

BMJ Open Study protocol for a cohort study of patients with advanced heart failure in Singapore

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ABSTRACT

Introduction Understanding the symptom and health expenditure burden among patients with advanced congestive heart failure (CHF) and their family caregivers is essential to reform policy and practice needed to provide quality care to these patients at affordable prices. The proposed cohort study titled Singapore Cohort of Patients with Advanced Heart Failure aims to describe trajectories of quality of life among patients and their primary informal caregivers, quantify healthcare utilisation and expenditures, assess changes in patient and caregiver awareness of and preferences for knowing diagnostic and prognostic information, awareness and utilisation of palliative care services, preferences for treatments and decision making, perceived quality of care, self-care, caregiver psychological distress and caregiver burden.

Methods This cohort study will recruit 250 patients with New York Heart Association Classification class III and IV CHF from inpatient wards at two public tertiary healthcare institutions in Singapore. Patients and their primary informal caregiver are being surveyed every 4 months until patients' death; caregivers are followed until 8 weeks postpatient death. Medical and billing records of patients are obtained and merged with patients' survey data.

Ethics and dissemination The study has been approved by an ethics board. Results from the study will be disseminated through publications and presentations targeting researchers, policy makers and clinicians interested in understanding and improving care for patients with advanced CHF.

Trial registration number NCT03089034.

BACKGROUND

Data from several countries shows that despite therapeutic advances and high health-care expenditures,¹ patients with advanced congestive heart failure (CHF) suffer from the physical and psychological effects of their illness.²⁻⁴ Unlike many patients with advanced cancer, patients with CHF typically experience a gradual decline in physical function over many months or years, with occasional periods of exacerbation.⁵ The non-linear deterioration in health leads to difficulties in prognostication and often delays referral to

Strengths and limitations of this study

- The main strength of the study is that will include a large sample of patients with advanced CHF followed prospectively over time until patients' death.
- The study assesses multiple dimensions of patients' end of life experiences incorporating standardised and validated instruments and merger with medical and billing records.
- Attrition may be a possible problem in the study.
- Most data collected is through patient and caregiver self-reports and is subject to reporting biases.
- A longer follow-up period may be required than originally anticipated to observe disease progression till death.

specialist palliative care services. Moreover, there is evidence that patients' understanding of their illness and communication with their physician is inadequate.^{6,7} These concerns suggest that patients may be receiving care that is suboptimal.

In Singapore, CHF is one of the leading causes of death.⁸ Although limited data from cross-sectional and qualitative studies suggests that patients with advanced CHF in Singapore experience physical, psychological and financial distress and do not understand their prognosis accurately,⁹ there has been no comprehensive longitudinal assessment of the experiences of patients with advanced CHF to assess gaps in care received.¹⁰ To assess patients' care needs, continuity of care received and identify areas of improvement for care for patients with advanced CHF, we aim to conduct a cohort study of patients with advanced CHF. The primary objectives of this study are to describe trajectories of quality of life among patients and their primary informal caregivers (mentioned as caregiver henceforth), and quantify healthcare utilisation and expenditures. Secondary objectives are to investigate longitudinal changes in

patient and caregiver awareness of and preferences for knowing diagnostic and prognostic information, awareness and utilisation of palliative care services, preferences for treatments and decision making, perceived quality of care, self-care, caregiver psychological distress and caregiver burden. Furthermore, heart failure, characterised by impaired skeletal muscle structure and metabolic function, is known to be associated with physical frailty.¹¹ Previous studies show handgrip strength to be a marker of physical frailty and to independently predict adverse health outcomes and mortality in several populations.^{12 13} Therefore, we will also examine longitudinal changes in handgrip strength as a marker of physical frailty among patients with advanced CHF to assess its relationship with death and disability. Finally for the caregivers of patients who pass away during the study period, we will assess their perception of patients' end of life (EOL) care. This paper presents the full protocol of this cohort study titled 'Singapore Cohort of Patients with Advanced Heart Failure (SCOPAH)'.

METHODS/DESIGN

Study setting and participants

SCOPAH is a cohort study of 250 patients with advanced CHF and their caregivers at two tertiary institutions in Singapore: National Heart Centre Singapore and Singapore General Hospital. The study recruits Singapore citizens or Permanent Residents aged 21 years or older when they are hospitalised at any of the two hospitals with symptoms severe enough to be classified as New York Heart Association (NYHA)¹⁴ class 3 or 4. CHF is established based on physician diagnosis with both systolic and diastolic CHF being included. Patients with major psychiatric disorders such as schizophrenia, bipolar disorder, personality disorder or emotional instability such as suicidal thoughts and depression, as stated in the electronic medical records, are excluded from participation. Caregiver participants are required to be aged 21 years or older and be a caregiver of the patient, defined as 1) main person or one of the main persons providing care to the patient (eg, accompanying patient for doctor's visits, helping the patient with day-to-day activities) or 2) main person or one of the main ensuring provision of care (eg, supervision of foreign domestic worker so that the patient is looked after or 3) main person or one of the main involved in making decisions regarding treatment the patient receives. Patients' paid domestic helpers are not included.

The study is registered at www.clinicaltrials.gov (NCT03089034).

Recruitment and follow-ups

Patients are prescreened for eligibility (ie, diagnosis, citizenship status, age) through their electronic medical records and those who meet study inclusion criteria are approached by a research coordinator during their inpatient stay for participation in the study. If the NYHA class

of patient is not stated in the electronic medical records, a NYHA screener is administered to the patients to assess the amount of exertion needed to provoke dyspnoea. Patients are further screened for their cognitive status through the Montreal Cognitive Assessment (MoCA) test; those scoring 10 or more are considered eligible to participate in the survey at that assessment point and their caregivers are also invited to take part in the survey. Patients scoring <10 on MoCA are deemed to be too cognitively impaired to participate in the survey. Their caregivers or legal guardian are approached for consent to access patient's medical and billing records, and the caregiver is invited to respond to the caregiver survey. Both patients and their caregivers who agree to participate provide informed consent and are informed that their identifying information will be kept confidential and that the study results will be reported in aggregate form. [Figure 1](#) shows the recruitment process.

Follow-up surveys with patients and caregivers are conducted every 4 months at outpatient, inpatient settings, or at patients' homes, depending on their preference. Patients are screened for cognitive function at each follow-up using MoCA. Those who fail the MoCA screening at three consecutive assessment points are no longer approached for the remaining follow-ups; however, the caregivers of such patients continue to be eligible for participation.

After patient's death, consenting caregivers complete a postdeath questionnaire at 8 weeks from the date of patient's death to investigate patient's healthcare utilisation during the last months of life and their perception of care received.

Survey data from both patient and caregiver participants is captured electronically using Qualtrics. Each participant is identified through a unique study code assigned on consent. Consent forms, screeners and surveys for both patients and caregivers are administered in their preferred language out of the following options: English, Mandarin and Malay. These three languages cover 99.5% of language literacy in Singapore.^{15 16} Patients complete surveys that are interviewer-administered (ie, interviewer reads the questions and answer options out to the patient), while caregivers have the option of doing it on their own; mode of survey administration is captured. Study participants are compensated with a SGD\$40 voucher for completion of each survey. At the end of the study period, their medical and billing records will be extracted and merged with their survey data to comprehensively capture their healthcare utilisation and expenditure patterns through the last year of their life.

[Table 1](#) summarises the several ways (categories A–F) patients and caregivers can participate in the study, depending on their eligibility and interest and the type of data that is ultimately captured.

Outcome measures

Patients and caregivers complete a survey assessing a broad range of topics regarding their quality of life,

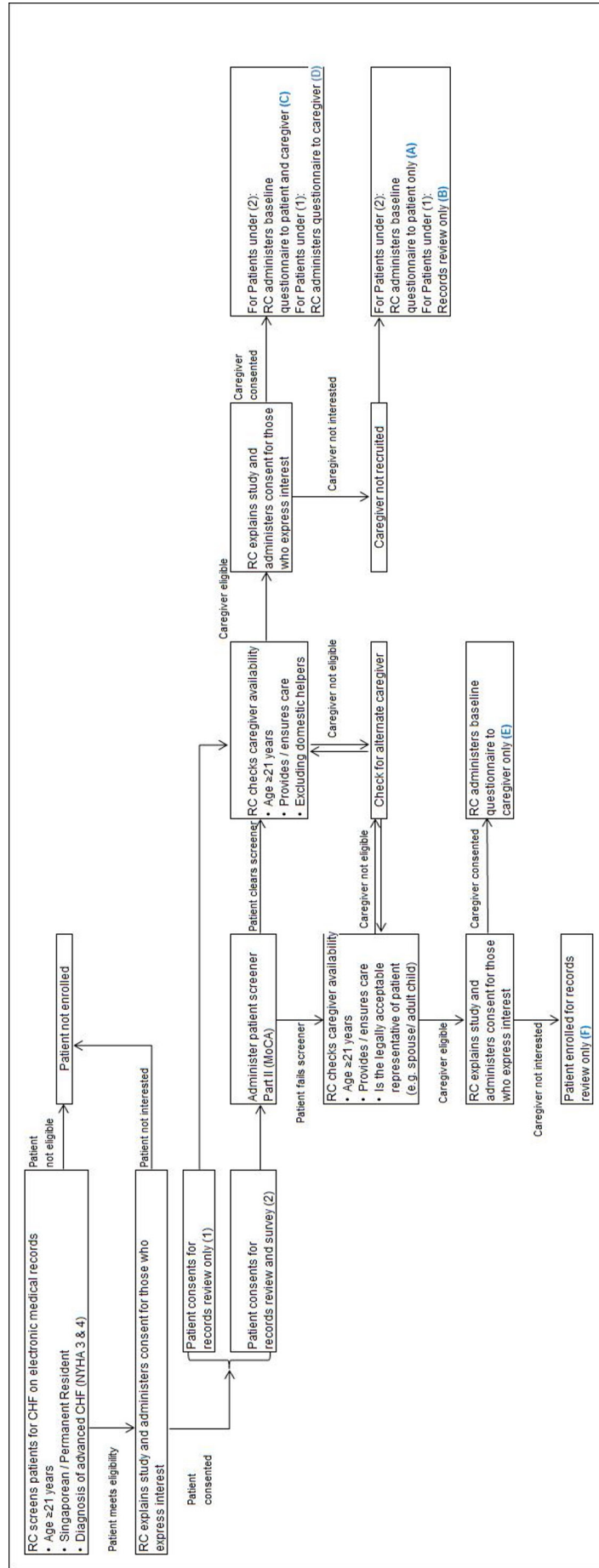


Figure 1 Workflow for recruitment of study participants. RC, Research Coordinator; CHF, Congestive heart failure; MoCA, Montreal Cognitive Assessment; NYHA, New York Heart Association.

Table 1 Type of data from patient and their caregiver

| Category | Patient cognitive status | Study participant(s) | Type of data consented to |
|----------|--------------------------|--|--|
| A | Patient passed MoCA* | Patient (caregiver declined/not available) | 1. Patient self-report survey 2. Patient records review† |
| B | MoCA not administered‡ | Patient (caregiver declined/not available) | 1. Patient records review† |
| C | Patient passed MoCA* | Patient and caregiver | 1. Patient self-report survey 2. Patient records review† 3. Caregiver self-report survey |
| D | MoCA not administered‡ | Patient and caregiver | 1. Patient records review† 2. Caregiver self-report survey and information as proxy for patient |
| E | Patient failed MoCA | Patient (consent from caregiver as legal representative) and caregiver | 1. Patient records review† 2. Caregiver self-report survey and information as proxy for patient |
| F | Patient failed MoCA | Patient (consent from caregiver as legal representative) | 1. Patient records review† |

*A cognitive assessment.

†Records review of medical and billing data.

‡Patients who fall under this category are not screened for their cognitive status since they have agreed to consent only for records review and not for the self-report survey.

MoCA, Montreal Cognitive Assessment.

perceived quality of care and healthcare utilisation/expenditure. Medical and billing records are accessed for patient diagnostic, treatment information and costs. Data from medical records is linked to information from the patient/caregiver surveys. The following outcomes are measured in the study:

1. *Quality of life.* Quality of life in this study comprises patient-reported outcomes of physical symptoms and functioning as well as psychosocial well-being. The Functional Assessment of Cancer Therapy-General (FACT-G)¹⁷ is a 27-item measure of quality of life of patients. This is an extensively used instrument and comprises four subscales: physical well-being, functional well-being, emotional well-being and social well-being. Seven items drawn from the palliative symptom-specific subscale¹⁸ are administered to measure symptom burden. Equivalence between English and Chinese version for the FACT-G has been reported using a Singaporean sample.¹⁹ Activities of daily living (ADLs) in patients are assessed using the Physical ADL section of the Older American Resources and Services ADL.²⁰
2. *Healthcare utilisation and expenditures.* Healthcare utilisation from hospitals is obtained through a combination of self-report and billing data, and consists of the total number of hospitalisations and visits to emergency department. Healthcare expenditures are classified by source of payment namely inpatient, outpatient, pharmacy and emergency department settings. Palliative care utilisation are also obtained through a combination of patient self-report and medical/billing records. Patients will be asked where they first received palliative care treatment, and billing records will then be traced at

those institutions. In addition, information on each patient's number of readmissions for CHF will be obtained.

3. *Awareness of and preferences for knowing diagnostic and prognostic information.* Patient and caregiver awareness of and preferences for diagnostic and prognostic information are assessed by asking questions developed specifically for the study and adapted from Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium and the Study to Understand Risks, Priority and Issues at End-of-Life.²¹ Items include whether patients perceive their treatments to cure their condition or extend their lives and whether patients would like to know how long they are likely to live under various treatment options.
4. *Awareness and utilisation of palliative care services.* Patients and caregivers are asked about their awareness and their source of getting informed about palliative care services. The utilisation of palliative care and the reasons for not using the services will be documented. These questions have been adapted from patient survey, V.7.0, used in observational study conducted by CanCORS Consortium.²² Treating physicians are asked about the timing of discussion with patients regarding enrolment to hospice.
5. *Preferences for treatments and decision making.* Patients and caregivers are asked about their preference for treatments trading off between treatment cost and survival. They will also be asked their experience in and preferences for making treatment decisions to investigate the extent to which patients' preferences for involvement in decision making are met. The questions on decision making have been adapted from patient survey, V.7.0, CanCORS.²³ In addition,

- physicians are asked about who makes the final treatment decision for their patients.
6. *Perceived quality of care.* Patient's and caregiver's perceived quality of care are assessed using a scale used by Ayanian *et al*²⁴ that consists of 13 questions addressing specific problems of care and 1 question eliciting overall rating of care on a 5-point scale ranging from poor to excellent (Cronbach's $\alpha=0.81-0.86$).
 7. *Self-care.* Self-care is measured in patients through the use of Self-Care of Heart Failure Index (SCHFI) V.6.2.²⁵ The SCHFI is a self-report measure, comprising 15 items divided into three subscales: self-care maintenance (Cronbach's $\alpha=0.55$),²⁶ self-care management (Cronbach's $\alpha=0.60$)²⁶ and self-care confidence (Cronbach's $\alpha=0.83$).²⁶ The items are rated on a 4-point response scale.
 8. *Caregiver psychological distress.* Caregiver psychological distress (defined as depression and anxiety) is assessed using the Hospital Anxiety and Depression Scale (HADS).²⁷ HADS has 14 items that yield two subscales: anxiety and depression subscale. This instrument has a Singapore Mandarin version reported to be valid and reliable (Cronbach's $\alpha=0.74-0.85$).²⁸
 9. *Caregiver burden.* The modified Caregiver Reaction Assessment scale, which consists of 21 items, is used to measure caregiver burden. The instrument yields four subscales: schedule and health, finances, family support and esteem. We will use the modified version that has been validated for use in Singapore and reported to be reliable (Cronbach's $\alpha=0.66-0.82$).²⁹
 10. *Hand grip strength.* Hand grip strength is assessed using a Smedley spring-type dynamometer (Hand Grip Meter, No. 6103 (75 kg), Tanita, Tokyo, Japan). After demonstrating its use, the interviewer asks the respondents to remove rings or other hand jewellery, to sit up straight as much as possible with arm straight down at side not touching the bed/chair and to squeeze the dynamometer as hard as possible and then let go. The elbow should not be supported or bent. Measurements are recorded to the nearest 0.5 kg. The process is conducted twice for each hand and the dynamometer is reset to zero after each measurement. Dominant hand for the respondent is also recorded.
 11. *Caregiver's perception of the patient's EOL care.* Caregivers are assessed at 8 weeks postpatient death on their experience and patient's experience at the EOL using the 13-item Caregiver Evaluation of the Quality of End-Of-Life Care (CEQUEL). The CEQUEL is a valid and reliable (Cronbach's $\alpha=0.52-0.78$)³⁰ measure of quality of EOL care from the caregiver's perspective, which includes measures of perceived suffering and prolongation of death.

All surveys that did not have Mandarin and Malay versions were translated with the assistance of a professional translation service. Questions that were developed specifically for this study were guided by the research aims and hypotheses and tailored specifically to our population

of interest. Cognitive interviews were conducted with 10 participants in each language to check the readability of the translated questionnaire.

Sample size calculation

As this study is not a randomised controlled trial, the sample size is not based on testing a single end point. Rather, the goal is to enrol an appropriate number of subjects such that the study is feasible, while simultaneously ensuring a sample size large enough to conduct analyses and estimate models as described above. A sample of 250 patients with advanced CHF, subject to 20% loss to follow-up will allow 95% CIs for proportions to be estimated with a margin of error of <0.05 and for means to be estimated with a margin of error of $<10\%$ of the associated observation SD. Furthermore, at $\alpha=0.05$, this sample size will provide $>80\%$ power for comparison of proportions differing by at least 0.20 between groups and for comparison of means differing by at least 0.4 SD between groups, under the assumption that the smaller group has at least 100 subjects.

Statistical analysis

To assess trajectories of quality of life of patients, we will use group-based trajectory modelling.^{31 32} Choice of the optimal number of trajectory classes will be based on a combination of the Bayesian Information Criterion value, number and/or proportion of individuals in each trajectory class and value of average predicted posterior probability of trajectory class membership. The functional form of the trajectory within each trajectory class will be based on significance of polynomial terms defining the trajectory.

To quantify healthcare expenditures, we will estimate total annual direct and indirect costs. We will also stratify costs by time from death (eg, last year or last 6 months) and by type of service (in total and separately for inpatient, non-inpatient, physician's office, prescription drug and alternative medicines). Annual healthcare utilisation will also be assessed as total number of hospitalisations, visits to emergency department and specialist consultants. We will use generalised linear models with the appropriate link function and distribution to model healthcare utilisation and expenditures from each source and age, socioeconomic status, health insurance status, funds in Medisave account and place of death as predictors.

To study possible predictors of, patient awareness of and preferences for diagnostic and prognostic information, awareness and utilisation of palliative care services, preferences for treatments and decision making, perceived quality of care, self-care, hand grip strength, and caregiver psychological distress and burden we will use mixed-effect generalised linear models.

Lastly, we will assess the relationship between hand-grip strength and mortality using both parametric and semi-parametric survival analysis approaches.

Patient and public involvement

Patients, patient advisors and public were not involved in the development of the research questions or in the design of the study. Patient involvement in the study includes answering survey questionnaires at baseline and at each follow-up. Results will be disseminated to patients and public through mass media releases.

DISCUSSION

The primary objective of this study is to describe trajectories of quality of life of patients with advanced CHF and their caregivers, and to quantify healthcare utilisation and costs of patients as they transit between care settings. We believe this study will be an important milestone in presenting a comprehensive picture of the experiences of patients with advanced CHF and their families including those during the patients' EOL period. These results will be used for policy analysis and for generating recommendations for ways to improve care, which can then be tested in future studies.

The study will allow us to describe trajectories of each outcome from the point of their enrolment into the study till they pass away. Describing and analysing time invariant and time variant factors that predict improvement or deterioration in these trajectories will help identify potentially modifiable risk factors for future interventions as well as patients/caregivers at risk of having these poor outcomes. Overall, this will help plan specific services, including those during the patients' EOL period, to address deterioration within each quality of life domain.

By mapping healthcare utilisation, transitions in healthcare settings and expenditures at different care settings at EOL, and the factors associated with each, we will predict future healthcare spending and develop models of care that will help improve continuity for care services, reduce burdensome interventions for patients, improve patient satisfaction with care received, reduce healthcare costs while improving patient's quality of life at the same time.

Assessing patient and caregiver awareness and preferences for diagnostic and prognostic information, their treatment preferences and their current and preferred involvement in decision making will inform development of decision aids and tailoring interventions to help patients receive the information they desire, to be involved in treatment decisions to the extent that they want and to receive treatments consistent with their preferences.

The study is challenging in that it aims to recruit a large number of patients with advanced CHF from two hospitals in a short period of time. However, we have a multidisciplinary research team that brings the experience required to successfully complete the proposed study. Attrition may be a problem. We try to minimise this through appropriate participant incentives and scheduling interviews at a time and place convenient for patients. This study was initiated in July 2017. We expect to recruit our target sample size by October 2018, and follow-up assessments to continue for at least 2 years.

To summarise, SCOPAH is a cohort study of patients with advanced CHF and their caregivers that will longitudinally capture the natural history of this illness among Singaporean patients, their healthcare preferences, experiences, utilisation and costs at the EOL. The data generated will help identify interventions and policies aimed to improve EOL experience of patients with advanced CHF in Singapore through expansion and delivery of palliative care services integrated with specialist care services.

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Competing interests None declared.

Patient consent Obtained.

Ethics approval This study was approved by the SingHealth Centralised Institutional Review Board (2016/3046).

Provenance and peer review Not commissioned; externally peer reviewed.

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