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Clinical paper

Physical, psychological, cognitive, social health outcomes, and health-related quality of life in out-of-hospital cardiac arrest survivors and their caregivers: Protocol of the quality cardiac arrest survivorship cohort study (QualiCAS)

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Abstract

Background: Out-of-hospital cardiac arrest (OHCA) is an emergency with historically low survival rates. Advances in resuscitation and post-resuscitation care have improved survival, precipitating greater scientific interest in OHCA patients' survivorship. However, there is insufficient high-quality population-based long-term survivorship data and limited research on the impact of OHCA sequelae on survivors' caregivers.

Objective: Our primary aim is to determine neurological function, physical, psychological, cognitive, social outcomes, and health-related quality of life (HRQoL) of OHCA survivors in Singapore. Secondary aims are to quantify caregivers' burden and its association with their HRQoL, and psychological well-being.

Methods: The Quality Cardiac Arrest Survivorship Cohort Study (QualiCAS) is a prospective population-based cohort study of OHCA survivors and their caregivers in Singapore. Participants aged ≥18 years and caregivers aged ≥21 years will be recruited from all public hospitals in Singapore. Health outcomes will be evaluated at 3, 6, and 12 months, and 3 and 5 years using the Hospital Anxiety and Depression Scale, PTSD Checklist for DSM-5, Fatigue Severity Scale, Montreal Cognitive Assessment Tool, EQ-5D-5L, Community Integration Questionnaire-Revised, Barthel Index, Lawton's Instrumental Activities of Daily Living, Timed Up and Go Test, Handgrip strength assessment, and Zarit Burden Interview.

Discussion: This study allows us to understand the natural history of OHCA survivorship and quantify the burdens on patients and their caregivers. Findings can guide clinical follow-up, identify high-risk patients, intervention targets, and inform rehabilitation strategies for OHCA sequelae.

Keywords: Cardiac Arrest, Survivorship-outcomes, Neurocognitive, Psychosocial, Caregiver, HRQoL (Health Related Quality of Life)

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https://doi.org/10.1016/j.resplu.2025.100938
Received 30 January 2025; Received in revised form 17 March 2025; Accepted 17 March 2025

Introduction

Out-of-hospital cardiac arrest (OHCA) poses a significant public health burden, with its rising incidence and historically poor survival rates.[1–3] In recent years however, survival rates have been increasing in part due to increased bystander intervention rates and improvement in post-resuscitation care.[4–6] A *meta*-analysis by Yan et al.[7] demonstrated an increase in pooled 1-year survival rate in adult OHCA patients from 6.0% between 2000 and 2009 to 12.3% between 2010 and 2019. Another meta-analysis reported that >60% of OHCA survivors can be expected to survive at least 5 years post-discharge.[8] In Singapore, survival rates have similarly improved from 11.6% in 2011 to 26.2% (Utstein survival) in 2019,[9] translating to approximately 200 OHCA survivors each year. Given the growing cohort of OHCA survivors in Singapore, there is a need to address questions on length and quality of survivorship amongst these patients.

While survival outcomes are improving for OHCA patients, recent literature suggests that, similar to survivors of other critical illnesses such as stroke, the sequelae of OHCA can be debilitating.[4,6,10] Common issues reported include psychological distress, fatigue, reduced societal participation, etc.,[10–14] illustrating the ubiquity of adverse complications in OHCA survivors and the need to adopt a multidimensional approach when assessing their health. Furthermore, the impact of an OHCA event extends beyond the survivors to their caregivers, with previous studies demonstrating that 11–32% of caregivers of OHCA survivors experienced high caregiver burden and poorer psychological well-being and HRQoL.[15,16] Understanding the needs of OHCA survivors' caregivers is also crucial as they form an integral part of survivors' recovery.[4,6]

While there is increasing scientific interest in the survivorship of OHCA patients, there is a paucity of high-quality population-based long-term survivorship data. To achieve quality survivorship, there is a need to establish baseline data on not only objective and crude clinician-reported outcomes such as cerebral performance categories (CPC) or modified Rankin Scale (mRS) but outcomes that are multi-dimensional, granular, and derived from survivors' perspectives.[4,6,17] We postulate that OHCA survivors and their caregivers in Singapore suffer from impediments in various domains, including physical, psychological, cognitive, and social functioning, and HRQoL. We further postulate that there are modifiable risk factors for poor long-term clinical progression, which can be targets for intervention. We aim to advance the field by addressing these important knowledge gaps using the approach of a population-based cohort study.

Objectives

The QualiCAS is a prospective, population-based cohort study of OHCA survivors which aims to describe the natural history of OHCA survivorship. The primary objective of QualiCAS is to establish neurological function, physical, psychological, cognitive, and social health outcomes, as well as HRQoL of OHCA survivors in Singapore at baseline (3rd month) and across 5 years. Our secondary objectives are to quantify the extent of caregivers' burden and its association with caregivers' HRQoL and psychological well-being.

Methods

Overall study design

This is a population-based cohort study that includes all OHCA cases attended to by Singapore's national ambulance service – the Singapore Civil Defence Force (SCDF) and all public hospitals. The subset of those who survive to hospital discharge and their primary caregivers will be recruited for in-person and telephone follow-up. Participants will be enrolled prior to their discharge from the hospital, with the first follow-up conducted at the 3rd month from the day they are discharged from the hospital. Follow-up time-points will be at the 3rd month, 6th month, 1st year, 3rd year, and 5th year. Depending on the date of enrolment, the duration of follow-up will be up to 5 years and for a minimum of 1 year (last patients enrolled). Visit schedule and instruments administered can be found in Table 1. Description of the instruments can be found in Table 2.

Outcomes

Primary outcome

With the inclusion of HRQoL as a core outcome in COSCA[17] and a supplemental outcome in Utstein template 2024,[18] we have identified HRQoL as our primary outcome. HRQoL will be assessed using the EQ-5D-5L (Table 2).

Secondary outcomes

Secondary outcomes include measurement of the following dimensions of health (Table 2):

- Physical function: activities of daily living, instrumental activities of daily living (IADL), muscular strength, and mobility as assessed by the Barthel Index, Lawton's IADL, handgrip strength, and Timed Up and Go (TUG) test, respectively.
- Psychological function: depression, anxiety, PTSD, and caregiver burden (for caregivers only) as assessed by the Hospital Anxiety and Depression scale (HADS), Post-traumatic stress disorder (PTSD) checklist for DSM-5 (PCL-5), and Zarit Burden Interview (ZBI), respectively.
- Cognitive function: attention, concentration, memory, executive functioning, language, visuospatial skills, and orientation as assessed by the Montreal Cognitive Assessment Tool (MOCA).
- Social function: community reintegration as assessed by the Community Integration Questionnaire-Revised (CIQ-R).
- Symptoms: fatigue as assessed by the Fatigue Severity Scale (FSS).

Additional variables

Additional variables collected include socio-demographics data such as age, sex, ethnicity, highest level of education, living arrangement, marital status, employment status, occupation, etc., and neurological status (mRS and CPC) of survivors. Key information about the arrest including dispatch information, ambulance and hospital treatment information, and survival outcomes, which are collected in the Pan-Asian Resuscitation Outcomes Study (PAROS)[2] will be linked to the QualiCAS cohort data.

Table 1 – Study schedule for out-of-hospital cardiac arrest survivors and their caregivers.

Domain	Instrument	Follow-up time points for survivors						Follow-up time points for caregivers				
		Upon discharge	3 months (in-person)	6 months	1 year (in-person)	3 years	5 years	3 months (in-person/ phone)	6 months	1 year (in-person/ phone)	3 years	5 years
Demographics	Baseline demographics record form	x	x					x				
Social	Community Integration Questionnaire-Revised			x	x							
Psychological	Hospital Anxiety and Depression Scale		x	x	x	x	x	x	x	x	x	x
	Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5)		x		x			x		x		
Cognitive	Montreal Cognitive Assessment Tool		x		x							
Physical	Lawton's Instrumental Activities of Daily Living		x		x							
	Barthel Index		x		x							
	Timed Up & Go Test		x		x							
	Handgrip Strength		x		x							
Quality of Life	EQ-5D-5L		x	x	x	x	x	x	x	x	x	x
Symptoms	Fatigue Severity Scale		x		x							
Caregiver	Zarit Burden Interview							x		x		

Table 2 – Description of study instruments.

Instrument	Author/License/Weblink	Conceptual focus	Description	Time taken (mins)	Scoring
Hospital Anxiety and Depression Scale	Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–370 License fees apply. No charge for non-funded academic use https://eprovide.mapi-trust.org/instruments/hospital-anxiety-and-depression-scale	Assessment of symptoms of anxiety and depression	7 items each for domains of anxiety and depression, with 4 response categories ranging from 0 to 3 for each item.	2–5	Total score for each scale ranges from 0 to 21. A score of $\leq$7 indicates normal range, 8–10 indicates mild anxiety/depression, 11–14 indicates moderate anxiety/depression, and 15–21 indicates severe anxiety/depression.
Montreal Cognitive Assessment Tool (MoCA)	Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JLC, Chertkow H. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. J Am Geriatr Soc 53:695–699, 2005 Licensed free of charge with for research purposes https://mocacognition.com/	Brief screening tool for mild cognitive impairment	Tests the domains of executive functioning, visuospatial abilities, attention, concentration, memory abstraction, language, concentration.	10–15	Overall score from 0 to 30. A score of $\geq$26 is considered normal. An additional point is added for those with 12 or fewer years of education.
EQ-5D-5L	Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011 Dec;20 (10):1727–36 Licensed free of charge for research purposes https://euroqol.org/	Standardized, preference-based measure of health status	Self-reported tool to measure HRQoL across 5 domains, consisting of 5 questions with 5 response levels. Domains assessed: pain/discomfort, mobility, self-care, anxiety/depression and usual activities.	5	Digits from the 5 domains may be combined into a 5-digit number that describes a health state. Responses may also be converted into a single utility index. The visual analogue scale records patient's self-rated health on a vertical numerical scale (0–100).
Community Integration Questionnaire-Revised (CIQ-R)	Willer B, Rosenthal M, Kreutzer JS. Assessment of community integration following rehabilitation for traumatic brain injury. Journal of Head Trauma Rehabilitation. June 1993;8(2):75–87 Licensed free of charge https://www.summerfoundation.org.au/resources/the-community-integration-questionnaire-revised/	Assessment of individuals' level of integration into home and community	18 items across 4 sub-scales. Home integration, social integration, productivity, participation in electronic social networking.	15	Overall score ranges from 0 to 35. Higher scores indicate better integration, lower scores indicate less integration.
Barthel Index	Mahoney FI, Barthel DW. Functional evaluation: The Barthel Index. Md State Med J. 1965 Feb;14:56–61 Licensed free of charge for non-commercial purposes https://eprovide.mapi-trust.org/instruments/barthel-index#need_this_questionnaire	Measurement of daily function; activities of daily living	Consists of 10 items including feeding, toileting, etc.	2–5	Scored from 0 to 20. Higher scores indicate higher levels of independence.

Table 2 (continued)

Instrument	Author/License/Weblink	Conceptual focus	Description	Time taken (mins)	Scoring
Lawton's instrumental activities of daily living (IADL) questionnaire	Lawton MP, Brody E. Assessment of older people: self-maintaining and instrumental activities of daily living. The Gerontologist 1969;9(3):179–186Licensed free of charge (https://www.cgakit.com/f-1-lawton-scale) https://eprovide.mapi-trust.org/instruments/instrumental-activities-of-daily-living-scale#coas_member_access_content	Measurementof daily function; instrumental activities of daily living	Consists of 8 items and assesses ability to use telephone, perform daily tasks such as household chores, shopping, etc., and handle finances	10–15	Scored from 0 to 8. Higher scores indicate higher levels of independence.
Fatigue Severity Scale	Krupp LB, LaRocca NG, Muir-Nash J. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121–1123 Licensed free of charge for non-commercial purposes https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/fss.php https://eprovide.mapi-trust.org/instruments/fatigue-severity-scale#coas_member_access_content	Measurement of severity of fatigue symptoms indaily activities	Consists of 9 items and assessed severity of fatigue symptoms and their impact on daily functioning	5–8	Total score is from 9 to 63. A higher score reflects greater fatigue.
Timed Up and Go (TUG) test	Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991 Feb;39(2):142–8 https://pubmed.ncbi.nlm.nih.gov/1991946/	Assessment of physical and functional mobility	Participants are asked to stand from a chair, walk 3 m, turn around, walk back to the chair and sit down. Participants are timed with the verbal instruction "go" and stops when the patient returns to seated position and the amount of time taken to complete the task will be recorded.	Subjective	A score of <10 s indicates complete independence, <20 s indicates independence for main transfers (e.g. stairs climbing, in and out of shower/tubs), and >30 s indicates dependence in most activities.
Handgrip strength	NIL	Assessment of grip strength using ahandgrip dynamometer	Participants are asked to stand upright, with their arms let down naturally, and clasp the grip with full force. Two such procedures are performed for each hand.	Subjective	Overall handgrip strength will be calculated as the mean of the measurements from the left and right hands.
Post-traumatic stress disorder (PTSD) checklist for DSM-5 (PCL-5)	Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P.A., Marx, B.P., & Schnurr, P. P. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov. Licensed for use by researchers. https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp	Assessment of PTSD symptoms based on DSM-5 criteria	20-item self-report measure that assesses the presence and severity of PTSD symptoms. Participants rate how bothered they have been by each of 20 items in the past month on a Likert scale ranging from 0 (not at all) to 4 (extremely).	5–10	Items are summed to derive a total severity score ranging from 0 to 80. A total score of 31–33 or highersuggests probable PTSD.

(*continued on next page*)

Table 2 (continued)

Instrument	Author/License/Weblink	Conceptual focus	Description	Time taken (mins)	Scoring
Zarit Burden Interview	Zarit SH, Reever KE, Bach-Peterson J. Relatives of the Impaired Elderly: Correlates of Feelings of Burden. Gerontologist. 1980;20(6):649–55 License fees apply. No charge for non-funded academic use https://eprovide.mapi-trust.org/instruments/zarit-burden-interview	Evaluation of caregivers' burden	22-item self-report questionnaire that evaluates level of caregivers' burden	<10	A score of <21 indicates absent or minor burden, a score between 21 and 40 indicates light burden, a score between 40 and 60 indicates moderate burden and a score >60 indicates heavy burden.

Mortality, lost-to-follow-up, and withdrawal from study are also documented.

Participant eligibility

Inclusion criteria for all OHCA survivors:

1. Aged $\geq$ 18 years
2. Presented to a public hospital via SCDF ambulance, private, or public transport; transferred from another hospital facility to the emergency department of a public hospital; or transferred from another hospital facility to an inpatient area of a public hospital.
3. Non-traumatic aetiology
4. Plans to reside in Singapore for at least 1 year after their OHCA

Inclusion criteria for caregivers:

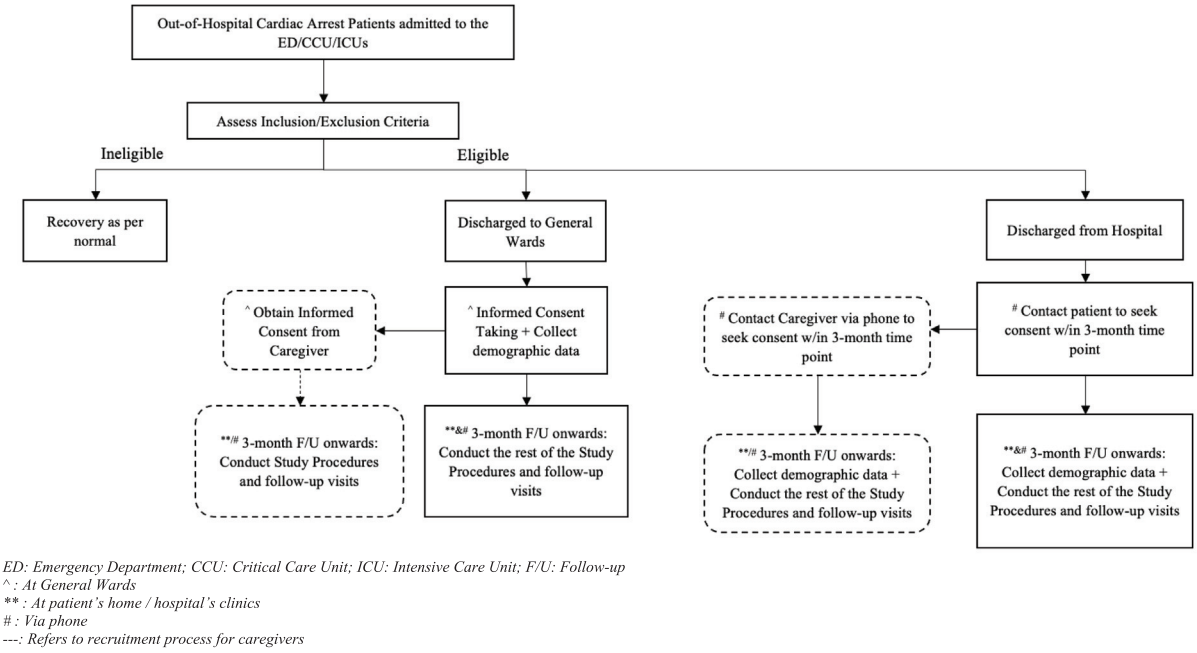
1. Aged $\geq$ 21 years (caregivers must be of legal age to consent for OHCA survivors aged < 21 years or those who are cognitively impaired).
2. Is a family member, a relative or a friend identified by the survivor/survivor's primary physician to be the primary caregiver.

Exclusion criteria for OHCA survivors and caregivers:

All OHCA survivors and caregivers who are unable to understand English or Mandarin (which are the two most commonly spoken languages in Singapore) will be excluded from the study. Caregivers who are formal caregivers such as healthcare professionals or hired help of the survivor will also be excluded.

Study procedure

Investigators and trained study personnel will screen for potential study participants amongst patients admitted to the Intensive Care Units (ICUs) of the study sites after OHCA. Informed consent will be obtained from the patient, next-of-kin, or legal representatives after patients are discharged from the intensive care units to the general wards, as well as from the patients' primary caregivers before they are recruited as participants (see Fig. 1 for study flowchart). Patients without a participating caregiver may still be recruited, while sole caregivers without a patient enrolled in the study will not be invited to participate as the primary focus of the study is on OHCA survivorship. In the event that an OHCA survivor acquires a new caregiver during the study, data from the recruited caregiver will be analysed until the point of their withdrawal before they are considered as lost to follow-up. However, data collection for the OHCA survivor will continue, and no new caregiver data will be collected. In-person follow-up visits will be conducted at either participants' homes, hospital clinics, nursing homes, etc. depending on participants' preference or convenience. Trained study personnel will administer (self-administered or interviewer-administered) the list of instruments as described in Table 1 to participants in-person or via telephone. Depending on participants' primary language, English or Chinese versions of the instruments will be administered. If participants are unable to consent or answer the questionnaires due to cognitive impairment, their caregivers will be asked to consent and complete the questionnaires (except for the PCL-5, MoCA, FSS, TUG Test, and handgrip strength) on their behalf. A minimum of five attempts will be made to contact participants at different days of the week and timings (e.g. weekday evenings, weekend mornings, etc.) before they are considered as lost-to-follow up. Data collection will cease if participants withdraw consent, are lost-to-follow up, or pass away (in the event of a survivor's death, data collection will also



ED: Emergency Department; CCU: Critical Care Unit; ICU: Intensive Care Unit; F/U: Follow-up
^ : At General Wards
*** : At patient's home / hospital's clinics*
 # : Via phone
---: Refers to recruitment process for caregivers

Fig. 1 – Study flowchart.

cease for caregivers). Recruitment for the study commenced in February 2023 and data collection is planned to continue for approximately 4 years.

Data collection

At inclusion, socio-demographic data will be collected. During follow-up interviews, the data collected can be found in Table 1. Data will be collected on paper-based versions of the instruments and entered into REDCap.[19,20].

Sample size

Based on data from the Pan-Asian Resuscitation Outcomes Study (PAROS),[9,21] we expect to recruit up to 1,000 OHCA survivors aged $\geq$ 18 years and 1,000 caregivers aged $\geq$ 21 years over a period of 5 years. Survivors and caregivers will be followed up for a period of up to 5 years upon survivors' discharge from the hospital.

Statistical analysis plan

Baseline characteristics will be presented as frequencies and proportions for categorical variables, and median (IQR) or mean (SD) for continuous variables, as appropriate for the distribution of the data. Outcomes at the time-points of interest will be summarised appropriately. Binary outcomes such as survival will be summarised as percentages. The Kaplan-Meier (KM) method will be used to construct survival functions to estimate median survival. The KM method, log-rank test and Cox regressions will be used to identify independent correlates with survival duration. Descriptive statistics will be used to summarise all instrument survey results. Where relevant, e.g. for HRQoL, estimates will be compared to appropriate controls (such as general population, or chronic heart failure patients). Standardised Mortality Ratio (SMR) per year of follow up will be computed. Disease burden will be quantified using Disability-Adjusted Life Years, given by the summation of Years of Life Lost (YLL) and Years Lost due to Disability (YLD). We anticipate participants to drop-out from the study as is typical of cohort studies. We will minimise the dropout rate using a range of strategies, including: (1) reimbursement of participants, (2) conducting follow-up measurements at convenient locations (i.e. participants' homes), (3) engaging participants to provide suggestions on next-phase study design. We will assess the severity of loss to follow-up by tracking the number and proportion of participants that drop out, and compare the characteristics of participants who drop out against those who do not.

Ethics

This study was approved by the Singhealth institutional review board (2022/2400) with requirement for written informed consent prior to enrolment of any participant into the study.

Discussion

The QualiCAS is a prospective, population-based cohort study of OHCA survivors which aims to describe the natural history of OHCA survivorship. Given the paucity of high-quality population-based data on the long-term survivorship outcomes of OHCA survivors, our study can fill this critical knowledge gap by providing comprehensive insights into the long-term neurological function, as well as physical, psychological, cognitive, and social health outcomes, and HRQoL of OHCA survivors. The inclusion of patient-reported outcomes (PRO) in our study extends and enriches previous work we had established through PAROS,[2,22] which focused only on short-term proximal clinical outcomes, such as survival to discharge/30th day and neurological status upon discharge/30th day.

With the establishment of QualiCAS, there are opportunities to 1) nest clinical trials within the cohort, e.g. cohort multiple randomised controlled trial design,[23] which is more cost-efficient and helps miti-

gate issues such as attrition; 2) evaluate the impact of public health and clinical programs on both clinical outcomes and PRO; 3) develop and validate OHCA-specific HRQoL and other PRO instruments; 4) conduct comparative analysis with other disease groups (e.g. stroke, AMI); 5) identify modifiable risk factors for development of targeted interventions; and 6) develop OHCA-specific disability-weights for estimation of disability adjusted life-years and healthy life expectancy.

One of the key challenges in cohort studies is the risk of selection bias including non-response and attrition, which can threaten the validity of our study findings. To reduce non-response rate, regular training sessions, including role-playing of the recruitment process with study team members, will be conducted to enhance their ability to effectively explain the study's aims, benefits, and procedures to participants. Apart from building mechanisms at the design stage to reduce attrition (see methodology section), our study will also utilise passive monitoring of outcomes via linkages to national disease and death registries to minimise data loss. If attrition rate is high, the cohort sample may have limited generalizability to the target population, i.e. all OHCA survivors in Singapore. We would then interpret with caution any analysis findings that attempt to use sample findings to make an inference on population parameters but to focus on analysis findings on correlations within the cohort, which remain valid.

Future directions

With the growing global interest in OHCA survivorship, there are opportunities to harmonize global survivorship cohorts for the conduct of joint comparative analysis, embed trials, and use patient-centred outcomes as clinically-oriented endpoints in studies of efficacy in resuscitation.[24,25] Such analyses will allow us to benchmark systems and practices and identify areas for improvement of care and patient outcomes. Our vision is to develop and sustain QualiCAS as a long-term registry. However, while in-person data collection method is likely to increase participation and reduce attrition, it is costly and resource intensive. To sustain such a registry would require consistent and multiple sources of funding, whether through philanthropic or governmental support. Low-cost solutions (e.g. postal, online tools, etc.) that could reduce data collection burden as well as respondent fatigue and burden (e.g. computerized adaptive testing), while maintaining data quality, would need to be explored and established as part of the long-term plan of the study.

Conclusion

The long-term systematic follow-up with repeated assessments of this population allows us to understand the natural history of OHCA survivorship and the burden of impediments suffered by both the patients and their caregivers. Our study can allow for further studies to assess the effectiveness and cost-effectiveness of current and potential OHCA treatment strategies, as well as track the outcomes associated with policies or interventions implemented. We will also be able to identify modifiable and non-modifiable determinants of unfavorable long-term outcomes, including HRQoL. These findings can assist policymakers in resource allocation and healthcare providers in identifying high-risk patients and targets for intervention, formulating discharge plans, and developing multi-disciplinary rehabilitation strategies to address OHCA sequelae.

Funding sources

The study is supported by the National Medical Research Council Singapore Translational Research Investigator Award (MOH-000982-01). Andrew Fu Wah Ho is supported by the SingHealth Duke-NUS Academic Medical Centre under the Clinician Investigator Advancement Programme (award number 15/FY2022/CIVA/03-A03) and National Medical Research Council (NMRC/CS_Seedfd/012/2018). Dr Desmond Mao is supported by the Alexandra Health Fund Ltd through the Research Investigator-Scientist Enabler (RISE) Grant. He received conference support from Zoll Medical.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A

See Table 3.

Table 3 – STROBE[26] Statement—checklist of items that should be included in reports of cohort studies.

	ItemNo.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page	Physical, psychological, cognitive, social health outcomes, and health-related quality of life in out-of-hospital cardiac arrest survivors and their caregivers: Protocol of the Quality Cardiac Arrest Survivorship Cohort Study (QualiCAS).
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1	This information is stated in the study abstract (background, objective, methods, and discussion described).
Introduction				
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	3	Rationale and existing literature are stated in the introduction section.
Objectives	3	State specific objectives, including any prespecified hypotheses	4	Specific objectives are stated at the end of the introduction: "The QualiCAS is a prospective, population-based cohort study of OHCA survivors which aims to describe the natural history of OHCA survivorship. The primary objective of QualiCAS is to establish neurological function, physical, psychological, cognitive, and social health outcomes, as well as HRQoL of OHCA survivors in Singapore at baseline (3rd month) and across 5 years. Our secondary objectives are to quantify the extent of caregivers' burden and its association with caregivers' HRQoL and psychological well-being. Page 4 L19
Methods				
Study design	4	Present key elements of study design early in the paper	5	Study design with all key elements are stated in the first subsection of the Methods section. "This is a population-based cohort study that includes all OHCA cases attended to by Singapore's national ambulance service – the Singapore Civil Defence Force (SCDF) and all public hospitals". Page 5 L7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 8, 18	Setting, location, follow-up and data collection are stated in the method section under the heading "Overall study design" and in Table 1. Recruitment is detailed in the method section under the subheading "Study procedure". Page 8 L34

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	ItemNo.	Recommendation	Page No.	Relevant text from manuscript
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6	Participant eligibility and selection criteria is stated under the methods section. Page 6 L44
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	N/A	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	All outcomes and variables area stated under the "Outcomes" and "Additional variables" subsection of the methods section. "Additional variables measured include social demographic data collected at discharge [. . .] Mortality, loss-to-follow-up, and withdrawal from study will also be documented.". Page 6 L24
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*19;* Table 2	*Data sources, instrument description, conceptual focus and scoring systems are stated in* Table 2*; a description of study instruments. Page 19*
Bias	9	Describe any efforts to address potential sources of bias	10	Selection bias was reduced through methods to reduce non-response rate, attrition and data loss, stated in the discussion "One of the key challenges in cohort studies is the risk of selection bias including non-response and attrition, which can threaten the validity of our study findings. To reduce non-response rate, regular training sessions, including role-playing of the recruitment process with study team members, will be conducted to enhance their ability to effectively explain the study's aims, benefits, and procedures to participants. [. . .]We would then interpret with caution any analysis findings that attempt to use sample findings to make an inference on population parameters but to focus on analysis findings on correlations within the cohort, which remain valid.". Page 10 L46
Study size	10	Explain how the study size was arrived at	8	Study size is stated under the "Sample size" subheading of the methods section, the calculation of which is based on data linkage from the Pan-Asian Resuscitation Outcomes Study. Page 8 L41
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9	These are described in the methods section under the statistical analysis plan subheading. Page 9 L2
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9	These are described in the methods section under the statistical analysis plan subheading. "Baseline characteristics will be presented as frequencies and proportions for categorical variables, and median (IQR) or mean (SD) for continuous variables, as appropriate for the distribution of the data. [. . .]We will assess the severity of loss to follow-up by tracking the number and proportion of participants that drop out, and compare the characteristics of participants who drop out against those who do not." Page 9 L5

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	ItemNo.	Recommendation	Page No.	Relevant text from manuscript
		(*b*) Describe any methods used to examine subgroups and interactions	N/A	N/A
		(*c*) Explain how missing data were addressed	9	This is described in the methods section under the statistical analysis plan subheading. "We anticipate participants to drop-out from the study as is typical of cohort studies. We will minimise the dropout rate using a range of strategies, including: (1) reimbursement of participants, (2) conducting follow-up measurements at convenient locations (i.e. participants' homes), (3) engaging participants to provide suggestions on next-phase study design." Page 9 L27
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	9	This is described in the methods section under the statistical analysis plan subheading. "We will assess the severity of loss to follow-up by tracking the number and proportion of participants that drop out, and compare the characteristics of participants who drop out against those who do not." Page 9 L36
		(*e*) Describe any sensitivity analyses	N/A	N/A
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A	N/A. This is a protocol paper.
		(b) Give reasons for non-participation at each stage	N/A	N/A. This is a protocol paper.
		(c) Consider use of a flow diagram	N/A	N/A. This is a protocol paper.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6	The methods section describes the socio-demographic and clinical data collected from the study participants. "Additional variables measured include social demographic data collected at discharge (age, sex, ethnicity, highest level of education, living arrangements) and survivors' neurological status via the mRS and CPC, which is collected at discharge, the 3-month, and 5-month time points." Page 6 L24
		(b) Indicate number of participants with missing data for each variable of interest	N/A	N/A. This is a protocol paper.
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	5	This is stated in the methods section and detailed in Table 1. "Participants will be enrolled prior to their discharge from the hospital, with the first follow-up conducted at the 3rd month from the day they are discharged from the hospital. Follow-up time-points will be at the 3rd month, 6th month, 1st year, 3rd year, and 5th year. Depending on the date of enrolment, the duration of follow-up will be up to 5 years and for a minimum of 1 year (last patients enrolled)." Page 5 L14

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	ItemNo.	Recommendation	Page No.	Relevant text from manuscript
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A	N/A. This is a protocol paper.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A	N/A. This is a protocol paper.
		(*b*) Report category boundaries when continuous variables were categorized	N/A	N/A. This is a protocol paper.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	N/A. This is a protocol paper.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	N/A
Discussion				
Key results	18	Summarise key results with reference to study objectives	N/A	N/A. This is a protocol paper.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10	Selection bias was reduced through methods to reduce non-response rate, attrition and data loss, stated in the discussion "One of the key challenges in cohort studies is the risk of selection bias including non-response and attrition, which can threaten the validity of our study findings. To reduce non-response rate, regular training sessions, including role-playing of the recruitment process with study team members, will be conducted to enhance their ability to effectively explain the study's aims, benefits, and procedures to participants. [. . .]We would then interpret with caution any analysis findings that attempt to use sample findings to make an inference on population parameters but to focus on analysis findings on correlations within the cohort, which remain valid.". Page 10 L46
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	N/A	N/A. This is a protocol paper.
Generalisability	21	Discuss the generalisability (external validity) of the study results	N/A	N/A. This is a protocol paper.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13	Funding sources were stated at the end of the manuscript after the discussion. Page 13 L10

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

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

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