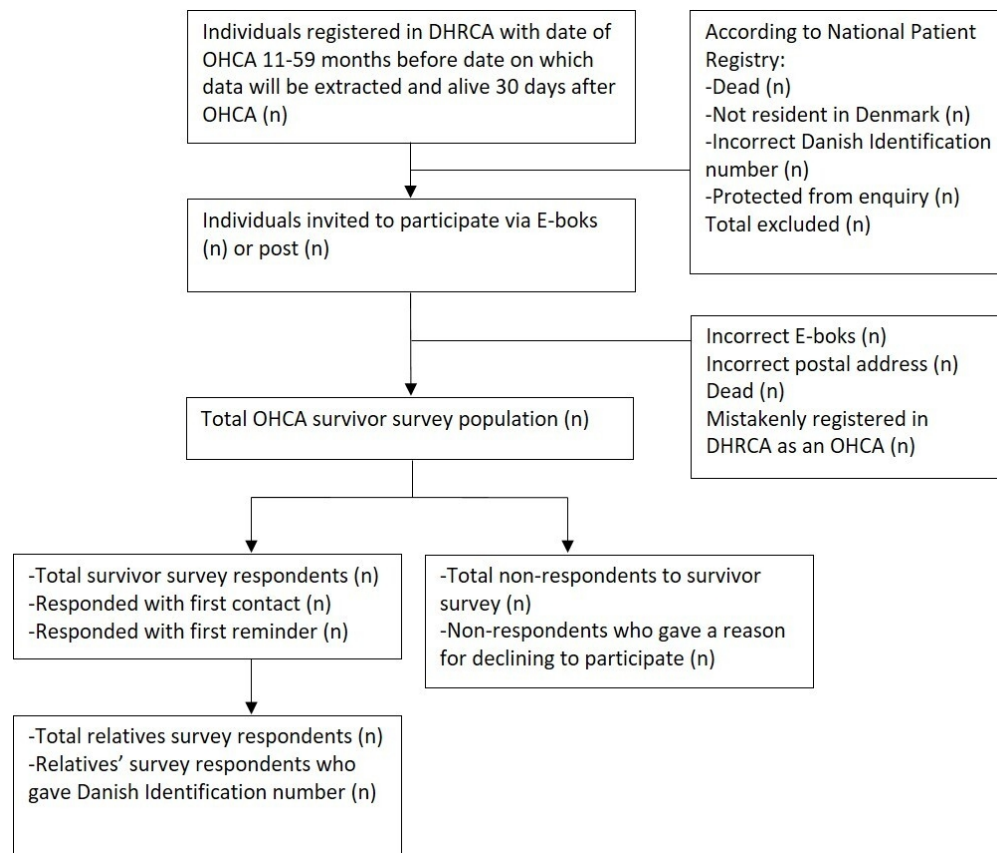
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Figure 1. Flow chart of Survey Population
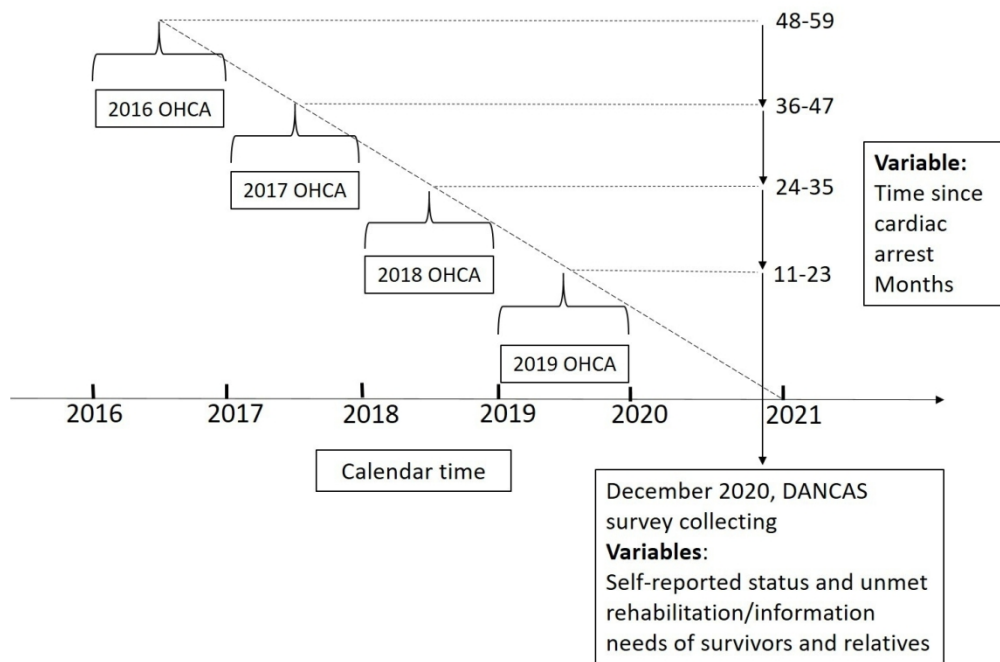
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Figure 2. Design of DANCAS survey and grouping according to time since OHCA

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Supplementary data.

Table 1. Detailed content of DANCAS surveys

Outcome domain	Outcome measure	Items, scoring	Danish translation	Notes
Survivors				
Generic health	EQ-5D-5L	Five item health dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Divided into five levels: 1='No problems' to 5= 'Extreme problems', scores ≥ 2 signifies a problem. Sixth item: Self-rating of health. Visual Analogue Scale, 0-100. Higher scores signify better health status.[1]	Received from the EuroQoL group	
Anxiety and depression	HADS	Seven-item symptoms of anxiety subscale (HADS-A) Seven-item subscale symptoms of depression (HADS-D). Four responses: 0='No symptoms' to 3= 'maximum number of symptoms'. Total subscale scores range: 0-21. <8 = no psychological distress, 8-10 = mild psychological distress, >10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[2]	Received from DenHeart study group[3]	Valid measure of anxiety and depression in Danish cardiac disease population[3]

Mental recovery/dependency	TSQ	Yes to Q1a + Yes to Q1b signify new problems with dependency after cardiac arrest. No to Q2 indicates problems with mental recovery after cardiac arrest.[4 5]	Received from TTM2 study group[4]	-
Fatigue impact on functional activities	MFIS	21 items in three sub-scales (physical, cognitive and psychosocial). Total scores range: 0-84. Total subscale scores: physical= 0 -36; cognitive=0=40; psychosocial= 0-8. ≥30 signify a fatigued individual (Antmann, 2012, Schiehser, 2015)	Translation received from e Provide, Mapi Research Trust.	Validated in people with multiple sclerosis.[6] and mild to moderate brain injury.[7]
Function and disability	12-item WHO DAS 2.0	12-item assessing 6 domains of functioning: 1) Understanding and communication; 2) Self-care; 3) Mobility; 4) Interpersonal relationships; 5) Work and household roles; and 6) Community and civic roles. Scored from 0= 'no difficulty' to 4= 'extreme difficulty or cannot do'. Total scores range: 0-48. Higher score indicating greater difficulty with activity and participation.	Available from:https://www w.etf.dk/ergotera pi-og-politik/hverdagsr ehabilitering	Used extensively to research neurological conditions including traumatic brain injury and spinal cord injury,[8] and rehabilitation and disability in a wide range of disease populations.[9] Validated in patients with chronic diseases.[10]
Life satisfaction/rehabilitat ion need	REHPA scale	A linear analogue scale, participants indicate how close they are to living the life they desire after their OHCA. Scale ranges from 0= 'goal reached' to 9= 'infinitely far from'.	By DANCAS study authors	

		Score of ≤3 will be considered as signifying having rehabilitation needs.		
Unmet rehabilitation needs		6-items asking if rehabilitation needs were met in different domains, for example, emotional reactions. Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[12]	Adapted by DANCAS authors	Questions adapted from existing survey 'The Experience of Cancer Patients during Diagnosis and Treatment'.[12 13]
Unmet information needs	Adapted from Zinckernagel et al., 2017	7-items asking if information needs were met in different domains, for example, 'treatment of your heart condition' Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[14]	Adapted by DANCAS authors for OHCA survivors from a Danish survey of patients with heart disease.[14]	
Relatives				
Anxiety and depression	HADS	As above		
Mental well-being	WHO-5	Five items with 6 responses from 0='At no time' to 5='all of the time'. Scores are totaled and multiplied by 4 to give range 0-100. Score <50 signifies poor emotional well-being.[15]	Developed in Denmark.[16]	Valid in multiple patient populations.[17]

Cognitive problems in daily life	IQCODE-CA	26-items scored on a five-point scale, 1= 'much improved' to 5= 'much worse'. Scores are totaled, divided by the number of questions to give a total, range 1-5. Score ≥3.04 signifies cognitive decline after cardiac arrest.[18]	Received from TTM2 study group	Relatives or close friends compare current cognitive function with pre-cardiac arrest cognitive function. Has been shown to accurately identify cardiac arrest survivors with potential cognitive problems.[18]
Caregiver strain	MCSI	13-items, scored: 2= 'Yes, On a Regular Basis', 1= 'Yes, sometimes', 0= 'No'. Range: 0-26, higher scores signify a higher level of carer strain.[19]	Translated by DANCAS study authors[a]	Found to have high internal validity with a population of family caregivers.[19]
Witness to OHCA	Questions designed for this survey	1-item on whether they witnessed the OHCA	Created by DANCAS study authors	
Labour market	Questions designed for this survey	7-items on educational level completed, current labour market status, status in pre-OHCA period and details of any sick leave in post-OHCA period.	Created by DANCAS study authors	These questions are asked of the relatives as their survey answers cannot be connected to Danish labour market registry data unless they provide their Danish personal identification number.
Social isolation	Question from Danish national health survey	One item: Does it ever happen that you are alone even though you would prefer to be with other people?"	Available at: http://www.dans kernessundhed.d k/Spoergeskema	

		Answers: "yes, often" and "yes, sometimes" signify loneliness. Other possible responses are "yes, but rarely" and "no.		
Support received post-OHCA	Questions designed for this survey	4-items on: whether relatives feel they have someone to talk to if they need support (yes, always/yes, mostly/yes, sometimes/no never or almost never); who have they received support from (multiple options); if they received the support they needed (Yes, No), and who would they have like to have received support from in the post-OHCA period (free text box).	Created by DANCAS study authors	

Abbreviations: HADS= Hospital Anxiety and Depression Scale; TSQ=Two Simple Questions; TTM2= Targeted Hypothermia versus Targeted Normothermia after OHCA trial 2; MFIS: Modified Fatigue Impact Scale, WHO DAS 2.0= World Health Organisation disability assessment schedule 2.0 Short; REHPA= Danish Knowledge Center for Rehabilitation and Palliative Care; OHCA=Out-of-hospital Cardiac Arrest; DANCAS=DANish Cardiac Arrest Survivorship; WHO-5= World Health Organisation-Five Well-Being index; IQCODE-CA: Informant Questionnaire on Cognitive Decline in the Elderly, Cardiac Arrest Version; MCSI= Modified Carer Strain Index.

aTranslation, cultural adaption and psychometric testing performed by study authors, results are planned to be available in a future publication.

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Long-term physical and psychological outcomes after out-of-hospital cardiac arrest– Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS survey)

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Long-term physical and psychological outcomes after out-of-hospital cardiac arrest– Protocol for a national cross-sectional survey of survivors and their relatives (the DANCAS survey)

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Word count manuscript: 3908

Key words: Out-of-hospital cardiac arrest survivor, relatives of out-of-hospital cardiac arrest survivors, cross-sectional survey, self-report.

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ABSTRACT

Introduction

The number of out-of-hospital cardiac arrest (OHCA) survivors is increasing. However, there remains limited knowledge on the long-term physical and psychological problems suffered by survivors and their relatives. The aims of the DANCAS (DANish cardiac arrest survivorship) survey are to describe the prevalence of physical and psychological problems, identify predictors associated with suffering them and to determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions.

Methods and analysis

The DANCAS survey has a cross-sectional design involving a survey of OHCA survivors and their relatives. OHCA survivors will be identified through the Danish Cardiac Arrest Registry as having suffered an OHCA between 1st January 2016 and 31st December 2019. Each survivor will be asked to identify their closest relative to complete the relatives' survey. Contents of survivor survey: EQ-5D-5L, Hospital Anxiety and Depression Scale, Two Simple Questions, Modified Fatigue Impact Scale, 12-item World Health Organisation Disability Assessment Scale 2.0, plus questions on unmet rehabilitation and information needs. Contents of relatives' survey: World Health Organisation-Five Well-Being Index, Hospital Anxiety and Depression Scale, Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest and the Modified Caregiver Strain Index. Self-report outcome data collected through the surveys will be enriched by data from Danish national registries including: demographic characteristics, circumstances of cardiac arrest and co-morbidities. The survey will be completed either electronically or by post December 2020-February 2021.

Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences.

Article Summary

Strengths and limitations of this study:

-Denmark has markedly improved the survival rate among OHCA survivors during the last five years.

-This will be one of the largest nationwide surveys of OHCA survivors to date with data collected from survivors and relatives up to five-years after cardiac arrest.

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-Data will be derived from both self-report measures and national registries providing a comprehensive picture of the problems experienced by OHCA survivors and the risk factors associated with suffering them.

-The response rate from OHCA survivors suffering from cognitive problems and/or fatigue may be lower due to difficulties completing the survey compared to those without these problems to counter this the survey will be available both electronically and on paper.

-The change in physical and psychological problems over time may be influenced by a treatment cohort effect and other unknown time-dependent modifying factors.

INTRODUCTION

The number of people surviving an out-of-hospital cardiac arrest (OHCA) is increasing every year due to advances in pre-hospital and acute medical care.[1 2] In Denmark, thirty-day survival after OHCA improved from 4% to 16% between 2001 and 2018.[3] This amounts to at least 800 new survivors every year.[3] Still, after the acute phase ends, the physical and psychological impact of OHCA may continue.[4] Most OHCA survivors will have a new or ongoing cardiac condition.[5 6] They may suffer from psychological trauma due to surviving a near-death experience.[7] Further, reduced oxygen levels to the brain during an OHCA can cause cognitive deficits in up to 50% of survivors.[8-10] Due to this combination of factors, OHCA survivors have been shown to suffer anxiety and depression, fatigue and reduced participation in society.[7 8 11 12] General health, return-to-work rates and quality of life do, however, appear to improve over time[13-15] but data regarding: health measures, return-to-work patterns and unmet rehabilitation needs beyond 12-months after OHCA are limited.[7 11 14 16 17]

As most OHCA occur in private homes, relatives are likely to witness the event.[18] Combined with the changes in both physical and psychological status of many OHCA survivors, quality of life and psychological health among relatives might be influenced. It has previously been described how relatives of OHCA survivors suffer from emotional problems including anxiety, depression and post-traumatic stress, due to becoming a carer for their loved one or fear of the cardiac arrest reocurring.[19 20] Likewise, lack of control, feelings of insecurity, mood and sleep disturbances have been reported among relatives.[21 22] Yet, very few research studies have investigated the consequences of OHCA for relatives in the longer term,[23 24] or how these are associated with witnessing the event or with the physical, psychological problems suffered by the OCHA survivor.

Rehabilitation for OHCA survivors is recommended in international guidelines[4 25] but the specific content and timing of these interventions has not been established. Survivors will commonly be

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offered cardiac rehabilitation related to their new or ongoing cardiac condition,[4 26] but it has been suggested that the psychological and neurological rehabilitation needs of OHCA are not met to the same degree.[27] Hence, the aims of this national cross-sectional study are to 1) describe the long-term prevalence of physical and psychological problems for OHCA survivors and their relatives and how these change over time 2) identify predictors associated with increased risk of suffering these problems and 3) determine unmet rehabilitation needs in order to make recommendations on the timing and content of future rehabilitation interventions. Specific objectives for each aim will be defined in future publications.

METHODS AND ANALYSIS

Study design

The DANCAS (DANish Cardiac Arrest Survivorship) survey aims will be achieved through a cross-sectional study design.

Setting and participants

In Denmark, pre-hospital care, hospital care and all cardiac treatment and rehabilitation are funded via the tax system and are free of charge for patients. The Danish Out-of-Hospital Cardiac Arrest (DHRCA) registry will be used to identify the Danish personal identification numbers of people who have suffered an OHCA from 1st January 2016 to 31st December 2019 and were alive 30-days after their cardiac arrest (figure 1). All patients in Denmark who have suffered an OHCA, where bystanders or paramedics attempted treatment are included in the DHRCA registry. Data is recorded electronically immediately after the OHCA in the pre-hospital patient record by paramedics from one of the five regional ambulance services and collected in the DHRCA. The DHRCA collects data on OHCA in Denmark for the purposes of quality improvement. The pre-hospital managers of the five Danish regions are responsible for collecting the data, have ownership of their own data, and give approval for data access on behalf of OHCA survivors. Access to DHRCA data is granted via approval of a research protocol by the DHRCA steering group.

The DHRCA started collecting data in 2001, however, before 2016, this was recorded by hand on paper and hence significant gaps in the data exist[3]. In addition, pre-hospital and medical management of OHCA has changed significantly in the period 2001-2015.[28] Consequently, the proposed timeframe of 1-5 years since OHCA provides both a long-term perspective and ensures data is relevant to the contemporary OHCA survivor population.

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The extracted Danish personal identification numbers will be matched by the Danish National Health Digital Board to names, and addresses in the Danish National Patient Registry retrieve.

The information letter received by the OHCA survivors will ask them to identify their closest relative and ask them to complete the relatives' survey. This method of recruitment has been tested in the development of the survey and is feasible. Closest relative is defined as a partner, spouse, sibling, or parent that is closest to the survivor.

Eligibility criteria

OHCA survivor participants included in the survey will have a Danish personal identification number, be alive at least 30-days post-cardiac arrest, resident in Denmark, over 18-years of age and able to read and write in Danish and not protected from receiving inquiries during scientific surveys.

Relative participants must have a relative who has survived an OHCA, be over 18 years of age and be able to read and write in Danish. The relatives do not need to have a Danish personal identification number, as they will be invited to complete their survey via the information letter to the OHCA survivor participants. However, they will be asked to provide their Danish personal identification number to allow linkage with Danish national registries.

Data collection

All OHCA survivor participants that meet the eligibility criteria will receive an invitation to participate in the survey via REDCap (Research Electronic Data Capture) software to their e-Boks (government electronic mail account) or via post if they do not have an E-boks address. Based on the age profile of OHCA survivors over the last 5-years and the age-profile of Danes with e-Boks addresses it is estimated that 20% of participants will require a postal survey.

The link to complete the separate relatives' survey will be included in the invitation sent to the OHCA survivors' eBoks. Invitations sent via post to the OHCA survivor will include a paper copy of both surveys, two stamped addressed envelopes (for survivor and relative) and information on how to complete the surveys online rather than by post if they wish. A participant information sheet will be included with all invitations to participate in the survey. This will detail the purpose of the research study, how data will be used and will explain that by returning the survey, they are consenting to take part. The information sheet will include a telephone number to call a member of the research team if participants have any questions. Participants who receive the E-boks survey will

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have the option to request a paper survey by post. A reminder invitation will be sent via E-boks/post after two-weeks.

Additional data from the DHRCA will provide information on circumstances of the OHCA (Table 1).

Table. 1 Data on circumstances of OHCA from DHRCA

Table. 1 Data on circumstances of OHCA from DHRCA
Location of cardiac arrest (Private/public)
First observed heart rhythm (shockable/not shockable)
Cardiopulmonary resuscitation was given before the arrival of the ambulance (Yes/No)
Defibrillated before the arrival of the ambulance (Yes/No)
Time to return of spontaneous circulation (minutes: second)

Development of the DANCAS surveys

The outcome domains for the two DANCAS surveys were developed from a public and patient involvement (PPI) event held in Denmark[29] (see PPI section below) and from the outcomes identified as important by participants in the COSCA (core outcome set for cardiac arrest) initiative.[30] For each of these outcome domains, appropriate existing self-report outcome measures were chosen. For domains where no outcome measure existed, questions from other patient groups were adapted for OHCA survivors or new questions were developed.

The PPI group participants tested individual outcome measures for acceptability and face validity where there was more than one outcome measure available (for example, in the domain 'function and disability'). The PPI group also gave feedback on draft versions of the whole DANCAS surveys, and the participant information sheet. Feedback was received from eight survivors, three relatives, and three clinicians with experience of treating OHCA survivors and relatives. Based on this feedback, we reduced the number of questions, removed any outcome measures where the item content overlapped and improved the clarity of the participation information sheet.

Self-report outcome measures in the DANCAS surveys

Full details on the self-report outcome measures, scoring, and Danish translations can be found in the Supplementary data.

The following self-report outcome measures will be completed by OHCA survivors:

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EQ-5D-5L: This is a six-item standardised instrument for measuring current health status.[31] The questionnaire covers five-dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into five-levels: no problems, slight, moderate, severe or extreme problems. The sixth-item, a Visual Analogue Scale, 0-100, allows the respondent to provide a self-rating of his or her health. A higher score signifies a better health status.

Hospital Anxiety and Depression Scale (HADS): The HADS consists of a seven-item subscale measuring symptoms of anxiety (HADS-A) and a seven-item subscale measuring symptoms of depression (HADS-D).[32] Each item has a four-choice response, with scores ranging from 0 (no symptoms) to 3 (maximum number of symptoms). The total scores on each subscale range from 0 to 21. A score of less than 8 indicates no psychological distress, 8 to 10 mild psychological distress and over 10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[33]

Two Simple Questions (TSQ): Consists of three-items. Developed to assess the survivor's own perception of mental recovery and dependency in daily activities after cardiac arrest.[34 35]

Modified Fatigue Impact Scale (MFIS): The MFIS assesses impact of fatigue on performance of functional activities and consists of 21-items in three-sub-scales (physical, cognitive and psychosocial). Total scores range from 0 to 84 with a score of 30 or more signifying a fatigued individual. It has been validated in people with multiple sclerosis and traumatic brain injury.[36 37]

12-item World Health Organisation Disability Assessment Schedule 2.0 (12-item WHO DAS 2.0): This assesses disability and functioning in the prior month on six adult life tasks. There are twelve-items scored from 0=no difficulty to 4=extreme difficulty, total score 0 to 48 with higher scores indicating greater difficulty. Used extensively to research rehabilitation and disability in a wide range of disease populations[38] and validated in patients with chronic diseases[39] including traumatic brain injury.[40]

REHPA scale: A linear analogue self-assessment scale, where participants indicate how close they are to living the life they desire after their OHCA, indicating rehabilitation need. The scale is rated between 0 (goal reached) to 9 (infinitely far from).

Questions on unmet rehabilitation needs have been adapted from the Danish Cancer Society questionnaire 'The experiences of cancer patients during diagnosis and treatment'.[41 42]. Participants are asked if they received the help they needed after their cardiac arrest in six areas: emotional

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reactions, cognitive problems, physical activity, peer-support and family (supplementary data). Questions on unmet information needs after cardiac arrest were adapted from a questionnaire evaluating experiences of healthcare quality in Denmark among patients with heart disease.[43] Participants are asked if they felt informed after their cardiac arrest on seven subjects: treatment of heart condition, medication for heart condition, emotional reaction, cognitive problems, physical activity, return-to-work and impact on family.

In addition to the HADS, the relatives' survey includes:

World Health Organisation Five Well-Being Index: The WHO-5 is a self-report measure of current mental well-being[44] that has been shown to be a valid tool across a wide range of study fields.[45] The tool consists of five statements with six responses on a scale from 'At no time' to 'All of the time' scoring 0-5. Scores are totaled and multiplied by 4 with 0 representing the worst imaginable well-being and 100 representing the best imaginable well-being. The WHO-5 was chosen as a generic global measure of health for the survey, as opposed to using the EQ-5D-5L as in the OHCA survivor survey. This choice was based on feedback from a PPI workshop asking relatives to fill-in and provide feedback on individual questionnaires. The relatives felt the EQ-5D-5L was about medical problems and was for their relative (who had suffered the OHCA) to complete and they were unsure how to answer the questions. Conversely, they understood why the WHO-5 might be relevant to their life situation and felt able to complete it.

The Informant Questionnaire on Cognitive Decline in the Elderly – Cardiac Arrest (IQCODE-CA): This is a modified version of the observer-reported questionnaire designed to measure global cognitive decline in the dementia population.[46] Informants, defined as relatives or close friends are requested to compare current cognitive function of the survivor with pre-cardiac arrest cognitive function. The tool contains 26-items scored on a five-point scale with higher scores indicating greater impairment. It has been shown to identify cardiac arrest survivors with possible cognitive problems.[46]

Modified caregiver strain index (MCSI): This is a self-reported questionnaire that screens for caregiver strain in caregivers.[47] The tool has 13 questions scoring 2 points for 'yes', 1 point for 'sometimes' and 0 for 'no'. Scores range from 26-0 with higher scores indicating a higher level of caregiver strain. The MCSI has been found to be easily administered and a reliable test of strain in an informal caregiver population.[47]

Further, one question derived from the Danish National Health Survey 2017[48] on loneliness and four questions on support received in the post-cardiac arrest period (created for this survey,

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supplementary data). Seven questions on educational level, labour market status and sick leave are also asked in the relatives section as their survey answers can only be connected to Danish labour market registry data if relatives choose to provide their Danish personal identification number in their survey response. One question will ask if they witnessed the OHCA.

Data enrichment from registries

Following data collection via the two surveys, data enrichment will occur via Danish national registries for both survivors and relatives. The Danish Civil Registration System will provide gender, age and marital status. The Danish Education Register:[49] education level and the Danish Register on personal income[50]: income.

The Danish National Patient Register,[51] provides data on 19 selected somatic co-morbidities scored on a 3-point scale. This data will be used to calculate the Charlson Comorbidity Index,[52] based on the 10 years previous to the date of the surveys. The Charlson Comorbidity Index has three categories: 0, 1-2 and ≥3. This registry will also provide data on hospital admissions and healthcare use for the potential sub-study on societal costs after surviving OHCA.

Current and pre-OHCA employment status for the working-age population will be obtained from the Danish Register for Evaluation of Marginalization.(DREAM)[53] Participants who are not on any social benefits or participants who are on State Education Fund grants, maternity leave pay, or leave-of-absence schemes will be classified as being part of the workforce.[54] Accordingly, patients receiving unemployment benefits, being on paid sick leave, on early retirement payment or disability pension will be defined as being on social benefits. Pre-OHCA employment status will be assessed in a 5-week span before cardiac arrest to classify patients as either working or receiving social benefits.

Information from the DHRCA and other national registries will be collected for all eligible study participants both responders and non-responders to the survey (figure 1).

Data handling and record-keeping

The study has been registered on the Region of Southern Denmark's record of data processing activities (19/8559). A license agreement has been made with Odense Patient Data Explorative Network (OPEN) (OP_843) to establish the REDCap system, secure data storage, data analysis and data linkage with national registries. REDCap will be used to import Danish personal identification

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numbers for survey distribution via E-boks. Postal surveys received will be scanned, and the data imported into REDCap and destroyed.

Sample size considerations

Each year approximately 800 people are alive 30-days after surviving an OHCA in Denmark.[3] Hence, we estimate the survey could be sent to approximately n=3200 survivors. Based on similar studies in heart diseases,[17 55] we are assuming a 20% (n=640) loss due to a person having moved out of Denmark, being protected from inquiries or having died,[16] and a response rate of 60%. Hence, the estimated total study population would be approximately n= 1540 OHCA survivors. The response rate to the relatives' survey is likely to be less as not all survivors will have a relative able to complete the survey. Hence, estimated 50% (770) of relatives will respond and 50% (380) of responders will provide Danish personal identification numbers.

Planned analysis

Continuous data will be checked for normality and described as mean and standard deviation (SD) or median with 25th and 75th quartiles [IQR, interquartile range], as appropriate. Categorical variables will be described as numbers and percentages (n (%)). To investigate changes in physical and psychological outcomes over time, participants will be stratified into four groups: those suffering an OHCA in 2016, 2017, 2018 and 2019 (figure 2). Differences in the prevalence of self-report problems between the groups will be determined by Chi-squared test or Fisher's Exact test as appropriate and time-trend analyses will be performed. The OHCA survivor and relatives' surveys will be linked via a unique identifying number to discover if associations exist between each groups' self-report outcomes.

Predictors of physical and psychological problems will be identified from self-report outcomes, demographic characteristics, circumstances of OHCA and unmet rehabilitation/information needs using univariate binary logistic regression. All univariate predictors with p<0.10 will be entered into a multivariate binary logistic regression, with description of odds ratios or β and 95% confidence intervals. In all regression analyses, both crude and adjusted models will be presented. Level of statistical significance will be set at p<0.05.

A potential sub-study is planned to calculate the total societal costs (healthcare costs and absenteeism from work) of surviving OHCA using the EQ-5D-5L data and registry data (National Prescription Registry,[56] and DREAM database).

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Ethics and dissemination

The study will be conducted in accordance with the Declaration of Helsinki. Surveys and registry-based research studies do not normally require ethical approval in Denmark. This has been confirmed for this study by the Region of Southern Denmark ethics committee (20192000_19). Participants will be informed about the study via the participant information sheet. Consent to participate will be implied through the return of the completed survey.

Results of the study will be disseminated via several peer-reviewed publications and will be presented at national and international conferences. The results of the proposed study will be reported with reference to the international statement in the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist for cross-sectional studies[57]. Health professionals will be informed of the study results through professional literature via new national clinical guidelines on rehabilitation after OHCA. Finally, the survey is part of a larger project on rehabilitation after surviving a cardiac arrest and all results, including the survey results, will be presented at a project-closing event to which all participants, stakeholders and interested parties will be invited.

Patient and public involvement

The themes for the survey were developed from a PPI event involving OHCA survivors, relatives and clinicians.[29] A further group of survivors and relatives have helped to develop the survey by testing individual questionnaires and by providing feedback on the whole survey. At the end of the study, the research advisory group and PPI group will discuss and comment on the findings and contribute to how the results will be disseminated and implemented in the next stage of the research.

Discussion

Recovery after OHCA can be complicated by a new or ongoing cardiac condition, mental trauma from surviving a near-death experience or possible anoxic brain injury. Small scale, short term studies suggest these complications can lead to an increased physical and psychological burden for both survivors and their relatives. However, little is known about the long-term prevalence of physical and psychological problems or who is at most risk of developing them. Rehabilitation has been recommended to meet the secondary physical and psychological consequences of OHCA but more knowledge is needed including establishing the perceived unmet rehabilitation and information needs from OHCA survivors and their relatives themselves.

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The results from this study will be used to identify the most prevalent problems suffered by OHCA survivors and their families and those at most risk of suffering them. This will allow researchers and managers within the Danish healthcare system to design assessment tools to ensure problems are detected early after OHCA, and survivors and relatives are offered rehabilitation plans tailored to their needs. Further, currently there are few high quality studies investigating the effectiveness of rehabilitation interventions for OHCA survivors. Results from the DANCAS survey will provide researchers with specific information to design the content and timing of new rehabilitation interventions for OHCA survivors and their relatives.

Although this study will be one of the largest surveys involving OHCA survivors and one of the first to survey both survivors and relatives, with the ability to link between the two, there are several potential limitations. The majority of the self-report questionnaires have undergone some validation testing. However, not all these tools have been validated in Danish or in the OHCA survivor population and some questions have been written specifically for this survey (see supplementary data).

The survey uses questionnaires based on self-report. However, approximately 50% of OHCA survivors suffer from cognitive deficits and/or fatigue, leading to difficulties completing the survey and hence potentially a lower response rate from survivors with these problems. To counter this, the survey will available both electronically and on paper, survivors will be allowed to have help to complete the survey and asked to state if they had help. In addition, the relatives' section of the survey will include an observer-reported cognitive questionnaire and relatives will be asked to complete this even if the survivor questionnaire is not completed. However, it remains possible that those with cognitive deficits and/or fatigue will be underrepresented in the survey response group and this has to be accepted as a limitation of the self-report method chosen to gain data from as many OHCA survivors as possible. Surveys will only be received by OHCA survivors able to access e-Boks or living at home, so we are very unlikely to receive responses from any survivor living in long-term residential care. Further, the DHRCA only records OHCA and therefore people who have suffered an in-hospital cardiac arrest will not be included in this study. To ensure the characteristics of the survey population are clear, baseline characteristics of non-responders will also be presented.

One aim of the survey is to describe how the prevalence of physical and psychological problems suffered by survivors and their relatives changes over time since OHCA. Ideally, this would be investigated using a prospective longitudinal study with data from the same population at multiple follow-up points. The disadvantage of this design is the results would not be available for five-years,

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and participants are asked to complete multiple surveys. The design of our survey groups participants dependent on time since OHCA to describe changes over time. However, as these are not the same participants in each time interval group, there is a risk of an unknown time-dependent confounding factor effecting one of the groups more than another. Further, the cross-sectional design, by definition, does not allow the formation of solid conclusions but the generation of hypotheses based on associations between variables.

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Data statement: Within the boundaries of Danish legislation, the anonymised data from the study will be available for other researchers upon reasonable request when the results have been published.

Figure legends:

Figure 1. Flow chart of Survey Population

Figure 2. Design of DANCAS survey and grouping according to time since OHCA

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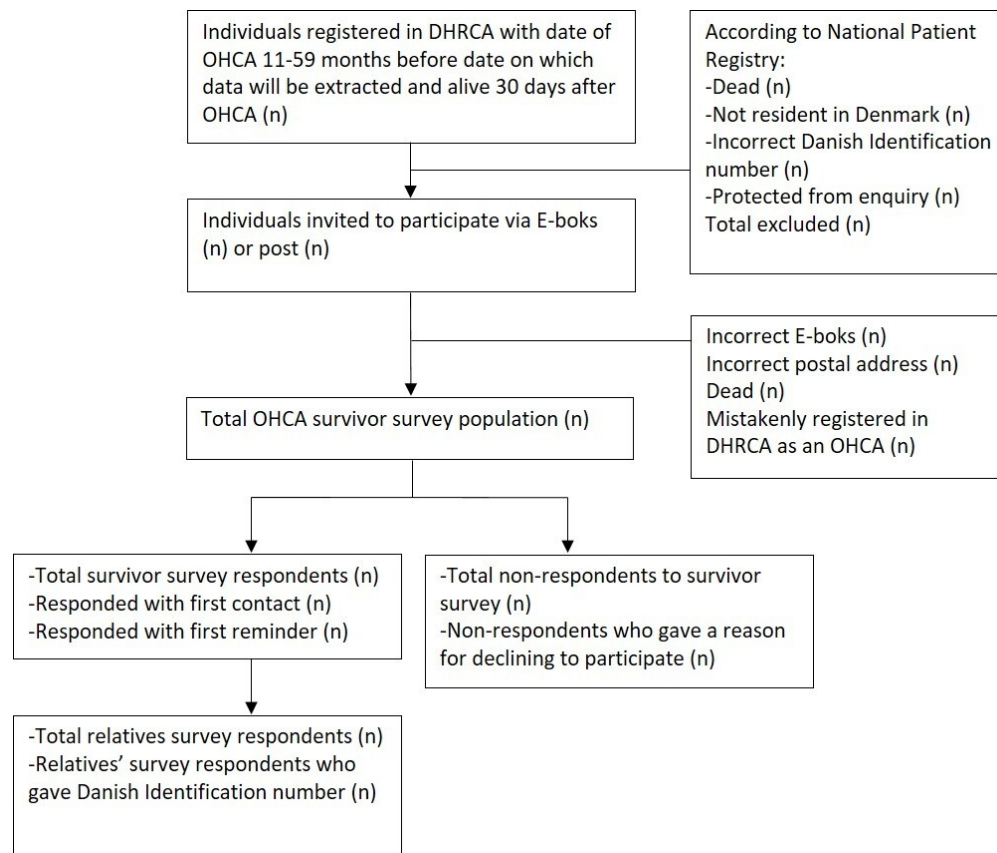
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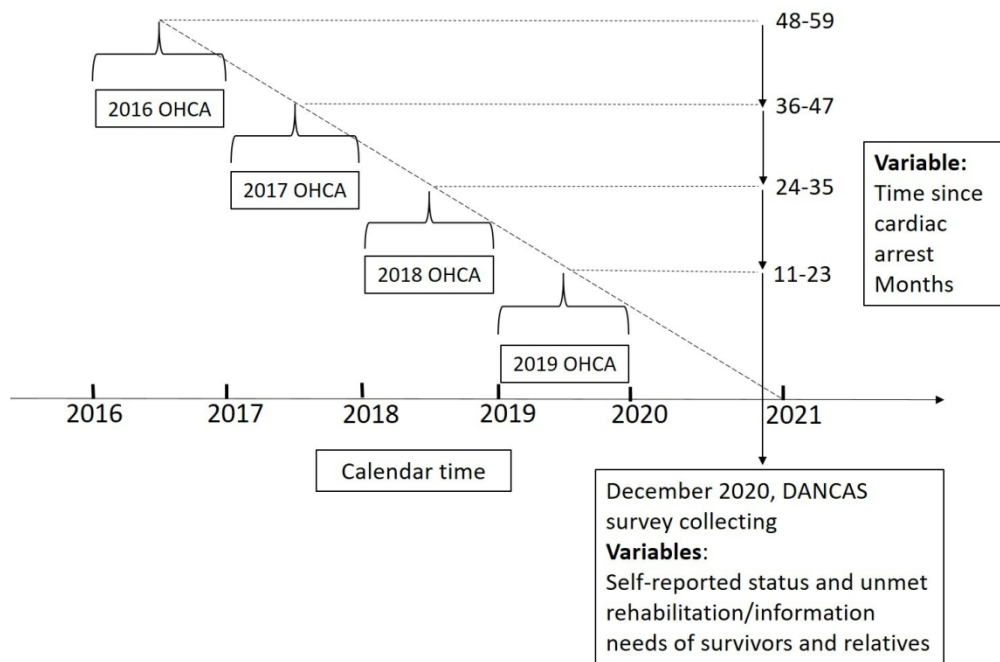Figure 1. Flow chart of Survey Population

84x71mm (300 x 300 DPI)

Figure 2. Design of DANCAS survey and grouping according to time since OHCA

125x84mm (300 x 300 DPI)

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Supplementary data.

Table 1. Detailed content of DANCAS surveys

Outcome domain	Outcome measure	Items, scoring	Danish translation	Notes
Survivors				
Generic health	EQ-5D-5L	Five item health dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Divided into five levels: 1='No problems' to 5= 'Extreme problems', scores ≥ 2 signifies a problem. Sixth item: Self-rating of health. Visual Analogue Scale, 0-100. Higher scores signify better health status.[1]	Received from the EuroQoL group	
Anxiety and depression	HADS	Seven-item symptoms of anxiety subscale (HADS-A) Seven-item subscale symptoms of depression (HADS-D). Four responses: 0='No symptoms' to 3= 'maximum number of symptoms'. Total subscale scores range: 0-21. <8 = no psychological distress, 8-10 = mild psychological distress, >10 definite psychological distress. It has recently been shown to be a valid measure of anxiety and depression in a Danish cardiac disease population.[2]	Received from DenHeart study group[3]	Valid measure of anxiety and depression in Danish cardiac disease population[3]

Mental recovery/dependency	TSQ	Yes to Q1a + Yes to Q1b signify new problems with dependency after cardiac arrest. No to Q2 indicates problems with mental recovery after cardiac arrest.[4][5]	Received from TTM2 study group[4]	-
Fatigue impact on functional activities	MFIS	21 items in three sub-scales (physical, cognitive and psychosocial). Total scores range: 0-84. Total subscale scores: physical= 0 -36; cognitive=0=40; psychosocial= 0-8. ≥30 signify a fatigued individual (Antmann, 2012, Schiehser, 2015)	Translation received from e Provide, Mapi Research Trust.	Validated in people with multiple sclerosis.[6] and mild to moderate brain injury.[7]
Function and disability	12-item WHO DAS 2.0	12-item assessing 6 domains of functioning: 1) Understanding and communication; 2) Self-care; 3) Mobility; 4) Interpersonal relationships; 5) Work and household roles; and 6) Community and civic roles. Scored from 0= 'no difficulty' to 4= 'extreme difficulty or cannot do'. Total scores range: 0-48. Higher score indicating greater difficulty with activity and participation.	Available from:https://www w.etf.dk/ergotera pi-og- politik/hverdagsr ehabilitering	Used extensively to research neurological conditions including traumatic brain injury and spinal cord injury,[8] and rehabilitation and disability in a wide range of disease populations.[9] Validated in patients with chronic diseases.[10]
Life satisfaction/rehabilitation need	REHPA scale	A linear analogue scale, participants indicate how close they are to living the life they desire after their OHCA. Scale ranges from 0= 'goal reached' to 9= 'infinitely far from'.	By DANCAS study authors	

		Score of ≤3 will be considered as signifying having rehabilitation needs.		
Unmet rehabilitation needs		6-items asking if rehabilitation needs were met in different domains, for example, emotional reactions. Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[12]	Adapted by DANCAS authors	Questions adapted from existing survey 'The Experience of Cancer Patients during Diagnosis and Treatment'.[12 13]
Unmet information needs	Adapted from Zinckernagel et al., 2017	7-items asking if information needs were met in different domains, for example, 'treatment of your heart condition' Scored on a 4-point Likert type scale from 'Yes to a high level' to 'No, not at all'.[14]	Adapted by DANCAS authors for OHCA survivors from a Danish survey of patients with heart disease.[14]	
Relatives				
Anxiety and depression	HADS	As above		
Mental well-being	WHO-5	Five items with 6 responses from 0='At no time' to 5='all of the time'. Scores are totaled and multiplied by 4 to give range 0-100. Score <50 signifies poor emotional well-being.[15]	Developed in Denmark.[16]	Valid in multiple patient populations.[17]

Cognitive problems in daily life	IQCODE-CA	26-items scored on a five-point scale, 1= 'much improved' to 5= 'much worse'. Scores are totaled, divided by the number of questions to give a total, range 1-5. Score ≥3.04 signifies cognitive decline after cardiac arrest.[18]	Received from TTM2 study group	Relatives or close friends compare current cognitive function with pre-cardiac arrest cognitive function. Has been shown to accurately identify cardiac arrest survivors with potential cognitive problems.[18]
Caregiver strain	MCSI	13-items, scored: 2= 'Yes, On a Regular Basis', 1= 'Yes, sometimes', 0= 'No'. Range: 0-26, higher scores signify a higher level of carer strain.[19]	Translated by DANCAS study authors[a]	Found to have high internal validity with a population of family caregivers.[19]
Witness to OHCA	Questions designed for this survey	1-item on whether they witnessed the OHCA	Created by DANCAS study authors	
Labour market	Questions designed for this survey	7-items on educational level completed, current labour market status, status in pre-OHCA period and details of any sick leave in post-OHCA period.	Created by DANCAS study authors	These questions are asked of the relatives as their survey answers cannot be connected to Danish labour market registry data unless they provide their Danish personal identification number.
Social isolation	Question from Danish national health survey	One item: Does it ever happen that you are alone even though you would prefer to be with other people?"	Available at: http://www.dans kernessundhed.d k/Spoergeskema	

		Answers: "yes, often" and "yes, sometimes" signify loneliness. Other possible responses are "yes, but rarely" and "no.		
Support received post-OHCA	Questions designed for this survey	4-items on: whether relatives feel they have someone to talk to if they need support (yes, always/yes, mostly/yes, sometimes/no never or almost never); who have they received support from (multiple options); if they received the support they needed (Yes, No), and who would they have like to have received support from in the post-OHCA period (free text box).	Created by DANCAS study authors	

Abbreviations: HADS= Hospital Anxiety and Depression Scale; TSQ=Two Simple Questions; TTM2= Targeted Hypothermia versus Targeted Normothermia after OHCA trial 2; MFIS: Modified Fatigue Impact Scale, WHO DAS 2.0= World Health Organisation disability assessment schedule 2.0 Short; REHPA= Danish Knowledge Center for Rehabilitation and Palliative Care; OHCA=Out-of-hospital Cardiac Arrest; DANCAS=DANish Cardiac Arrest Survivorship; WHO-5= World Health Organisation-Five Well-Being index; IQCODE-CA: Informant Questionnaire on Cognitive Decline in the Elderly, Cardiac Arrest Version; MCSI= Modified Carer Strain Index.

[a]Translation, cultural adaption and psychometric testing performed by study authors, results are planned to be available in a future publication.

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