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Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers, with Palliative Care (TIER-HF-PC) – a study protocol

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TITLE PAGE

Full title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers, with Palliative Care (TIER-HF-PC) – a study protocol

Short title:

TIER-HF-PC: evaluation of a needs-based patient directed model of care

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Key words: palliative care, heart failure, randomized controlled trial, health coaching, screening

Abstract (word limit 300)

Background

Palliative care (PC) improves quality-of-life (QOL). However, PC is currently delivered "too little, too late" in heart failure (HF).

Aims and Hypothesis

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers, with Palliative Care (TIER-HF-PC) is a novel, nurse coach-led model of PC that integrates PC into HF care. We will compare the effectiveness of TIER-HF-PC against usual care for improving patient and caregiver health outcomes. We will also evaluate implementation outcomes (such as care experience) of TIER-HF-PC.

Methods

In TIER-HF-PC, patients undergo regular distress screening. Intensity of PC treatments will be tiered based upon the severity of problems detected. Minimally, all patients will receive PC education resources. Patients with moderate-intensity needs will receive PC health coaching. Patients with high intensity needs will receive a PC physician consultation, on top of PC health coaching. Patients in usual care are not screened but can be referred to a PC physician based upon cardiologist discretion.

We will recruit 240 English or Mandarin-speaking patients with HF and up to 240 caregivers from 3 sites across 2 cardiac centers. Patients will be randomized in a 1:1 ratio to TIER-HF-PC or usual care. We will utilize an intention-to-treat approach for data analysis. Our primary outcome is patient QOL on Kansas City Cardiomyopathy Questionnaire at 24 weeks. Secondary outcomes include patient healthcare utilization, caregiver QOL, and cost-effectiveness. All participants who received palliative care treatments will receive a service evaluation survey. Additionally, a sample of these participants and their treating healthcare staff will be purposively recruited for in-depth semi-structured interviews on their TIER-HF-PC experience. Interviews will be thematically analyzed. We will evaluate protocol fidelity through case notes and study processes audits.

Significance

An effective, satisfactory, TIER-HF-PC model of care allows timely, needs-based PC integration, improving QOL and other outcomes.

Strengths

- Assessment of implementation outcomes, in addition to health outcomes
- Adequately powered study
- Recruitment from more than 1 site, allowing generalizability of results

Limitations

- Limited to English and Mandarin speaking patients, with potential to expand to Asian patients speaking other languages in future

Ethics and dissemination

This study was approved by the SingHealth Institutional Ethics Review Board- review number: 2024-2213. Results of the study will be disseminated when data analysis is complete.

Trial registration

This study was registered on clinicaltrials.gov (trials ID: NCT06244953)

Main paper

Introduction

Heart failure is a serious, life-threatening condition that threatens the well-being of approximately 26 million people worldwide [1]. In Singapore, cardiovascular disease is a common cause of death, accounting for 30.9% of all deaths in 2023 [2]. The illness trajectory of heart failure is undulating and unpredictable, with the risk of sudden death increasing exponentially as heart failure progresses towards its advanced stages [3-5]. Patients with advanced heart failure have high physical and psycho-emotional burden, poor quality-of-life, and are prone to recurrent hospitalizations, especially at the end of life [6-8]. Besides the distress heart failure places on patients, caregivers also have significant caregiving burden, which increases as heart failure advances [9].

Palliative care is an approach that improves the quality-of-life of patients and their families who are facing problems associated with life-threatening illness [10]. Palliative care interventions for heart failure in cohort studies and pilot studies have been shown to improve patient-centred outcomes, documentation of preferences, and reduce inappropriate healthcare utilization [11]. There are strong recommendations from European, American, and Singaporean heart failure societies for palliative care to be integrated as early as possible, from the point of diagnosis of symptomatic heart failure, to death and bereavement [12-16]. According to the 2014 World Health Assembly mandate, all governments should aim to "strengthen palliative care as a component of comprehensive care throughout the life course" [17]. The Singapore Ministry of Health in its 2022 work plan for a healthier Singapore similarly exhorted the healthcare workforce to improve palliative care provision for all patients, as well as embrace holistic approaches to improve wellness for patients and their caregivers [18].

However, despite the strong mandate and need for palliative care [19], patients with heart failure receive palliative care "too little, too late". In Singapore, the National Palliative Care Minimum Data set (MDS) was developed to provide information on the longitudinal trends of the demographic and clinical profile of patients who receive palliative care [20]. In the 2022 MDS report, it was estimated that patients with non-cancer diagnoses such as heart failure, the median time from first specialist palliative care assessment to death was only 9 days [20].

There are multiple reasons why patients receive palliative care "too little, too late". First, current palliative care services are heavily dependent on a scarce resource of specialist palliative care clinicians. Palliative care reviews are comprehensive and holistic, which is often an intensive "all-or-nothing" approach for palliative care delivery. As a result, current palliative care services will not be able to scale up quickly enough to support the rapidly growing and changing needs of the heart failure population [21-22]. Second, palliative care service provision is dependent on cardiologist referring practices. Current cardiology practices for referring to palliative care differ widely [23-24], and there are no mechanisms in place that systemically support cardiologists to know when the opportune moment would be to refer palliative care. Third, there currently does not exist a system for regular screening of patients for needs to allow proactive engagement of patients and caregivers prior to crises. [25] Palliative care services are often referred only when symptoms are escalating and uncontrolled, limiting the window of opportunity in which palliative care can make a significant difference.

Therefore, our team developed a novel model of palliative care - Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC). TIER-HF-PC is a tiered model of palliative care, that is led by a nurse coach who has background training in palliative care, with support from a specialist palliative care physician. In TIER-HF-PC, patients will undergo regular distress screening. The type and intensity of palliative care treatments will be subsequently tailored to the type and severity of problems reported. The coach will also engage and empower patients and their caregivers to take a proactive approach to their care.

TIER-HF-PC is a complex intervention [26-27] with multiple interacting components (screening for needs, tailoring of treatments, provision of treatments). The incorporation of a screening mechanism to detect concerns of patients with heart failure reduces dependency on heterogenous cardiologist referral patterns. At the same time, the allocation of palliative care resources according to needs allows specialist physician resources to be preserved for those who are in severe distress, without compromising access to lower intensity palliative care treatments. The use of health coaching as a palliative care treatment allows patients and caregivers to be actively engaged in self-care as a strategy, rather than healthcare services being deployed reactively during times of crises.

To evaluate TIER-HF-PC, we will conduct a two-armed parallel group, open label, randomized controlled trial. The overall aim of this study is to test the effectiveness and implementation of the interacting components in TIER-HF-PC. [28]

Our specific aims include to evaluate the:

1) Impact of TIER-HF-PC on patients reported outcomes
2) Impact of TIER-HF-PC on caregiver reported outcomes
3) Care experience in TIER-HF-PC
4) Implementation fidelity of TIER-HF-PC
5) Impact of TIER-HF-PC on health care utilization and survival
6) Cost effectiveness of TIER-HF-PC.

We hypothesize that TIER-HF-PC will be superior to usual care in improving patient and caregiver quality-of-life. We also hypothesize that patients and caregivers will be satisfied with the interventions in TIER-HF-PC, while recognizing that specific process modifications might be needed to improve the implementation of TIER-HF-PC.

Methods

Study design

We will conduct a randomized controlled trial comparing TIER-HF-PC (intervention arm) against usual care (control arm) amongst 240 patients with heart failure, and up to 240 caregivers.

Study setting

Recruitment will take place at two cardiac centres across 3 sites: The National Heart Centre Singapore (NHCS), a national and regional referral centre for cardiology which has two campuses/recruitment sites (Outram in the central region and Sengkang in the north-east region) [29] and Khoo Teck Puat Hospital (KTPH), a 795-bed general and acute hospital in the northern region of Singapore [30]. NHCS manages over 120,000 outpatient consultations each year whilst KTPH serves over 550,000 people in their region. In NHCS, patients who require palliative care at the Outram campus are referred to palliative care services from the National Cancer Centre Singapore (NCCS) [31], and patients who require palliative care at the Sengkang campus are referred to the palliative care service in Seng Kang Hospital. [32] In KTPH, patients who require palliative care are referred to the palliative care department in KTPH.

Study participants

Inclusion criteria for patients: (i) 21 years or older and (ii) able to communicate in English or Chinese and (iii) be of stage C or D heart failure, as defined by American College of Cardiology/American Heart Association (ACC/AHA) classification system and (iv) have functional limitation of New York Heart Association (NYHA) functional status of at least 2 or worse and (v) be deemed by their cardiologist's clinical judgement to have an expected prognosis of at least 6 months survival, and (vi) have had a heart failure related hospitalization event (e.g. symptomatic decompensated heart failure) within 6 months prior to recruitment and (vii) have a phone that allows telecommunication. Criteria (iii) to (vi) are based on medical records documentation. Cardiologists can use current literature on prognostication to guide their clinical prognostication. [33-34]

Exclusion criteria for patients: Participants who have (i) cognitive impairment (e.g., dementia) (ii) severe, untreated, active mental illness (e.g., major depressive disorder) or (iii) ventricular assist device implant or (iv) non-reversible hearing or visual loss or (v) active drug abuse or (vi) already known to a palliative care service. Criteria (i) to (vi) will be based on medical record documentation.

*Inclusion criteria for caregiver*s: We will recruit the direct, unpaid, family caregiver of the patient, who is self-reported by the patient to be the main person to be either responsible for up to 4 hours a day of caregiving tasks and/or decision maker/spokesperson with the medical team [35-36]. This caregiver may or may not live in the same residence as the patient. Caregivers must be 21 years or above and be able to communicate in English or Chinese.

Exclusion criteria for caregivers: Participants who have self-reported (i) cognitive impairment (e.g., dementia) or (ii) severe, untreated, active mental illness (e.g., major depressive disorder) or (iii) non-reversible hearing or visual loss (iv) active drug abuse or (v) are a domestic helper for the patient.

Recruitment

A research coordinator will screen the clinic lists of participating cardiology clinics to identify potentially eligible patients. Patients can also be referred to the research coordinator from the study team investigators. The research coordinator will then approach these patients during their visits to the study sites to confirm their eligibility and obtain informed consent. Research coordinators will not be involved in their clinical care. Participants can be recruited in patient-caregiver dyads, or as patients alone.

Randomization

Patient participants will be randomized in a 1:1 ratio to either the TIER-HF-PC intervention or usual care. If the patient's caregiver is also recruited, he/she will follow the patient's allocation assignment. Patients will be randomized using the permuted block technique, stratified by recruitment site and by whether patient has a participating caregiver. The randomization scheme will be generated by an independent statistician, with block size kept unknown to the clinical investigators as per the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines. A randomizer who does not participate in the recruitment procedures will reveal the allocation status (generated by the statistician) to the research coordinator. Allocation status will only be made known to the research coordinator after informed consent is taken for the participants. Participants will not be blinded to their allocation status.

Usual Care

Guided by the National institutes of Health (NIH) consensus panel recommendations [37], usual care will be the best comparator to test whether patients with heart failure and their caregivers can be better supported beyond what is currently offered. Patients in usual care will continue to receive clinical care by their cardiologist. If their cardiologist picks up their symptoms or other concerns, they can be referred to a specialist palliative care physician by the cardiologist.

TIER-HF-PC

Figure 1 shows the TIER-HF-PC structure. Every 4 weeks, patients will be screened using the distress thermometer (DT). [38-40] This screening will last for a total of 24 weeks from baseline recruitment. The screening results will be used to inform the tier of care that they will receive. If a caregiver is recruited together with the patient, the caregiver will be placed in the same tier as the patient.

Patients with DT score ≤ 3 will be triaged to the first tier (lowest needs). This is consistent with the cut-off score of 4 being the optimal score for screening for patients whose distress level warrants palliative care. [40]. Patients who have a DT score ≥4 will be further assessed with the Integrated Palliative Care Outcome Scale (IPOS) [41] to allow characterization of the palliative care issue. Patients with slight to moderate problems on the IPOS will be triaged to the second (moderate needs) tier whilst those with severe to overwhelming problems on the IPOS will be triaged to the third (highest needs) tier. Intensity of palliative care interventions will be matched accordingly to the tier with the highest tier requiring the most palliative care intervention. As screening will occur every 4 weeks, should DT scores increase during the period of screening, patients can be escalated up the tiers accordingly. Patients in TIER-HF-PC will continue to receive clinical care from their cardiologist.

Procedures for the screening process

The DT will be first be sent *via* text message by the study coordinator. However, if the patient does not respond within the same day, follow-up phone calls for 3 consecutive working days (up to twice a day) will be made by the research coordinator, to ensure we will receive the DT results are captured in a timely manner. All patients will be contacted by the nurse coach within 3 days of receiving their DT score, so that patients can be further assessed with the IPOS and a timely decision about their tier-placement can be made.

In all three tiers, participants will be given English or Chinese educational resources. This can be given either in hard copy or soft copy, by the research coordinator.

Further details on the tiers follows:
First tier (lowest needs): Educational resources will contain information on palliative care services, management of heart failure symptoms and co-morbidities, and practical information on caregiving resources in Singapore. These resources have been used in our prior research studies. [42-44]
Second tier (moderate needs): The health coach will start coaching with patients and their caregivers within 1 week of IPOS screening. Health coaching sessions for patients and caregivers will be

conducted separately whenever possible, to ensure patients and caregivers have enough privacy and time to work with the health coach. Depending on the technological literacy and logistical availability of the participants, health coaching can be conducted using videoconferencing methods, over the phone, or face-to-face. Each health coaching session is expected to last about 1 hour. We anticipate the health coaching to last over a period of 4 to 8 weeks. After completion of health coaching, patients and caregivers will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on concerns and reinforce skills taught during coaching. The nurse coach will also facilitate participants to initiate contact back, should concerns arise out of the coaching period. During the coaching period, should a patient have severe or overwhelming concerns, the nurse coach will escalate palliative care support to the third tier.

Content of health coaching (patient): A structured manual for health coaching will be used. This manual has been prior adapted [42,45-46] from the (Educate, Nurture, Advise, Before Life Ends, or ENABLE) program in the U.S.A. [47-53] The ENABLE program is a nurse-led palliative care and health coaching program. The culturally adapted ENABLE topics are "maintaining positivity and problem solving", "self-care", "coping with stress and spirituality", "symptom management", "talking about what matters most, making choices" and "sharing your journey and legacy". The sequence of the ENABLE topics will be individualized, based upon patient's requests and results on the IPOS.

Content of health coaching (caregiver): Health coaching topics for caregivers are "maintaining positivity and problem solving", "self-care", "coping with stress and spirituality", "being a partner in managing symptoms".

Third tier (highest needs): Patient participants will be reviewed by a specialist palliative care physician within 1 week of IPOS screening. There will be structured assessments by the physician to evaluate their physical, emotional, and social problems, with the specific purpose of allowing medication titration and referrals to other clinical services as necessary. Physician review will be done face-to-face whenever possible. Alternative methods for consulting include video-consultation, with the caveat that patients who need physical examination would be called back to the hospital for physical consult, should the physician deem necessary. After completion of physician review, participants will receive health coaching and follow-up, as per what is done for participants in the second tier.

Participants in all 3 tiers who are still alive after week 48 will be transited by the nurse coach to relevant services in current care. This transition will be determined by their needs, and in consultation with the palliative care physician.

Study instruments and data collection procedures

Collection procedure

All patient and caregiver reported outcome measures will be collected over the phone, by the study research coordinator. If participants are not contactable over the phone despite attempts, we will collect the outcome measures face-to-face to ensure timely data collection and to minimize missing data.

Study instruments for patients only:

Cardiac specific Quality-of-life (QOL) measure: Kansas City Cardiomyopathy Questionnaire (KCCQ-12), [54-55] a 12-item QOL scale, composed of physical function, symptoms, QOL, social interference and a summary score. It is validated in the cardiac population and commonly used in cardiology trials for assessment of QOL. The KCCQ-12 has similar validity to the 23-item version and is shorter with less respondent burden. [55] The KCCQ-12 can be self-reported by patients or read to patients over the phone by a research coordinator. The total summary score can range from 0 to 100, with higher scores representing better health status. A clinically meaningful change is defined as a change of at least 5 points on the KCCQ. [56] The KCCQ-12 will be measured every 8 weeks from baseline, till the point of patient death, or till week 48, whichever is earlier. The frequency of our proposed KCCQ tracking is referenced from trials which used KCCQ to track longitudinal changes in QOL. [56]

Non-cardiac specific health-related quality of life: EUROQOL EQ-5D-5L [57-59] provides a global assessment of the patient's quality-of-life in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It can be administered over the phone. [58] Each patient's health state utility can be derived from their responses to the 5 dimensions.

Hospital Anxiety and Depression Scale (HADS) [60]: A 14-item scale with a score range of 0 to 42, that can be administered over the phone [61]. It is composed of two subscales- anxiety and depression- with a cut-off point of 11 for each subscale, that determines anxiety and depression of clinical significance.

Study instruments for caregivers only

Singapore Caregiver Quality of Life Scale -15 (SCQOLS-15): a 15-item scale with 5 domains measuring QOL of life caregivers in domains: physical well-being, mental well-being, experience and meaning, impact on daily life, and financial well-being. [62-64] This will be measured every 8 weeks from baseline, till the point of patient death, or till week 48, whichever is earlier.

Study instruments for patients and caregivers

Brief Coping with Problems Experienced (Brief-COPE) scale [65]: A 28-item scale measuring the ways people cope with stressful events. It has been used in the heart failure population, where the coping style was shown to correlate with the level of physical functioning. [66]

Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being 12 Item Scale (Facit-SP-12) [67]: A 12-item survey that measures the spiritual well-being of patients and caregivers. The Facit-SP-12 has been used as a secondary outcome measure in the palliative care population for heart failure trials. [68] The total of Facit-SP-12 ranges from 0 to 48 with higher scores representing increased spirituality.

Data collection on experience on TIER-HF-PC and its acceptability

Client Satisfaction Questionnaire (CSQ-4) [69]: A 4-item scale consisting of 3 items (measuring the experience of the client with a program) and an item measuring improvement in client self-efficacy. This service evaluation questionnaire will be measured for participants randomized to TIER-HF-PC. The CSQ-4 has been used as an outcome measure in our prior studies [42-43,70] and has also been used in other studies to evaluate health services programs. [71] The CSQ-4 can be administered over the phone.

Semi-structured interviews: We will purposively recruit patients, caregivers from TIER-HF-PC and healthcare staff whose patients were managed using TIER-HF-PC. To capture diverse views across different demographics, functional status (patients only), background specialty (palliative care versus heart failure, physician versus nurse) and years of clinical experience (healthcare staff only), we will utilize purposive and iterative sampling techniques. An interview guide will be developed based on elements and selected outcomes in Proctor's taxonomy of implementation outcomes, such as acceptability, appropriateness and timeliness and the RE-AIM/ PRISM framework. [72] The RE-AIM framework stands for outcomes such as reach, effectiveness and adoption. The PRISM (Practical, Robust, Implementation and Sustainability Model) framework is complementary to RE-AIM and is used to identify the multilevel contextual factors that affect the implementation outcomes in RE-AIM.

Data collection for assessment of fidelity to the TIER-HF-PC intervention and study procedures

The fidelity to procedures, and extent to which TIER-HF-PC is implemented as planned will follow recommendations from the NIH behavior change consortium [73] and be determined by the following processes measures: (i) number of patients who complete the screening DT and IPOS assessments (ii) percentage of patients and/or caregivers who manage to complete health coaching sessions and specialist palliative care physician review, according to their assigned tier (iii) case note audit and review of clinical entries by TIER-HF-PC staff. All clinical entries by nurse coach and specialist palliative care doctor that were entered into the electronic healthcare notes from NHCS and KTPH will be audited to review the main themes of palliative care treatments that were covered during specialist palliative care review and health coaching. Due to the anticipated high load of clinical entries, we will audit using the techniques of natural language processing (NLP). [74-75]

Data collection on healthcare utilization

We will collect data on referral to community palliative care services and other community support services that patients in both arms might utilize, such as community nursing services. The date and number of hospital admissions, hospital length of stay for each admission, number of emergency department visits, number and length of intensive care unit admissions and date and location of death will also be collected. We will track if usual care patients are referred to palliative care consult services.

Data collection on health care cost

We will collect data on the cost of hospitalization bills, emergency department bills and outpatient bills from the hospital record systems. We will also estimate the cost of healthcare provision, based upon estimated time staff spend on caring for patients within this trial.

Figure 2 describes a diagram of our study flow and timeline for data collection procedures.

Statistical justification

Sample size calculation

For the purposes of evaluation of primary outcome- assuming a common standard deviation of 12 points for the KCCQ overall summary score, [68] the planned sample size will be 200 subjects (100 per arm) to provide 80% power at 5% two-sided type 1 error rate, to detect a difference of 5 points at 24 weeks, which is the smallest change that is clinically significant at the individual patient level. [51] To account for dropouts and attrition, we will aim to recruit 120 patients per arm (240 patients). As caregiver recruitment is based on the patient sample, we will aim to recruit up to 120 caregivers per arm (up to 240 caregivers). We estimate we will recruit 80% of the participants from NHCS campuses (192 patients and 192 caregivers), and 20% of the participants (48 patients and 48 caregivers) from KTPH. Based on screening logs from previous studies recruiting similar patients from same settings, it is estimated that there will be 40 eligible patients per month. Assuming a recruitment rate of 50% and 20 patients recruited per month, the sample size could be achieved within 12 months. A more conservative estimation of a 40% recruitment rate (16 patients are recruited per month) would allow us to achieve the required sample size within 15 months. For the semi-structured interviews, based upon our prior research in the same setting, [76-78] we will reach data saturation by 30-40 patients, 30-40 caregivers, and 30 staff across two sites. These will be our target sample sizes.

Analysis of patient and caregiver outcome measures

We will adopt the official scoring method to obtain the summary scores and domain scores of the various questionnaires – KCCQ-12, SCQOLS-15, HADS, EQ-5D-5L, Facit-SP-12,; subject to imputation for item nonresponse by the "half rule", if applicable. Descriptive statistics, and measures of effect size will be used to compare the study groups at baseline, 8 weeks, 16 weeks, and 24 weeks. Analysis will follow an intention-to-treat principle. Longitudinal data analyses will be conducted to examine intervention effects using linear mixed-effects-modelling for repeated measures at baseline, 8 through 16 and 24 weeks, constraining the baseline mean to be equal between intervention and control groups with indicators for time, group, and time by group interactions. Mixed-effects models using maximum likelihood estimation provide robust estimate despite missing values or early dropouts if the data are Missing Completely At Random or Missing At Random. [79] Estimate of standard deviation of residuals from the mixed-effects model will be used to compute effect sizes (Cohen's d). We will also chart the trajectories of quality of life from baseline till patient death or week 48 whichever is earlier, to evaluate the differences in quality-of-life across time between arms. In addition, we will perform pre-planned subgroup analyses, to evaluate associations of outcomes with variables including recruitment site, time since diagnoses of heart failure, NYHA status, and number of palliative care health coaching and physician review sessions received. We will also examine changes in coping style over time, using BRIEF-COPE scores as an outcome.

Assessment of experience with TIER-HF-PC

The total score of the CSQ per participant will be computed. We will analyze patient and caregiver scores separately and will calculate the percentage of participants in TIER-HF-PC who have at least a CSQ score of 12 and above, which indicates good experience with care.

Regarding the analysis of semi-structured interviews, we will form a qualitative coding team (consisting of 2 research coordinators, the principal investigator and a co-investigator. All members of the coding team will be required to have training in qualitative analysis. All audio-taped interviews will be transcribed verbatim by our research coordinators, and the accuracy of each transcript cross-checked by another research coordinator. Interviews conducted in Chinese will be translated to English prior to analysis by the coordinators. Coding of up to 30% of our interviews will be initially undertaken by both research coordinators to ensure inter-coder reliability in accordance with current guidelines. [80] Coding will subsequently be done independently by the 2 coordinators once inter-coder reliability is established. Interviews will be open coded line by line. Code categories will be developed and iteratively adjusted through discussions. The code categories will be subsequently mapped back to the main domains of the RE-AIM and PRISM framework to identify key multi-level contextual factors influencing the TIER-HF-PC outcomes as well as to assess the adoption, implementation, and impact of TIER-HF-PC. Hence, the analysis will involve both inductive and deductive approaches.

Analysis of fidelity to TIER-HF-PC

For the purpose of auditing TIER-HF-PC, we will follow guidance from literature for auditing using NLP. [74-75] A sample of 30% of extracted medical notes will be annotated, to highlight keywords/phrases and develop a standard codebook that will delineate the specific components of our palliative care health coaching and physician treatments. These will include documentation around: self-care, symptoms, psycho-emotional concerns, spirituality, decision making, care planning, financial and legacy planning. Regarding the NLP techniques, we will leverage on a class of models pre-trained on vast electronic health records. Among these are ClinicalBERT, [81] BioBERT,[82] BioMegatron, [83] and GatorTron [84] which have been shown to be performant on clinical concept extraction, natural language inference, medical question answering, and semantic textual similarity tasks. We propose the use and exploration of these models as feature extractors in conjunction with other traditional machine learning models (i.e., tree-based models) for downstream classification of interview notes into concepts relevant to the TIER-HF-PC objectives. The feature extraction step uses the model to transform an input (i.e., text) into an array of numbers that hold information about the input's structure and semantics from medical notes. This approach leverages existing pre-trained models to form the corpus necessary for fine-tuning of specific use cases, in this case, the auditing of TIER-HF-PC clinical notes. For the development of the automated audit algorithm, the annotated notes will be split into 80% training and 20% test datasets for the development of the NLP algorithm. Validation will be based on the 20% of data unseen in the training phase. If the machine-annotated notes appear out of context, they will be examined, and the code book will be tuned accordingly. We will report on the sensitivity, specificity, area under the receiver operating curve (AUROC), F1-Score and the area under the precision recall curve (AUPRC). Once the target performance is achieved, we will run the software to annotate the remaining 70% of the medical notes.

Assessment of impact of TIER-HF-PC on healthcare utilization and survival

We will estimate the differences in community hospice usage, number and length of hospital admissions, number of emergency visits, number, and length of intensive care visits between TIER-HF-PC participants and those in usual care using generalized linear models, with binomial model for community hospice usage and Poisson model with robust standard effort for other healthcare utilization outcomes.

We will quantify the differences in survival between TIER-HF-PC and usual care by Cox model, censoring at week 48 or death, whichever occurs earlier.

Healthcare cost analysis

We will sum up the total cost of inpatient bills and outpatient bills including emergency visit bills for TIER-HF-PC participants and usual care participants from week 1 to week 24 and quantify the cost differences between both groups by generalized linear model with Gamma model and robust standard error. The net cost of TIER-HF-PC will be calculated based upon the cost of care provision in TIER-HF-PC minus the cost savings from the reduction in health care utilization. We will also calculate incremental cost-effectiveness ratios (ICERs) to measure the average net cost per quality-adjusted-life-year (QALY) gained for TIER-HF-PC versus usual care participants. The QALY will be calculated by the product of quality-of-life (EQ-5D-5L) and survival.

Fidelity, standardization, and monitoring

The study team at NCCS will remain responsible for keeping track of the overall study recruitment rate, randomizing participants, and managing data collection, cleaning, and analysis. The data monitoring committee will include the study principal investigator, the statistician, and the site principal investigators. Access to data set is governed through a data sharing agreement with all participating investigators in the study team, governed by the study principal investigator, as per institutional rules. The study principal investigator will coordinate study logistics through regular site meetings between NCCS, NHCS and KTPH. These will ensure timely solving of recruitment, retention, and other study issues. Health coaches will have mandatory training using current available resources for ENABLE coaching training prior to the start of TIER-HF-PC. They will utilize checklists to ensure the coaching and assessments are standardized. They will also have monthly meetings with the PI to troubleshoot problems that arise during the process of health coaching and assessment.

Participant safety

Provisions will be made to recruit patient participants after their acute heart failure exacerbations have been resolved. Participants might be emotional during health coaching and palliative care physician

review. If this occurs, the principal investigator will refer to existing clinical networks for emotional support. Participants will be allowed to withdraw from the program at any point in time if requested.

Ethics

This study has been approved by the SingHealth institutional ethics review board- study review number 2024-2213. All participants must sign informed consent prior to participation and privacy of data will be adhered to as per institutional requirements.

Patient and public involvement

We did not involve any patients or member of the public in the design of this trial.

Discussion

We describe a novel tiered model of palliative care which we aim to evaluate if it could be effective in improving outcomes in patients with heart failure and that of their caregivers. Besides effectiveness, we also aim to determine if this model of care would be acceptable, cost-effective, and can be implemented with fidelity. In this study, we will also be utilizing novel methods of analysis such as NLP to audit TIER-HF-PC.

Empowering patients to self-care through nurse-led early palliative care, [47-53] and implementation of regular symptom monitoring in patients with advanced illness have been studied in various studies separately, but there has not been a model of care that has effectively evaluated if patient-reported screening measures can be used to trigger and personalize the type and intensity of palliative care treatments. We believe that TIER-HF-PC is the first and will bring novel insights into how we can provide palliative care most sustainably for a rapidly aging population and workforce. TIER-HF-PC allows us to evaluate if limited specialist resource can be directed at those most in need whilst ensuring that all patients have access to a patient determined, appropriate level of palliative care, delivered through established care escalation pathways and regular screening.

We do anticipate challenges within this study, such as differing levels of technological literacy within our participants, thus we have allowed for both telehealth and face-to-face methods for conducting the palliative care treatments in TIER-HF-PC. We also anticipate that there might be difficulty recruiting caregivers face-to-face, as not all caregivers would accompany patients to their outpatient appointments. Therefore, we will contact caregivers *via* the phone and allow mail-back options for consent. We are also allowing for recruitment from two cardiac centres with access to three campuses, to have a larger population of patients with heart failure to recruit from and strengthen the overall generalizability of our study to different healthcare settings. To minimize trial dropouts, we will utilize phone-based collection of outcome measures to reduce trial fatigue.

If TIER-HF-PC is shown to be beneficial, we will iterate and disseminate TIER-HF-PC to other care settings for heart failure care in the medium-term. In the long-term, TIER-HF-PC can potentially be expanded to other serious life-limiting illnesses that have limited palliative care access. These will include non-cancer illnesses such as chronic kidney disease, chronic respiratory disease, and chronic neurological disease.

Conclusion

TIER-HF-PC is a novel model of care that allows us to deliver timely, personalized palliative care, at an intensity that matches the severity of patient-reported problems. Our study will evaluate if this model of care improves quality of life, is acceptable, cost-effective and can be implemented with fidelity to the planned study protocol.

If TIER-HF-PC is shown effective, it has the potential to be expanded to other settings of care for heart failure, as well as other serious illnesses. This will allow us to achieve our long-term goal of improving quality of life of all patients with serious illness, in a manner that is cost-effective and sustainable.

Acknowledgements

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Data availability: Data from this study will not be posted on any data repository.

Dissemination of results: Results of this study will be disseminated upon completion of data analysis. This manuscript, or any related manuscript, is not currently under consideration or accepted elsewhere

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Trial registration: clinicaltrials.govID NCT06244953. Registered in January 2024.

Current protocol version: Version 1.0, version date 25th December 2023**.** Any protocol modifications will be updated on clinicaltrials.gov

Ethics board approval reference number: SingHealth ethics review board: 2024-2213

Supporting instruments- SPIRIT checklist

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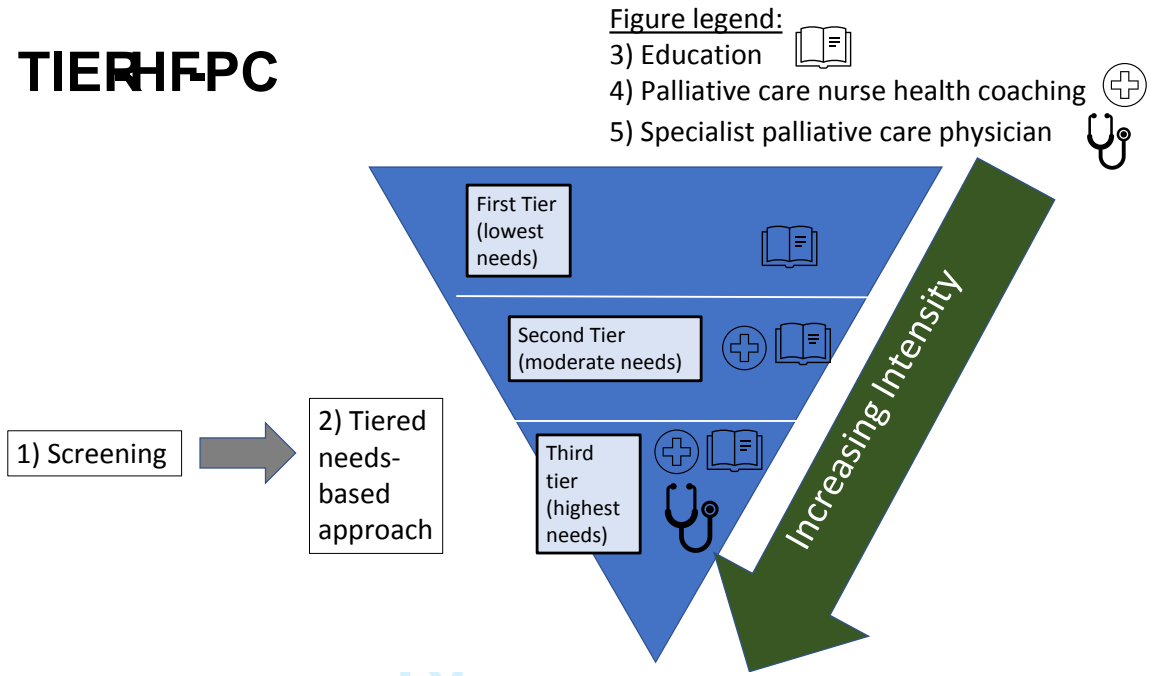
Figure 1- Components of TIER-HF-PC

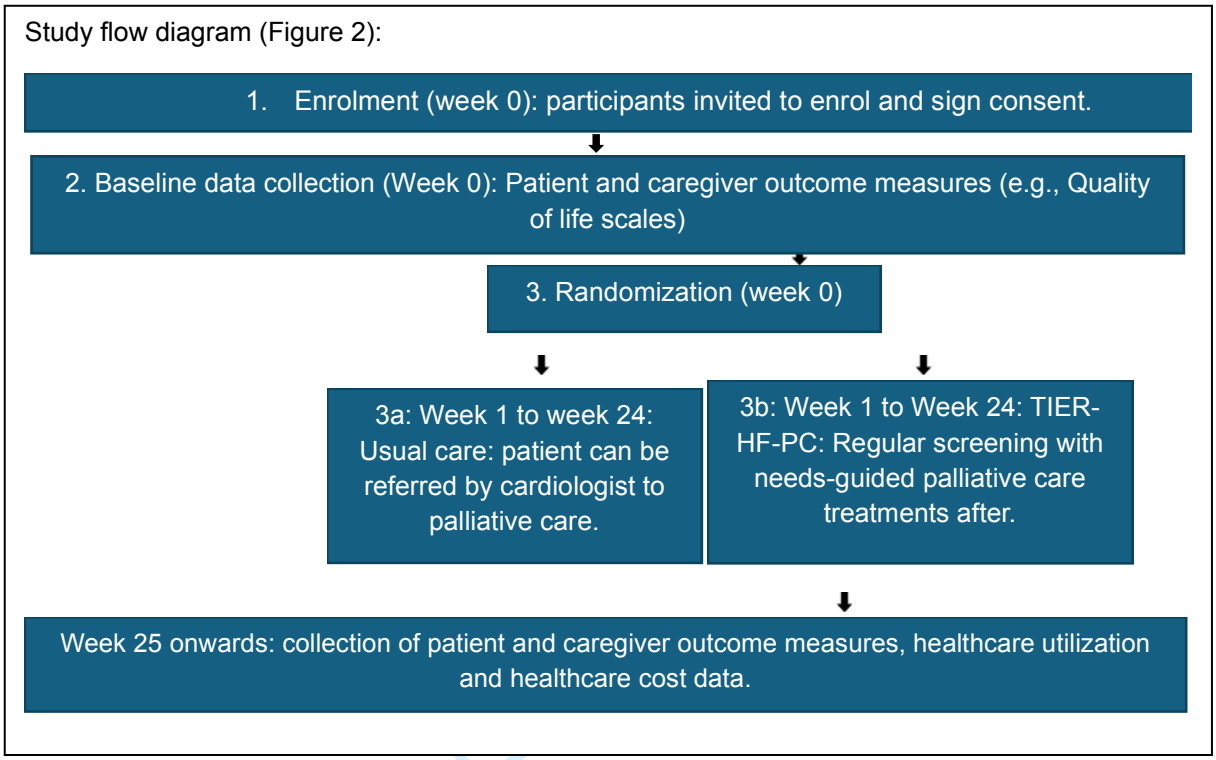


First tier: Distress thermometer (DT) < 4

Second tier: DT ≥4, Integrated Palliative Care Outcomes Scale (IPOS) slight to moderate problems

Third tier: DT ≥ 4, IPOS severe to overwhelming problems

Figure 2– Study flow diagram



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1 of title page
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Cover letter to editor, page18 of manuscript
	2b	All items from the World Health Organization Trial Registration Data Set	Page 2 of title page
Protocol version	3	Date and version identifier	Page 18 of manuscript
Funding	4	Sources and types of financial, material, and other support	page 18 of manuscript
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	title page
	5b	Name and contact information for the trial sponsor	page 18 of manuscript
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	page 18 of manuscript

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Methods, page 15 of manuscript
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Introduction, page 3 of manuscript
	6b	Explanation for choice of comparators	Methods, page 7 of manuscript
Objectives	7	Specific objectives or hypotheses	Introduction, page 5 of manuscript
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Methods, page 5 of manuscript
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Methods, page 5 of manuscript
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Methods, page 6 of manuscript
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Methods, page 7-9 of manuscript
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Methods, page 16 of manuscript

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Methods, page 15 of manuscript
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Methods, page 7 of manuscript
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Methods, page 10-11 of manuscript
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Methods, page 11-12 of manuscript
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Methods, page 15 of manuscript
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Methods, page 6 of manuscript
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Methods, page 7 of manuscript
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Methods, page 7 of manuscript
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_methods page 7 of manuscript

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Methods page 7 of manuscript
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Not applicable
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Methods page 9-11 of manuscript
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Methods page 15 of manuscript
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Methods page 15 of manuscript
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Methods page 12-13 of manuscript
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Methods page 12-13 of manuscript
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	methods page 12-13 of manuscript
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	methods page 15 of manuscript

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Methods page 12 of manuscript
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Methods page 16 of manuscript
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Methods page 15 of manuscript
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Methods page 16 of manuscript
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Manuscript page 18 of manuscript
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Manuscript page 18 of manuscript
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Methods page 11 of manuscript
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Manuscript page 18 of manuscript
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Methods page 16 of manuscript
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Methods page 9 of manuscript

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Other information, Manuscript page 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	Title page
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset and statistical code	Manuscript page 18
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Attached.
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Interventions to Enable and Reach patients with Heart Failure, and their caregivers, with Palliative Care (TIER-HF-PC) – a study protocol of a two-armed parallel group, open label randomized controlled trial that evaluates the effectiveness of a tiered model of palliative care in tertiary cardiac institutes in Singapore

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TITLE PAGE

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Short title:

TIER-HF-PC: evaluation of a needs-based patient directed model of care

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Key words: palliative care, heart failure, randomized controlled trial, health coaching, screening

Abstract (word limit 300)

Introduction

Palliative care (PC) improves quality-of-life (QOL). However, PC is currently delivered "too little, too late" in heart failure (HF). Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers, with Palliative Care (TIER-HF-PC) is a novel, nurse coach-led model of PC that integrates PC into HF care. We will compare the effectiveness of TIER-HF-PC against usual care for improving patient and caregiver health outcomes. We will also evaluate implementation outcomes (such as care experience) of TIER-HF-PC.

Methods and analysis

In TIER-HF-PC, patients undergo regular distress screening. Intensity of PC treatments will be tiered based upon the severity of problems detected. Minimally, all patients will receive PC education resources. Patients with moderate-intensity needs will receive PC health coaching. Patients with high intensity needs will receive a PC physician consultation, on top of PC health coaching. Patients in usual care are not screened but can be referred to a PC physician based upon cardiologist discretion.

We will recruit 240 English or Mandarin-speaking patients with HF and up to 240 caregivers from 3 sites across 2 cardiac centers. Patients will be randomized in a 1:1 ratio to TIER-HF-PC or usual care. We will utilize an intention-to-treat approach for data analysis. Our primary outcome is patient QOL on Kansas City Cardiomyopathy Questionnaire at 24 weeks. Secondary outcomes include patient healthcare utilization, caregiver QOL, and cost-effectiveness. All participants who received palliative care treatments will receive a service evaluation survey. Additionally, a sample of these participants and their treating healthcare staff will be purposively recruited for in-depth semi-structured interviews on their TIER-HF-PC experience. Interviews will be thematically analyzed. We will evaluate protocol fidelity through case notes and study processes audits.

Ethics and dissemination

This study was approved by the SingHealth Institutional Ethics Review Board- review number: 2024-2213. Results of the study will be disseminated when data analysis is complete.

Registration details

This study was registered on clinicaltrials.gov (trials ID: NCT06244953)

Strengths

- Assessment of implementation outcomes, in addition to health outcomes
- Adequately powered study
- Recruitment from more than 1 site, allowing generalizability of results

Limitations

- Limited to English and Mandarin speaking patients, with potential to expand to Asian patients speaking other languages in future

Main paper

Introduction

Heart failure is a serious, life-threatening condition that threatens the well-being of approximately 26 million people worldwide [1]. In Singapore, cardiovascular disease is a common cause of death, accounting for 30.9% of all deaths in 2023 [2]. The illness trajectory of heart failure is undulating and unpredictable, with the risk of sudden death increasing exponentially as heart failure progresses towards its advanced stages [3-5]. Patients with advanced heart failure have high physical and psycho-emotional burden, poor quality-of-life, and are prone to recurrent hospitalizations, especially at the end of life [6-8]. Besides the distress heart failure places on patients, caregivers also have significant caregiving burden, which increases as heart failure advances [9].

Palliative care is an approach that improves the quality-of-life of patients and their families who are facing problems associated with life-threatening illness [10]. Palliative care interventions for heart failure in cohort studies and pilot studies have been shown to improve patient-centred outcomes, documentation of preferences, and reduce inappropriate healthcare utilization [11]. There are strong recommendations from European, American, and Singaporean heart failure societies for palliative care to be integrated as early as possible, from the point of diagnosis of symptomatic heart failure, to death and bereavement [12-16]. According to the 2014 World Health Assembly mandate, all governments should aim to "strengthen palliative care as a component of comprehensive care throughout the life course" [17]. The Singapore Ministry of Health in its 2022 work plan for a healthier Singapore similarly exhorted the healthcare workforce to improve palliative care provision for all patients, as well as embrace holistic approaches to improve wellness for patients and their caregivers [18].

However, despite the strong mandate and need for palliative care [19], patients with heart failure receive palliative care "too little, too late". In Singapore, the National Palliative Care Minimum Data set (MDS) was developed to provide information on the longitudinal trends of the demographic and clinical profile of patients who receive palliative care [20]. In the 2022 MDS report, it was estimated that patients with non-cancer diagnoses such as heart failure, the median time from first specialist palliative care assessment to death was only 9 days [20].

There are multiple reasons why patients receive palliative care "too little, too late". First, current palliative care services are heavily dependent on a scarce resource of specialist palliative care clinicians. Palliative care reviews are comprehensive and holistic, which is often an intensive "all-or-nothing" approach for palliative care delivery. As a result, current palliative care services will not be able to scale up quickly enough to support the rapidly growing and changing needs of the heart failure population [21-22]. Second, palliative care service provision is dependent on cardiologist referring practices. Current cardiology practices for referring to palliative care differ widely [23-24], and there are no mechanisms in place that systemically support cardiologists to know when the opportune moment would be to refer palliative care. Third, there currently does not exist a system for regular screening of patients for needs to allow proactive engagement of patients and caregivers prior to crises. [25] Palliative care services are often referred only when symptoms are escalating and uncontrolled, limiting the window of opportunity in which palliative care can make a significant difference.

Therefore, our team developed a novel model of palliative care - Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC). TIER-HF-PC is a tiered model of palliative care, that is led by a nurse coach who has background training in palliative care, with support from a specialist palliative care physician. In TIER-HF-PC, patients will undergo regular distress screening. The type and intensity of palliative care treatments will be subsequently tailored to the type and severity of problems reported. The coach will also engage and empower patients and their caregivers to take a proactive approach to their care.

TIER-HF-PC is a complex intervention [26-27] with multiple interacting components (screening for needs, tailoring of treatments, provision of treatments). The incorporation of a screening mechanism to detect concerns of patients with heart failure reduces dependency on heterogenous cardiologist referral patterns. At the same time, the allocation of palliative care resources according to needs allows specialist physician resources to be preserved for those who are in severe distress, without compromising access to lower intensity palliative care treatments. The use of health coaching as a palliative care treatment allows patients and caregivers to be actively engaged in self-care as a strategy, rather than healthcare services being deployed reactively during times of crises.

To evaluate TIER-HF-PC, we will conduct a two-armed parallel group, open label, randomized controlled trial. The overall aim of this study is to test the effectiveness and implementation of the interacting components in TIER-HF-PC. [28]

Our specific aims include to evaluate the:

1) Impact of TIER-HF-PC on patients reported outcomes
2) Impact of TIER-HF-PC on caregiver reported outcomes
3) Care experience in TIER-HF-PC
4) Implementation fidelity of TIER-HF-PC
5) Impact of TIER-HF-PC on health care utilization and survival
6) Cost effectiveness of TIER-HF-PC.

We hypothesize that TIER-HF-PC will be superior to usual care in improving patient and caregiver quality-of-life. We also hypothesize that patients and caregivers will be satisfied with the interventions in TIER-HF-PC, while recognizing that specific process modifications might be needed to improve the implementation of TIER-HF-PC.

Methods

Study design

We will conduct a randomized controlled trial comparing TIER-HF-PC (intervention arm) against usual care (control arm) amongst 240 patients with heart failure, and up to 240 caregivers.

Study setting

Recruitment will take place at two cardiac centres across 3 sites: The National Heart Centre Singapore (NHCS), a national and regional referral centre for cardiology which has two campuses/recruitment sites (Outram in the central region and Sengkang in the north-east region) [29] and Khoo Teck Puat Hospital (KTPH), a 795-bed general and acute hospital in the northern region of Singapore [30]. NHCS manages over 120,000 outpatient consultations each year whilst KTPH serves over 550,000 people in their region. In NHCS, patients who require palliative care at the Outram campus are referred to palliative care services from the National Cancer Centre Singapore (NCCS) [31], and patients who require palliative care at the Sengkang campus are referred to the palliative care service in Seng Kang Hospital. [32] In KTPH, patients who require palliative care are referred to the palliative care department in KTPH.

Study timeline

The study is planned to start on14 August 2024 and is estimated to complete by 31 October 2027.

Study participants

Inclusion criteria for patients: (i) 21 years or older and (ii) able to communicate in English or Chinese and (iii) be of stage C or D heart failure, as defined by American College of Cardiology/American Heart Association (ACC/AHA) classification system and (iv) have functional limitation of New York Heart Association (NYHA) functional status of at least 2 or worse and (v) be deemed by their cardiologist's clinical judgement to have an expected prognosis of at least 6 months survival, and (vi) have had a heart failure related hospitalization event (e.g. symptomatic decompensated heart failure) within 6 months prior to recruitment and (vii) have a phone that allows telecommunication. Criteria (iii) to (vi) are based on medical records documentation. Cardiologists can use current literature on prognostication to guide their clinical prognostication. [33-34]

Exclusion criteria for patients: Participants who have (i) cognitive impairment (e.g., dementia) (ii) severe, untreated, active mental illness (e.g., major depressive disorder) or (iii) ventricular assist device implant or (iv) non-reversible hearing or visual loss or (v) active drug abuse or (vi) already known to a palliative care service. Criteria (i) to (vi) will be based on medical record documentation.

*Inclusion criteria for caregiver*s: We will recruit the direct, unpaid, family caregiver of the patient, who is self-reported by the patient to be the main person to be either responsible for up to 4 hours a day of caregiving tasks and/or decision maker/spokesperson with the medical team [35-36]. This caregiver may or may not live in the same residence as the patient. Caregivers must be 21 years or above and be able to communicate in English or Chinese.

Exclusion criteria for caregivers: Participants who have self-reported (i) cognitive impairment (e.g., dementia) or (ii) severe, untreated, active mental illness (e.g., major depressive disorder) or (iii) non-

reversible hearing or visual loss (iv) active drug abuse or (v) are a domestic helper for the patient.

Recruitment

A research coordinator will screen the clinic lists of participating cardiology clinics to identify potentially eligible patients. Patients can also be referred to the research coordinator from the study team investigators. The research coordinator will then approach these patients during their visits to the study sites to confirm their eligibility and obtain informed consent. Research coordinators will not be involved in their clinical care. Participants can be recruited in patient-caregiver dyads, or as patients alone.

Randomization

Patient participants will be randomized in a 1:1 ratio to either the TIER-HF-PC intervention or usual care. If the patient's caregiver is also recruited, he/she will follow the patient's allocation assignment. Patients will be randomized using the permuted block technique, stratified by recruitment site and by whether patient has a participating caregiver. The randomization scheme will be generated by an independent statistician, with block size kept unknown to the clinical investigators as per the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines. A randomizer who does not participate in the recruitment procedures will reveal the allocation status (generated by the statistician) to the research coordinator. Allocation status will only be made known to the research coordinator after informed consent is taken for the participants. Participants will not be blinded to their allocation status.

Usual Care

Guided by the National institutes of Health (NIH) consensus panel recommendations [37], usual care will be the best comparator to test whether patients with heart failure and their caregivers can be better supported beyond what is currently offered. Patients in usual care will continue to receive clinical care by their cardiologist. If their cardiologist picks up their symptoms or other concerns, they can be referred to a specialist palliative care physician by the cardiologist.

TIER-HF-PC

Figure 1 shows the TIER-HF-PC structure. Every 4 weeks, patients will be screened using the distress thermometer (DT). [38-40] This screening will last for a total of 24 weeks from baseline recruitment. The screening results will be used to inform the tier of care that they will receive. If a caregiver is recruited together with the patient, the caregiver will be placed in the same tier as the patient.

Patients with DT score ≤ 3 will be triaged to the first tier (lowest needs). This is consistent with the cut-off score of 4 being the optimal score for screening for patients whose distress level warrants palliative care. [40]. Patients who have a DT score ≥4 will be further assessed with the Integrated Palliative Care Outcome Scale (IPOS) [41] to allow characterization of the palliative care issue. Patients with slight to moderate problems on the IPOS will be triaged to the second (moderate needs) tier whilst those with severe to overwhelming problems on the IPOS will be triaged to the third (highest needs) tier. Intensity of palliative care interventions will be matched accordingly to the tier with the highest tier requiring the most palliative care intervention. As screening will occur every 4 weeks, should DT scores increase during the period of screening, patients can be escalated up the tiers accordingly. Patients in TIER-HF-PC will continue to receive clinical care from their cardiologist.

Procedures for the screening process

The DT will be first be sent *via* text message by the study coordinator. However, if the patient does not respond within the same day, follow-up phone calls for 3 consecutive working days (up to twice a day) will be made by the research coordinator, to ensure we will receive the DT results are captured in a timely manner. All patients will be contacted by the nurse coach within 3 days of receiving their DT score, so that patients can be further assessed with the IPOS and a timely decision about their tier-placement can be made.

In all three tiers, participants will be given English or Chinese educational resources. This can be given either in hard copy or soft copy, by the research coordinator.

Further details on the tiers follows:

First tier (lowest needs): Educational resources will contain information on palliative care services, management of heart failure symptoms and co-morbidities, and practical information on caregiving resources in Singapore. These resources have been used in our prior research studies. [42-44]
Second tier (moderate needs): The health coach will start coaching with patients and their caregivers within 1 week of IPOS screening. Health coaching sessions for patients and caregivers will be conducted separately whenever possible, to ensure patients and caregivers have enough privacy and time to work with the health coach. Depending on the technological literacy and logistical availability of the participants, health coaching can be conducted using videoconferencing methods, over the phone, or face-to-face. Each health coaching session is expected to last about 1 hour. We anticipate the health coaching to last over a period of 4 to 8 weeks. After completion of health coaching, patients and caregivers will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on concerns and reinforce skills taught during coaching. The nurse coach will also facilitate participants to initiate contact back, should concerns arise out of the coaching period. During the coaching period, should a patient have severe or overwhelming concerns, the nurse coach will escalate palliative care support to the third tier.

Content of health coaching (patient): A structured manual for health coaching will be used. This manual has been prior adapted [42,45-46] from the (Educate, Nurture, Advise, Before Life Ends, or ENABLE) program in the U.S.A. [47-53] The ENABLE program is a nurse-led palliative care and health coaching program. The culturally adapted ENABLE topics are “maintaining positivity and problem solving”, “self-care”, “coping with stress and spirituality”, “symptom management”, “talking about what matters most, making choices” and “sharing your journey and legacy”. The sequence of the ENABLE topics will be individualized, based upon patient’s requests and results on the IPOS.

Content of health coaching (caregiver): Health coaching topics for caregivers are “maintaining positivity and problem solving”, “self-care”, “coping with stress and spirituality”, “being a partner in managing symptoms”.

Third tier (highest needs): Patient participants will be reviewed by a specialist palliative care physician within 1 week of IPOS screening. There will be structured assessments by the physician to evaluate their physical, emotional, and social problems, with the specific purpose of allowing medication titration and referrals to other clinical services as necessary. Physician review will be done face-to-face whenever possible. Alternative methods for consulting include video-consultation, with the caveat that patients who need physical examination would be called back to the hospital for physical consult, should the physician deem necessary. After completion of physician review, participants will receive health coaching and follow-up, as per what is done for participants in the second tier.

Participants in all 3 tiers who are still alive after week 48 will be transited by the nurse coach to relevant services in current care. This transition will be determined by their needs, and in consultation with the palliative care physician.

Study instruments and data collection procedures
Collection procedure
All patient and caregiver reported outcome measures will be collected over the phone, by the study research coordinator. If participants are not contactable over the phone despite attempts, we will collect the outcome measures face-to-face to ensure timely data collection and to minimize missing data.

Study instruments selections
Study instruments were chosen as they have been used in the heart failure population and in local studies in Singapore in the English and Chinese language.

Study instruments for patients only:
Cardiac specific Quality-of-life (QOL) measure: Kansas City Cardiomyopathy Questionnaire (KCCQ-12), [54-55] a 12-item QOL scale, composed of physical function, symptoms, QOL, social interference and a summary score. It is validated in the cardiac population and commonly used in cardiology trials for assessment of QOL. The KCCQ-12 has similar validity to the 23-item version and is shorter with less respondent burden. [55] The KCCQ-12 can be self-reported by patients or read to patients over the phone by a research coordinator. The total summary score can range from 0 to 100, with higher scores representing better health status. A clinically meaningful change is defined as a change of at least 5 points on the KCCQ. [56] The KCCQ-12 will be measured every 8 weeks from baseline, till the point of patient death, or till week 48, whichever is earlier. The frequency of our proposed KCCQ tracking

is referenced from trials which used KCCQ to track longitudinal changes in QOL. [56]
Non-cardiac specific health-related quality of life: EUROQOL EQ-5D-5L [57-59] provides a global assessment of the patient's quality-of-life in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It can be administered over the phone. [58] Each patient's health state utility can be derived from their responses to the 5 dimensions.
Hospital Anxiety and Depression Scale (HADS) [60]: A 14-item scale with a score range of 0 to 42, that can be administered over the phone [61]. It is composed of two subscales- anxiety and depression- with a cut-off point of 11 for each subscale, that determines anxiety and depression of clinical significance.

Study instruments for caregivers only
Singapore Caregiver Quality of Life Scale -15 (SCQOLS-15): a 15-item scale with 5 domains measuring QOL of life caregivers in domains: physical well-being, mental well-being, experience and meaning, impact on daily life, and financial well-being. [62-64] This will be measured every 8 weeks from baseline, till the point of patient death, or till week 48, whichever is earlier.

Study instruments for patients and caregivers
Brief Coping with Problems Experienced (Brief-COPE) scale [65]: A 28-item scale measuring the ways people cope with stressful events. It has been used in the heart failure population, where the coping style was shown to correlate with the level of physical functioning. [66]
Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being 12 Item Scale (Facit-SP-12) [67]: A 12-item survey that measures the spiritual well-being of patients and caregivers. The Facit-SP-12 has been used as a secondary outcome measure in the palliative care population for heart failure trials. [68] The total of Facit-SP-12 ranges from 0 to 48 with higher scores representing increased spirituality.

Data collection on experience on TIER-HF-PC and its acceptability
Client Satisfaction Questionnaire (CSQ-4) [69]: A 4-item scale consisting of 3 items (measuring the experience of the client with a program) and an item measuring improvement in client self-efficacy. This service evaluation questionnaire will be measured for participants randomized to TIER-HF-PC. The CSQ-4 has been used as an outcome measure in our prior studies [42-43,70] and has also been used in other studies to evaluate health services programs. [71] The CSQ-4 can be administered over the phone.
Semi-structured interviews: We will purposively recruit patients, caregivers from TIER-HF-PC and healthcare staff whose patients were managed using TIER-HF-PC. To capture diverse views across different demographics, functional status (patients only), background specialty (palliative care versus heart failure, physician versus nurse) and years of clinical experience (healthcare staff only), we will utilize purposive and iterative sampling techniques. An interview guide will be developed based on elements and selected outcomes in Proctor's taxonomy of implementation outcomes, such as acceptability, appropriateness and timeliness and the RE-AIM/ PRISM framework. [72] The RE-AIM framework stands for outcomes such as reach, effectiveness and adoption. The PRISM (Practical, Robust, Implementation and Sustainability Model) framework is complementary to RE-AIM and is used to identify the multilevel contextual factors that affect the implementation outcomes in RE-AIM.

Data collection for assessment of fidelity to the TIER-HF-PC intervention and study procedures
The fidelity to procedures, and extent to which TIER-HF-PC is implemented as planned will follow recommendations from the NIH behavior change consortium [73] and be determined by the following processes measures: (i) number of patients who complete the screening DT and IPOS assessments (ii) percentage of patients and/or caregivers who manage to complete health coaching sessions and specialist palliative care physician review, according to their assigned tier (iii) case note audit and review of clinical entries by TIER-HF-PC staff. All clinical entries by nurse coach and specialist palliative care doctor that were entered into the electronic healthcare notes from NHCS and KTPH will be audited to review the main themes of palliative care treatments that were covered during specialist palliative care review and health coaching. Due to the anticipated high load of clinical entries, we will audit using the techniques of natural language processing (NLP). [74-75]

Data collection on healthcare utilization
We will collect data on referral to community palliative care services and other community support services that patients in both arms might utilize, such as community nursing services. The date and number of hospital admissions, hospital length of stay for each admission, number of emergency

department visits, number and length of intensive care unit admissions and date and location of death will also be collected. We will track if usual care patients are referred to palliative care consult services.

Data collection on health care cost
We will collect data on the cost of hospitalization bills, emergency department bills and outpatient bills from the hospital record systems. We will also estimate the cost of healthcare provision, based upon estimated time staff spend on caring for patients within this trial.

Figure 2 describes a diagram of our study flow and timeline for data collection procedures.

Statistical justification

Sample size calculation
For the purposes of evaluation of primary outcome- assuming a common standard deviation of 12 points for the KCCQ overall summary score, [68] the planned sample size will be 200 subjects (100 per arm) to provide 80% power at 5% two-sided type 1 error rate, to detect a difference of 5 points at 24 weeks, which is the smallest change that is clinically significant at the individual patient level. [51] To account for dropouts and attrition, we will aim to recruit 120 patients per arm (240 patients). As caregiver recruitment is based on the patient sample, we will aim to recruit up to 120 caregivers per arm (up to 240 caregivers). We estimate we will recruit 80% of the participants from NHCS campuses (192 patients and 192 caregivers), and 20% of the participants (48 patients and 48 caregivers) from KTPH. Based on screening logs from previous studies recruiting similar patients from same settings, it is estimated that there will be 40 eligible patients per month. Assuming a recruitment rate of 50% and 20 patients recruited per month, the sample size could be achieved within 12 months. A more conservative estimation of a 40% recruitment rate (16 patients are recruited per month) would allow us to achieve the required sample size within 15 months. For the semi-structured interviews, based upon our prior research in the same setting, [76-78] we will reach data saturation by 30-40 patients, 30-40 caregivers, and 30 staff across two sites. These will be our target sample sizes.

Analysis of patient and caregiver outcome measures
We will adopt the official scoring method to obtain the summary scores and domain scores of the various questionnaires – KCCQ-12, SCQOLS-15, HADS, EQ-5D-5L, Facit-SP-12,; subject to imputation for item nonresponse by the "half rule", if applicable. Descriptive statistics, and measures of effect size will be used to compare the study groups at baseline, 8 weeks, 16 weeks, and 24 weeks. Analysis will follow an intention-to-treat principle. Longitudinal data analyses will be conducted to examine intervention effects using linear mixed-effects-modelling for repeated measures at baseline, 8 through 16 and 24 weeks, constraining the baseline mean to be equal between intervention and control groups with indicators for time, group, and time by group interactions. Mixed-effects models using maximum likelihood estimation provide robust estimate despite missing values or early dropouts if the data are Missing Completely At Random or Missing At Random. [79] Estimate of standard deviation of residuals from the mixed-effects model will be used to compute effect sizes (Cohen's d). We will also chart the trajectories of quality of life from baseline till patient death or week 48 whichever is earlier, to evaluate the differences in quality-of-life across time between arms. In addition, we will perform pre-planned subgroup analyses, to evaluate associations of outcomes with variables including recruitment site, time since diagnoses of heart failure, NYHA status, and number of palliative care health coaching and physician review sessions received. We will also examine changes in coping style over time, using BRIEF-COPE scores as an outcome.

Assessment of experience with TIER-HF-PC
The total score of the CSQ per participant will be computed. We will analyze patient and caregiver scores separately and will calculate the percentage of participants in TIER-HF-PC who have at least a CSQ score of 12 and above, which indicates good experience with care.

Regarding the analysis of semi-structured interviews, we will form a qualitative coding team (consisting of 2 research coordinators, the principal investigator and a co-investigator. All members of the coding team will be required to have training in qualitative analysis. All audio-taped interviews will be transcribed verbatim by our research coordinators, and the accuracy of each transcript cross-checked by another research coordinator. Interviews conducted in Chinese will be translated to English prior to

analysis by the coordinators. Coding of up to 30% of our interviews will be initially undertaken by both research coordinators to ensure inter-coder reliability in accordance with current guidelines. [80] Coding will subsequently be done independently by the 2 coordinators once inter-coder reliability is established. Interviews will be open coded line by line. Code categories will be developed and iteratively adjusted through discussions. The code categories will be subsequently mapped back to the main domains of the RE-AIM and PRISM framework to identify key multi-level contextual factors influencing the TIER-HF-PC outcomes as well as to assess the adoption, implementation, and impact of TIER-HF-PC. Hence, the analysis will involve both inductive and deductive approaches.

Analysis of fidelity to TIER-HF-PC

For the purpose of auditing TIER-HF-PC, we will follow guidance from literature for auditing using NLP. [74-75] A sample of 30% of extracted medical notes will be annotated, to highlight keywords/phrases and develop a standard codebook that will delineate the specific components of our palliative care health coaching and physician treatments. These will include documentation around: self-care, symptoms, psycho-emotional concerns, spirituality, decision making, care planning, financial and legacy planning. Regarding the NLP techniques, we will leverage on a class of models pre-trained on vast electronic health records. Among these are ClinicalBERT, [81] BioBERT,[82] BioMegatron, [83] and GatorTron [84] which have been shown to be performant on clinical concept extraction, natural language inference, medical question answering, and semantic textual similarity tasks. We propose the use and exploration of these models as feature extractors in conjunction with other traditional machine learning models (i.e., tree-based models) for downstream classification of interview notes into concepts relevant to the TIER-HF-PC objectives. The feature extraction step uses the model to transform an input (i.e., text) into an array of numbers that hold information about the input's structure and semantics from medical notes. This approach leverages existing pre-trained models to form the corpus necessary for fine-tuning of specific use cases, in this case, the auditing of TIER-HF-PC clinical notes. For the development of the automated audit algorithm, the annotated notes will be split into 80% training and 20% test datasets for the development of the NLP algorithm. Validation will be based on the 20% of data unseen in the training phase. If the machine-annotated notes appear out of context, they will be examined, and the code book will be tuned accordingly. We will report on the sensitivity, specificity, area under the receiver operating curve (AUROC), F1-Score and the area under the precision recall curve (AUPRC). Once the target performance is achieved, we will run the software to annotate the remaining 70% of the medical notes.

Assessment of impact of TIER-HF-PC on healthcare utilization and survival

We will estimate the differences in community hospice usage, number and length of hospital admissions, number of emergency visits, number, and length of intensive care visits between TIER-HF-PC participants and those in usual care using generalized linear models, with binomial model for community hospice usage and Poisson model with robust standard effort for other healthcare utilization outcomes.

We will quantify the differences in survival between TIER-HF-PC and usual care by Cox model, censoring at week 48 or death, whichever occurs earlier.

Healthcare cost analysis

We will sum up the total cost of inpatient bills and outpatient bills including emergency visit bills for TIER-HF-PC participants and usual care participants from week 1 to week 24 and quantify the cost differences between both groups by generalized linear model with Gamma model and robust standard error. The net cost of TIER-HF-PC will be calculated based upon the cost of care provision in TIER-HF-PC minus the cost savings from the reduction in health care utilization. We will also calculate incremental cost-effectiveness ratios (ICERs) to measure the average net cost per quality-adjusted-life-year (QALY) gained for TIER-HF-PC versus usual care participants. The QALY will be calculated by the product of quality-of-life (EQ-5D-5L) and survival.

Fidelity, standardization, and monitoring

The study team at NCCS will remain responsible for keeping track of the overall study recruitment rate, randomizing participants, and managing data collection, cleaning, and analysis. The data monitoring committee will include the study principal investigator, the statistician, and the site principal investigators. Access to data set is governed through a data sharing agreement with all participating investigators in the study team, governed by the study principal investigator, as per institutional rules. The study principal investigator will coordinate study logistics through regular site meetings between NCCS, NHCS and KTPH. These will ensure timely solving of recruitment, retention, and other study issues.

Health coaches will have mandatory training using current available resources for ENABLE coaching training prior to the start of TIER-HF-PC. They will utilize checklists to ensure the coaching and assessments are standardized. They will also have monthly meetings with the PI to troubleshoot problems that arise during the process of health coaching and assessment.

Participant safety

Provisions will be made to recruit patient participants after their acute heart failure exacerbations have been resolved. Participants might be emotional during health coaching and palliative care physician review. If this occurs, the principal investigator will refer to existing clinical networks for emotional support. Participants will be allowed to withdraw from the program at any point in time if requested.

Ethics and dissemination

This study has been approved by the SingHealth institutional ethics review board- study review number 2024-2213 and covers all participating sites All participants must sign informed consent (supplemental material) prior to participation and privacy of data will be adhered to as per institutional requirements. Results of the study will be disseminated through publications and research conferences when data analysis is complete.

Patient and public involvement

We did not involve any patients or member of the public in the design of this trial.

Discussion

We describe a novel tiered model of palliative care which we aim to evaluate if it could be effective in improving outcomes in patients with heart failure and that of their caregivers. Besides effectiveness, we also aim to determine if this model of care would be acceptable, cost-effective, and can be implemented with fidelity. In this study, we will also be utilizing novel methods of analysis such as NLP to audit TIER-HF-PC.

Empowering patients to self-care through nurse-led early palliative care, [47-53] and implementation of regular symptom monitoring in patients with advanced illness have been studied in various studies separately, but there has not been a model of care that has effectively evaluated if patient-reported screening measures can be used to trigger and personalize the type and intensity of palliative care treatments. We believe that TIER-HF-PC is the first and will bring novel insights into how we can provide palliative care most sustainably for a rapidly aging population and workforce. TIER-HF-PC allows us to evaluate if limited specialist resource can be directed at those most in need whilst ensuring that all patients have access to a patient determined, appropriate level of palliative care, delivered through established care escalation pathways and regular screening.

We do anticipate challenges within this study, such as differing levels of technological literacy within our participants, thus we have allowed for both telehealth and face-to-face methods for conducting the palliative care treatments in TIER-HF-PC. We also anticipate that there might be difficulty recruiting caregivers face-to-face, as not all caregivers would accompany patients to their outpatient appointments. Therefore, we will contact caregivers *via* the phone and allow mail-back options for consent. We are also allowing for recruitment from two cardiac centres with access to three campuses, to have a larger population of patients with heart failure to recruit from and strengthen the overall generalizability of our study to different healthcare settings. To minimize trial dropouts, we will utilize phone-based collection of outcome measures to reduce trial fatigue.

If TIER-HF-PC is shown to be beneficial, we will iterate and disseminate TIER-HF-PC to other care settings for heart failure care in the medium-term. In the long-term, TIER-HF-PC can potentially be expanded to other serious life-limiting illnesses that have limited palliative care access. These will include non-cancer illnesses such as chronic kidney disease, chronic respiratory disease, and chronic neurological disease.

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Author Contribution Statement

First author Dr Shirlyn Neo was responsible for drafting of the manuscript, design of the study and finalization of the manuscript.

Authors Dr Ke Yu and Dr Lee Chun Fan were responsible for conceptualizing the study methods and analysis.

Professor Cheung was responsible for guiding study design and methodology.

All authors approved the final version of the manuscript to be published.

Author Guarantor: Author Dr Shirlyn Neo is the guarantor.

Data availability: Data from this study will not be posted on any data repository.

Dissemination of results: Results of this study will be disseminated upon completion of data analysis. This manuscript, or any related manuscript, is not currently under consideration or accepted elsewhere

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Trial registration: clinicaltrials.govID NCT06244953. Registered in January 2024.

Current protocol version: Version 1.0, version date 25th December 2023**.** Any protocol modifications will be updated on clinicaltrials.gov

Ethics board approval reference number: SingHealth ethics review board: 2024-2213

Supporting instruments- SPIRIT checklist

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Figure Legend

Figure 1: Components of TIER-HF-PC

Figure 2: Study flow diagram

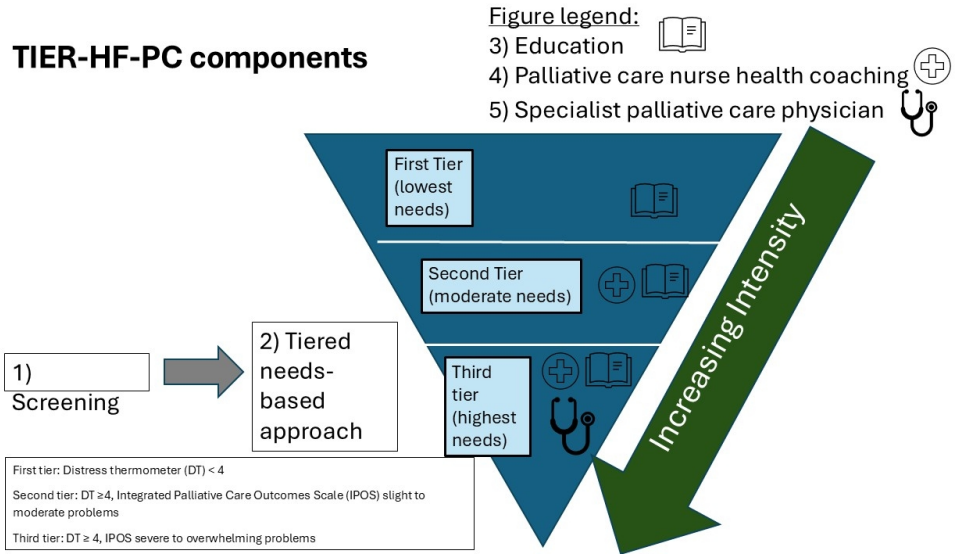

Figure 1- components of tier-hf-pc

338x190mm (96 x 96 DPI)

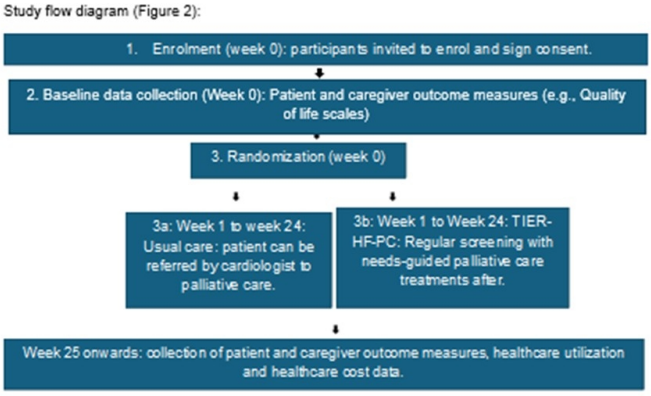

Figure 2- study flow diagram

338x190mm (96 x 96 DPI)

Restricted, Sensitive (Normal)

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

You are being invited to participate in a research study. Your participation in this study is entirely voluntary. Before you take part in this research study, the study must be explained to you, and you must be given the chance to ask questions. Your questions will be answered clearly and to your satisfaction. Please read carefully the information provided here. If you agree to participate, please sign the consent form. You will be given a copy of this document.

STUDY INFORMATION

Protocol Title:
Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

This research study is recruiting at the following SingHealth institution(s) and Alexandra Health Pte Ltd institution(s). Please note that the word “SingHealth” refers to the institutions NCCS, NHCS and, SKH. “Alexandra Health Pte Ltd” refers to KTPH. These are institution(s) where you are recruited into the study from.

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PURPOSE OF THE RESEARCH STUDY

The purpose of this study is to test the effectiveness and implementation of a novel model of palliative care to improve access to supportive and palliative care for patients with heart failure and their caregivers.

You were selected as a possible participant in this study because you have heart failure, are 21 years or older and able to communicate in English or Chinese

This study targets to recruit 10 participants from National Cancer Centre Singapore, 400 participants from National Heart Centre Singapore, 35 participants from Sengkang General Hospital and, 35 participants from Khoo Teck Puat Hospital. About 480 participants are expected to take part in this study at multiple hospitals and medical facilities in Singapore.

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STUDY PROCEDURES & YOUR RESPONSIBILITIES IN THIS STUDY

The study involves the following:

Randomization:
If you agree to participate in this study, you will be randomised. You will be randomised to receive “usual care” or “TIER-HF-PC” intervention. Randomisation means assigning you to one of the 2 groups by chance, like tossing a coin or rolling a dice.

Intervention (TIER-HF-PC):
“Usual care” arm
For participants who are randomised into the “usual care” arm, you will continue with your usual clinical care by your cardiologist. We will also monitor your quality of life and other measures regularly. If your cardiologist picks up their symptoms or other concerns, they can refer you to a specialist palliative care physician.

“TIER-HF-PC” arm
For participants who are randomised into the “TIER-HF-PC” arm, you will be further screened with the Distress thermometer (DT) and the Integrated Palliative Care Outcome Scale (IPOS). Your scores on the DT and IPOS will determine which tier of the intervention you are allocated to.

- First tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. You will continue to be screened every 4 weeks, for a total period of 24 weeks from baseline, using the DT. You will be escalated up the tiers according to your DT scores.

- Second tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. The palliative care team will also start health coaching with you and your caregiver within 1 week of DT/IPOS screening. Each health coaching session is expected to last about 1 hour, last over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. The team will also continue to assess your concerns during the health coaching period You will be escalated up the tiers according to the team’s assessment of your concerns.

- Third tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. Subsequently, you will be reviewed by a specialist palliative care physician within 1 week of IPOS/DT screening. After completion of physician review, you will receive health coaching. Each health coaching session is expected to last about 1 hour, last over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. The palliative care team will also continue to assess your concerns during the health coaching period.

Participants in all 3 tiers will be transited by the palliative care team to relevant services in current care after week 48.

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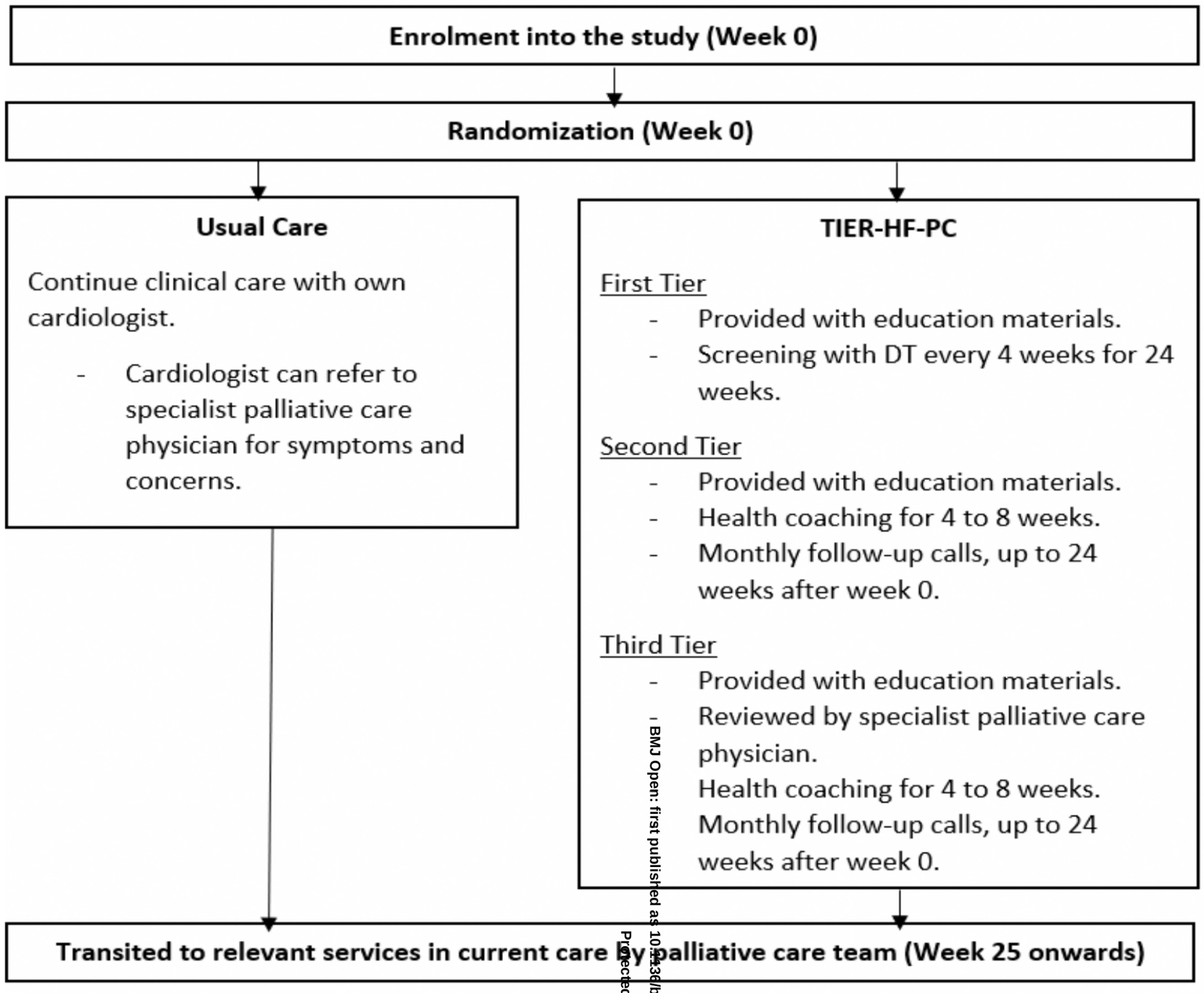
Content of health coaching

A structured manual for health coaching will be used. The culturally adapted topics of "maintaining positivity and problem solving", "self-care", "coping with stress and spirituality", "symptom management", "talking about what matters most, making choices" and "sharing your journey and legacy" will be coached. The sequence of the topics will be individualized, based upon participant's requests and results on the IPOS.



Questionnaire/ interview:

We will ask you to complete questionnaires about your quality of life, psycho-emotional status, coping methods, spirituality, and satisfaction with care, through your preferred medium (either hardcopy or softcopy).

"Usual care" arm

At week 0, 8, 16, 24, 32 and every 8 weeks after till week 48 the study team member would follow-up with you to complete the questionnaire.

"TIER-HF-PC" arm

You will have to complete some survey at week 0, 8, 16, 24, 25, 32 and every 8 weeks after till week 48.

After week 25, you will be invited to participate in a semi-structured interview to share about your experience and feedback about the intervention. The semi-structured interview will be

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conducted through your preferred medium (either face-to-face, phone call or video conferencing) at a mutually agreed time and date. Audio-recording of the interviews will be mandatory for the purpose of analysing the interviews.

	Week 0, Week 8, Week 16, Week 24	**Week 25 onwards**
TIER-HF-PC	KCCQ, EQ-5D-5L, HADS, Brief COPE, Facit-SP-12	Week 25: CSQ, semi-structured interviews. Week 32 and every 8 weeks after till week 48: KCCQ
Usual Care	KCCQ, EQ-5D-5L, HADS Brief COPE, Facit-SP-12	Week 32 and every 8 weeks after till week 48: KCCQ

KCCQ: Kansas City Cardiomyopathy Questionnaire
EQ-5D-5L: EuroQol Group – 5 Dimension – 5 Level questionnaire
HADS: Hospital Anxiety and Depression Scale
Brief COPE: abbreviated Coping Orientation to Problems Experienced Scale
Facit-SP-12: Functional Assessment of Chronic Illness Therapy-Spiritual Well-being Scale (12 items)
CSQ-4: Client Satisfaction Questionnaire (4 items)

Medical history:
We will collect information (data) from your medical records. The information will include, if any, healthcare utilization data (date of referral to community palliative care services and other community support services, date and number of hospital admissions, hospital length of stay for each admission, number of emergency department visits, number and length of intensive care unit admissions, , referred to palliative care consult services) and health care cost data (cost of hospitalization bills, emergency department bills, outpatient bills).

Data about you from other resources:
We will use data that identifies you like your name and national registration identity card (NRIC), to access and add data from other sources that is specific to you. This will give researchers more data about factors that might affect your health. For example, we may combine or link the data that we collect about you in this study with data from other sources. This includes but is not limited to healthcare billing information, government administrative data and/or research data such as health and health-related data, social data, education data, birth and death data, economic and housing data, and data from disease registries and databases, whether by itself or with the assistance of a data intermediary.

If you agree to participate in this study, you should follow the advice and directions given to you by the study team.

WHAT IS NOT STANDARD CARE OR IS EXPERIMENTAL IN THIS STUDY

The study is being conducted because TIER-HF-PC is not yet proven to be a standard method of increasing access to palliative care for patients with heart failure and their caregivers. We hope that your participation will help us to determine the effectiveness of the TIER-HF-PC method.

POSSIBLE RISKS, DISCOMFORTS, OR INCONVENIENCES

Questionnaires/ surveys/ interviews:
Some of the questions might make you feel uncomfortable or upset. You may refuse to answer any of the questions and/or take a break at any time during the study. Study

procedures can also be stopped upon your request. The Principal Investigator will then be informed, and you will be offered a referral to the appropriate support.

Personal privacy and confidentiality:

This study uses information that may affect your privacy. To protect your confidentiality, only a unique code will be used to identify data that we collected from you.

As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

For transcribing of the interviews, audio recording will be required. While we will protect your confidentiality to the best of our abilities, absolute confidentiality cannot be guaranteed. However, all data will be de-identified prior to analysis. We will also protect your data through the following ways:

- ☐ Audio recordings and transcribes for the purpose of this research study will not be labelled with your name or identifiable information. Instead, a study ID will be used and assigned.
- ☐ Audio recordings and transcribes collected (which will eventually be deleted after the end of the study) will only be stored in devices with secured and restricted access. Access to data will also be limited.
- ☐ We will only report information in its aggregated form and will not identify the responses of any individuals.

POTENTIAL BENEFITS

There is no assurance you will benefit from this study. However, your participation may help to implement a better model of palliative and supportive care for heart failure patients and their caregivers. A better care model would also potentially lead to better outcomes for patients and caregivers through the heart failure journey.

ALTERNATIVE IF YOU DO NOT PARTICIPATEIN THE STUDY

There is no alternative to the study procedures. You can choose not to take part in this study. The study procedures will not be carried out.

COSTS & PAYMENTS IF PARTICIPATINGIN THIS STUDY

There is no cost to you for participating in this research study. However, as a token of appreciation, you will be reimbursed a total of SGD 40 in cash upon completion of the intervention and all necessary procedures. Should you be selected and choose to participate in the interview after completing the intervention, you will be further reimbursed with SGD 10 in cash upon completion of the interview.

INCIDENTAL FINDINGS

During the course of the study, there is a possibility that we might unintentionally come to know of new information about your health condition from the outcome measures/ validated health surveys that is/are conducted as part of the study. These are called “incidental findings”.

“Incidental findings” are findings that have potential health or reproductive importance to a participant like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives, or variables of the study. These findings may cause you to feel anxious and may affect your current or future life and/or health insurance coverage. Examples of potential incidental findings that may be discovered during the course of this study may include but are not limited to emotional or psychological distress. You will be asked to indicate whether you wish to be re-identified and notified in the event of an important incidental finding that is related to you.

If you agree to be re-identified and notified, your study doctor/ a qualified healthcare professional will explain the incidental finding to you and discuss and advise you on the next steps to follow. You may wish to do more tests and seek advice to confirm this incidental finding. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

If you do not wish to be re-identified and notified, your decision will be respected. However, in exceptional situations such as discovery of life-threatening incidental findings with available treatment options, you will be contacted to confirm your decision whether to learn more about the incidental findings. In rare situations where the incidental findings have public health implications and as required by the law (e.g. under the Infectious Diseases Act), you will be contacted and informed of the incidental findings.

PARTICIPANT’S RIGHTS

Your participation in this study is entirely voluntary. You have a right to ask questions, which the study team will do their best to answer clearly and to your satisfaction.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legal representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative and will be contacted for further consent if required.

WITHDRAWAL FROM STUDY

You are free to withdraw your consent and discontinue your participation in the study at any time, without your medical care being affected. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, any research information or data obtained before your withdrawal of consent will be retained and may continue to be used. This is to allow a complete and comprehensive evaluation of the research study.

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Your study doctor, the Principal Investigator of this study may stop your participation in the study at any time for one or more of the following reasons:

- ☐ Failure to follow the instructions of the Principal Investigator and/or study staff.
- ☐ The Principal Investigator decides that continuing your participation could be harmful to your health or safety.
- ☐ The study is cancelled.

RESEARCH RELATED INJURY AND COMPENSATION

If you follow the directions of the Principal Investigator of this research study and you are injured due to the research procedure given under the plan for the research study, our institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS

Your participation in this study will involve the collection of Personal Data. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. Examples of personal data include name, national registration identity card (NRIC), nationality, passport information, date of birth, and telephone number.

Personal Data collected for this study will be kept confidential and stored in Singapore. Your study records and medical records (if applicable) to the extent required by the applicable laws and regulations, will not be made publicly available. To protect your identity, your Personal Data will be labelled with a unique code. The code will be used in place of your name and other information that directly and easily identifies you. The study team will keep a separate file that links your code to your Personal Data. This will be kept in a safe place with restricted access. In the event of any data sharing with third parties (e.g. funding agencies, research collaborators) whether locally or overseas and publication regarding this study, your identity will remain confidential.

However, the monitor(s), the auditor(s), the Institutional Review Board, and the regulatory authority(ies) will be granted direct access to your original medical records (if applicable) and study records to verify study procedures and data, without making any of your information public.

By signing the Consent Form, you consent to (i) the collection, access to, use and storage of your Personal Data by SingHealth, and (ii) the disclosure of such Personal Data to our authorised service providers and relevant third parties as mentioned above. To the fullest extent permitted by applicable law, under no circumstances will SingHealth and/or its

affiliates be liable for any direct, indirect, incidental, special or consequential loss or damages arising out of any data breach event.

All data collected in this study are the property of SingHealth. The data will be used for the purpose of this research study only.

By participating in this research study, you are confirming that you have read, understood and consent to the SingHealth Data Protection Policy, the full version of which is available at www.singhealth.com.sg/pdpa.

WHO HAS REVIEWED THE STUDY

This study has been reviewed by the SingHealth Centralised Institutional Review Board for ethics approval.

If you have questions about your rights as a participant, you can call the SingHealth Centralised Institutional Review Board at 8126 3660 during office hours (8:30 am to 5:30pm).

WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY

If you have questions about this research study or in the case of any injuries during the course of this study, you may contact your study doctor, the Principal Investigator listed under STUDY INFORMATION section, at the beginning of this document.

If you have any feedback about this research study, you may contact the Principal Investigator or the SingHealth Centralised Institutional Review Board.

CONSENT FORM FOR RESEARCH STUDY

Protocol Title:
Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Declaration by Research Participant

(i) I agree to participate in the research study as described and on the terms set out in the Participant Information Sheet. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

(ii) I understand the purpose and procedures of this study. I have been given the Participant Information Sheet and the opportunity to discuss and ask questions about this study and am satisfied with the information provided to me.

(iii) I understand that my individually identifiable information (Personal Data) and data collected about me may be combined or linked with data from other sources, including but

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not limited to healthcare billing information, government administrative data and/or research data such as health, and health-related data, social data, education data, birth and death data, economic and housing data, data from disease registries and database, whether by itself or with the assistance of a data intermediary.

(iv) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without my medical care being affected.

(v) By participating in this research study, I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

Consent to be Re-identified and Notified in the case of an Incidental Finding

There may be potential incidental findings arising from this research. Please indicate whether you consent to re-identification and notification about the incidental finding:

□ Yes, I wish to be re-identified and notified in the case of an incidental finding from this research. I can be reached by:

Phone/ Email:

□ In the event that I cannot be reached, please contact the following person nominated by me: [Optional]

Name/ Phone/ Email:

□ No, I do not wish to be re-identified and notified in the case of an incidental finding from this research. However, I understand that in exceptional or rare situations, I will be contacted as described in the Participant Information Sheet:

- In exceptional situations such as discovery of life-threatening incidental findings with available treatment options, I will be contacted to confirm my decision whether to learn more about the incidental findings.
- In rare situations where the incidental findings have public health implications and as required by the law (e.g. under the Infectious Diseases Act), I will be contacted and informed of the incidental findings.

Name of participant	Signature/Thumbprint (Right / Left)	Date of signing

To be completed by parent / legal guardian / legal representative, where applicable

I hereby give consent for _____(Name of Participant) to participate in the research study. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

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Name of participant's parent/ legal guardian/ legal representative	Signature/Thumbprint (Right / Left)	Date of signing

To be completed by translator, if required

The study has been explained to the participant/ legal representative in _____ by _____.
Language Name of translator

To be completed by witness, where applicable

I, the undersigned, certify that:

- ☐ I am 21 years of age or older.
- ☐ To the best of my knowledge, the participant or the participant's legal representative signing this informed consent form had the study fully explained to him/her in a language understood by him/ her and clearly understands the nature, risks and benefits of the participant's participation in the study.
- ☐ I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative giving the consent.
- ☐ I have taken reasonable steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Witnessed by: _____ _____
Name of witness Date of signing

_____
Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant' s legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant' s or legal representative' s thumbprint). After the written consent form and any written information to be provided to participant is read and explained to the participant or the participant' s legal representative, and after the participant or the participant' s legal representative has orally consented to the participant' s participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBRA.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant's legal representative is able to read, sign and date on the consent form.

Investigator's Statement

I, the undersigned, certify to the best of my knowledge that the participant/ participant's legal representative signing this consent form had the study fully explained to him/her and clearly understands the nature, risks, and benefits of the participant's participation in the study.

Restricted, Sensitive (Normal)

Name of Investigator/ Person obtaining consent	Signature	Date

Restricted, Sensitive (Normal)

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

You are being invited to participate in a research study. Your participation in this study is entirely voluntary. Before you take part in this research study, the study must be explained to you and you must be given the chance to ask questions. Your questions will be answered clearly and to your satisfaction. Please read carefully the information provided here. If you agree to participate, please sign the consent form. You will be given a copy of this document.

STUDY INFORMATION

Protocol Title:
Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

This research study is recruiting at the following SingHealth institution(s) and Alexandra Health Pte Ltd institution(s). Please note that the word “SingHealth” refers to the institutions NCCS, NHCS and, SKH. “Alexandra Health Pte Ltd” refers to KTPH. These are institution(s) where you are recruited into the study from.

□ **National Cancer Centre Singapore (NCCS)**
Principal Investigator:
Dr Shirlyn Neo Hui Shan
Division of Palliative and Supportive
Tel: 6436 8000
Institution Mainline: 6436 8000

□ **National Heart Centre Singapore (NHCS)**
Principal Investigator:
Dr David Sim Kheng Leng
Department of Cardiology
Tel: 6704 8000
Institution Mainline: 6704 8000

□ **Sengkang General Hospital (SKH)**
Principal Investigator:
Dr Lionel See Kee Yon
Department of Internal Medicine
Tel: 6930 5000
Institution Mainline: 6930 5000

PURPOSE OF THE RESEARCH STUDY

The purpose of this study is to test the effectiveness and implementation of a novel model of palliative care to improve access to supportive and palliative care for patients with heart failure and their caregivers.

You were selected as a possible participant in this study because you are a caregiver for a heart failure patient, are 21 years or older and able to communicate in English or Chinese

This study targets to recruit 10 participants from National Cancer Centre Singapore, 400 participants from National Heart Centre Singapore, 35 participants from Sengkang General Hospital and, 35 participants from Khoo Teck Puat Hospital. About 480 participants are expected to take part in this study at multiple hospitals and medical facilities in Singapore.

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STUDY PROCEDURES & YOUR RESPONSIBILITIES IN THIS STUDY

The study involves the following:

Randomization:

If you agree to participate in this study, your loved one (who is also a participant) will be randomised. They will be randomised to receive “usual care” or “TIER-HF-PC” intervention. Randomisation means assigning you to one of the 2 groups by chance, like tossing a coin or rolling a dice. The group that you are in will be dependent on which group your loved one is randomised into. You will be placed in the same group as your loved one.

Intervention (TIER-HF-PC):

“Usual care” arm

For participants who are randomised into the “usual care” arm, we will monitor your quality of life and other measures regularly. Your loved one will continue to receive their usual clinical care by their cardiologist.

“TIER-HF-PC” arm

For participants who are randomised into the “TIER-HF-PC” arm, your loved ones will be further screened with the Distress thermometer (DT) and the Integrated Palliative Care Outcome Scale (IPOS). Their scores on the DT and IPOS will determine which tier of the intervention you are allocated to.

- First tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. You will continue to be screened every 4 weeks, for a total period of 24 weeks from baseline, using the DT. You will be escalated up the tiers according to your love ones’ DT scores.

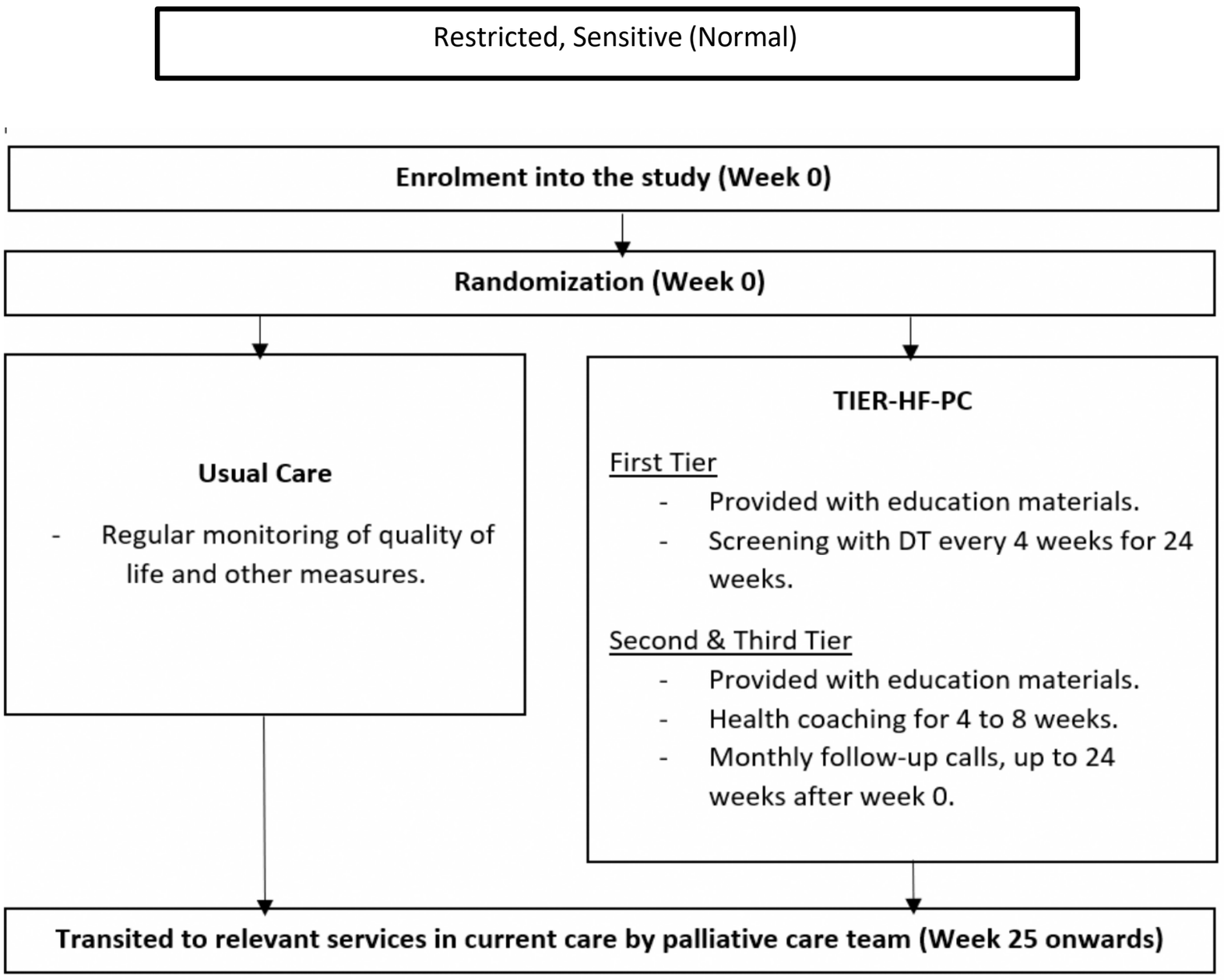
- Second and Third tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. The palliative care team will start health coaching with you and your loved ones within 1 week of DT screening. Each health coaching session is expected to last about 1 hour over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. If you are in the second tier, you may be escalated up the tier according to the team’s assessment of your loved one’s concerns.

Participants in all 3 tiers will be transited by the palliative care team to relevant services in current care after week 48.

<u>Content of health coaching</u>

A structured manual for health coaching will be used. The culturally adapted topics of are “maintaining positivity and problem solving”, “self-care”, “coping with stress and spirituality”, “being a partner in managing symptoms” will be coached. The sequence of the topics will be individualized, based upon participant’s requests.



Questionnaire/ interview:

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"Usual care" arm
At week 0, 8, 16, 24, 32 and every 8 weeks after till week 48 the study team member would follow-up with you to complete the questionnaire.

"TIER-HF-PC" arm
You will have to complete some survey at week 0, 8, 16, 24, 25, 32 and every 8 weeks after till week 48.

After week 25, you will be invited to participate in a semi-structured interview to share about your experience and feedback about the intervention. The semi-structured interview will be conducted through your preferred medium (either face-to-face, phone call or video conferencing) at a mutually agreed time and date. Audio-recording of the interviews will be mandatory for the purpose of analysing the interviews.

	Week 0, Week 8, Week 16, Week 24	**Week 25 onwards**
TIER-HF-PC	SCQOL, Brief COPE, Facit-SP-12	Week 25: CSQ, semi-structured interviews. Week 32 and every 8 weeks after till week 48: SCQOL
Usual Care	SCQOL, Brief COPE, Facit-SP-12	Week 32 and every 8 weeks after till week 48: SCQOL

SCQOL: Singapore Caregiver Quality Of Life Survey
Brief COPE: abbreviated Coping Orientation to Problems Experienced Scale
Facit-SP-12: Functional Assessment of Chronic Illness Therapy-Spiritual Well-being Scale (12 items)
CSQ-4: Client Satisfaction Questionnaire (4 items)

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If you agree to participate in this study, you should follow the advice and directions given to you by the study team.

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Questionnaires/ surveys/ interviews:
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Personal privacy and confidentiality:
This study uses information that may affect your privacy. To protect your confidentiality, only a unique code will be used to identify data that we collected from you.

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There is no assurance you will benefit from this study. However, your participation may help to implement a better model of palliative and supportive care for heart failure patients and their caregivers. A better care model would also potentially lead to better outcomes for patients and caregivers through the heart failure journey.

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ALTERNATIVE IF YOU DO NOT PARTICIPATEIN THE STUDY

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COSTS & PAYMENTS IF PARTICIPATINGIN THIS STUDY

There is no cost to you for participating in this research study. However, as a token of appreciation, you will be reimbursed a total of SGD 40 in cash upon completion of the intervention and all necessary procedures. Should you be selected and choose to participate in the interview after completing the intervention, you will be further reimbursed with SGD 10 in cash upon completion of the interview.

INCIDENTAL FINDINGS

There will not be any incidental findings arising in this research. “Incidental findings” are findings that have potential health or reproductive importance to research participants like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study.

PARTICIPANT’S RIGHTS

Your participation in this study is entirely voluntary. You have a right to ask questions, which the study team will do their best to answer clearly and to your satisfaction.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legal representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative and will be contacted for further consent if required.

WITHDRAWAL FROM STUDY

You are free to withdraw your consent and discontinue your participation in the study at any time, without the medical care of your loved ones being affected. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, any research information or data obtained before your withdrawal of consent will be retained and may continue to be used. This is to allow a complete and comprehensive evaluation of the research study.

Your study doctor, the Principal Investigator of this study may stop your participation in the study at any time for one or more of the following reasons:

- ☐ Failure to follow the instructions of the Principal Investigator and/or study staff.
- ☐ The Principal Investigator decides that continuing your participation could be harmful to your health or safety.
- ☐ The study is cancelled.

Restricted, Sensitive (Normal)

RESEARCH RELATED INJURY AND COMPENSATION

If you follow the directions of the Principal Investigator of this research study and you are injured due to the research procedure given under the plan for the research study, our institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS

Your participation in this study will involve the collection of Personal Data. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. Examples of personal data include name, national registration identity card (NRIC), nationality, passport information, date of birth, and telephone number.

Personal Data collected for this study will be kept confidential and stored in Singapore. Your study records and medical records (if applicable), to the extent required by the applicable laws and regulations, will not be made publicly available. To protect your identity, your Personal Data will be labelled with a unique code. The code will be used in place of your name and other information that directly and easily identifies you. The study team will keep a separate file that links your code to your Personal Data. This will be kept in a safe place with restricted access. In the event of any data sharing with third parties (e.g. funding agencies, research collaborators) whether locally or overseas and publication regarding this study, your identity will remain confidential.

However, the monitor(s), the auditor(s), the Institutional Review Board, and the regulatory authority(ies) will be granted direct access to your original medical records (if applicable) and study records to verify study procedures and data, without making any of your information public.

By signing the Consent Form, you consent to (i) the collection, access to, use and storage of your Personal Data by SingHealth, and (ii) the disclosure of such Personal Data to our authorised service providers and relevant third parties as mentioned above. To the fullest extent permitted by applicable law, under no circumstances will SingHealth and/or its affiliates be liable for any direct, indirect, incidental, special or consequential loss or damages arising out of any data breach event.

All data collected in this study are the property of SingHealth. The data will be used for the purpose of this research study only.

By participating in this research study, you are confirming that you have read, understood and consent to the SingHealth Data Protection Policy, the full version of which is available at www.singhealth.com.sg/pdpa.

Restricted, Sensitive (Normal)

WHO HAS REVIEWED THE STUDY

This study has been reviewed by the SingHealth Centralised Institutional Review Board for ethics approval.

If you have questions about your rights as a participant, you can call the SingHealth Centralised Institutional Review Board at 8126 3660 during office hours (8:30 am to 5:30pm).

WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY

If you have questions about this research study or in the case of any injuries during the course of this study, you may contact your study doctor, the Principal Investigator listed under STUDY INFORMATION section, at the beginning of this document.

If you have any feedback about this research study, you may contact the Principal Investigator or the SingHealth Centralised Institutional Review Board.

Restricted, Sensitive (Normal)

CONSENT FORM FOR RESEARCH STUDY

Protocol Title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Declaration by Research Participant

(i) I agree to participate in the research study as described and on the terms set out in the Participant Information Sheet. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

(ii) I understand the purpose and procedures of this study. I have been given the Participant Information Sheet and the opportunity to discuss and ask questions about this study and am satisfied with the information provided to me.

(iii) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without the medical care of my loved one being affected.

(v) By participating in this research study, I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

_____	_____	_____
Name of participant	Signature/Thumbprint (Right / Left)	Date of signing

To be completed by parent / legal guardian / legal representative, where applicable

I hereby give consent for _____(Name of Participant) to participate in the research study. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

_____	_____	_____
Name of participant's parent/ legal guardian/ legal representative	Signature/Thumbprint (Right / Left)	Date of signing

Restricted, Sensitive (Normal)

To be completed by translator, if required

The study has been explained to the participant/ legal representative in

_____ by _____.

Language Name of translator

To be completed by witness, where applicable

I, the undersigned, certify that:

☐ I am 21 years of age or older.

☐ To the best of my knowledge, the participant or the participant's legal representative signing this informed consent form had the study fully explained to him/her in a language understood by him/ her and clearly understands the nature, risks and benefits of the participant's participation in the study.

☐ I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative giving the consent.

☐ I have taken reasonable steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Witnessed by: _____ _____

Name of witness Date of signing

_____

Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant' s legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant' s or legal representative' s thumbprint). After the written consent form and any written information to be provided to participant is read and explained to the participant or the participant' s legal representative, and after the participant or the participant' s legal representative has orally consented to the participant' s participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBRA.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant's legal representative is able to read, sign and date on the consent form.

Investigator's Statement

I, the undersigned, certify to the best of my knowledge that the participant/ participant's legal representative signing this consent form had the study fully explained to him/her and clearly understands the nature, risks and benefits of the participant's participation in the study.

Name of Investigator/ Person obtaining consent	Signature	Date

OFFICIAL USE ONLY	
Doc Name : Informed Consent Form Template	
Doc Number : 207-001	
Doc Version : 13	**Date :** 31 Jan 2022

INFORMED CONSENT FORM

1. Study Information

Protocol Title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Principal Investigator & Contact Details:

Dr Laurence Tan Lean ChinD
epartment of Geriatric Medicine
Institution Mainline: 6555 8000

Study Sponsor:

National Medical Research Council (NMRC)

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Nevertheless, before you take part in this research study, the study will be explained to you and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign this informed consent form. You will be given a copy of this consent form to take home with you.

You are invited because you have heart failure, are 21 years or older and able to communicate in English or Chinese

This study is carried out to find out the effectiveness and implementation of a novel model of palliative care to improve access to supportive and palliative care for patients with heart failure and their caregivers.

This study will recruit 10 participants from National Cancer Centre Singapore, 400 participants from National Heart Centre Singapore, 35 participants from Sengkang General Hospital and, 35 participants from Khoo Teck Puat Hospital over a period of 3 years. About 480 participants will be involved in this study.

3. What procedures will be followed in this study

If you take part in this study, you will be randomized to receive “usual care” or “TIER-HF-PC” intervention. Randomization means assigning you to one of the two groups by chance, like tossing a coin or rolling dice.

If you take part in this study, you will be asked to follow certain study procedure based on the group you are randomized into.

Your participation in the study will last for 48 weeks. You will go through either the “usual care” or “TIER-HF-PC” intervention for about 24 weeks and be followed up with thereafter till the 48th week of your participation in the study.

If you agree to take part in this study, the following will happen to you:

Intervention (TIER-HF-PC):

"Usual care" arm

For participants who are randomized into the "usual care" arm, you will continue with your usual clinical care by your cardiologist. We will also monitor your quality of life and other measures regularly. If your cardiologist picks up their symptoms or other concerns, they can refer you to a specialist palliative care physician.

"TIER-HF-PC" arm

For participants who are randomized into the "TIER-HF-PC" arm, you will be further screened with the Distress thermometer (DT) and the Integrated Palliative Care Outcome Scale (IPOS). Your scores on the DT and IPOS will determine which tier of the intervention you are allocated to.

- First tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. You will continue to be screened every 4 weeks, for a total period of 24 weeks from baseline, using the DT. You will be escalated up the tiers according to your DT scores.

- Second tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. The palliative care team will also start health coaching with you and your caregiver within 1 week of DT/IPOS screening. Each health coaching session is expected to last about 1 hour, last over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. The team will also continue to assess your concerns during the health coaching period You will be escalated up the tiers according to the team's assessment of your concerns.

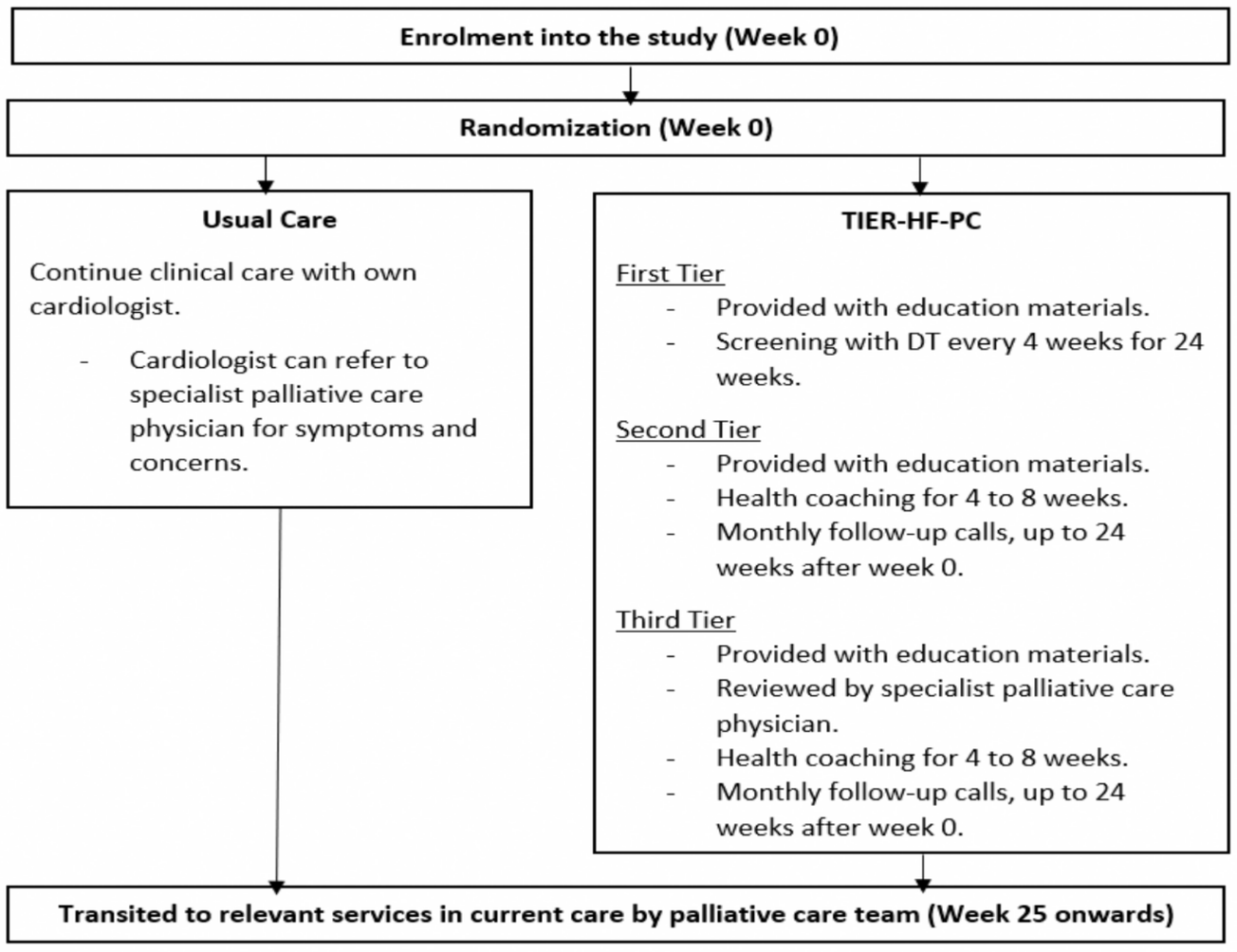
- Third tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. Subsequently, you will be reviewed by a specialist palliative care physician within 1 week of IPOS/DT screening. After completion of physician review, you will receive health coaching. Each health coaching session is expected to last about 1 hour, last over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. The palliative care team will also continue to assess your concerns during the health coaching period.

Participants in all 3 tiers will be transited by the palliative care team to relevant services in current care after week 48.

<u>Content of health coaching</u>

A structured manual for health coaching will be used. The culturally adapted topics of "maintaining positivity and problem solving", "self-care", "coping with stress and spirituality", "symptom management", "talking about what matters most, making choices" and "sharing your journey and legacy" will be coached. The sequence of the topics will be individualized, based upon participant's requests and results on the IPOS.



Questionnaire/ interview:

We will ask you to complete questionnaires about your quality of life, psycho-emotional status, coping methods, spirituality, and satisfaction with care, through your preferred medium (either hardcopy or softcopy).

"Usual care" arm

At week 0, 8, 16, 24, 32 and every 8 weeks after till week 48 the study team member would follow-up with you to complete the questionnaire.

"TIER-HF-PC" arm

You will have to complete some survey at week 0, 8, 16, 24, 25, 32 and every 8 weeks after till week 48.

After week 25, you will be invited to participate in a semi-structured interview to share about your experience and feedback about the intervention. The semi-structured interview will be conducted through your preferred medium (either face-to-face, phone call or video conferencing) at a mutually agreed time and date. Audio-recording of the interviews will be mandatory for the purpose of analysing the interviews.

	Week 0, Week 8, Week 16, Week 24	**Week 25 onwards**
TIER-HF-PC	KCCQ, EQ-5D-5L, HADS, Brief COPE, Facit-SP-12	Week 25: CSQ, semi-structured interviews. Week 32 and every 8 weeks after till week 48: KCCQ
Usual Care	KCCQ, EQ-5D-5L, HADS Brief COPE, Facit-SP-12	Week 32 and every 8 weeks after till week 48: KCCQ

KCCQ: Kansas City Cardiomyopathy Questionnaire
EQ-5D-5L: EuroQol Group – 5 Dimension – 5 Level questionnaire
HADS: Hospital Anxiety and Depression Scale
Brief COPE: abbreviated Coping Orientation to Problems Experienced Scale
Facit-SP-12: Functional Assessment of Chronic Illness Therapy-Spiritual Well-being Scale (12 items)
CSQ-4: Client Satisfaction Questionnaire (4 items)

Incidental Findings

Any individually-identifiable data obtained during the course of this study will be stored and analysed for the purposes of this study and will not be used for future biomedical research.

During the course of the study, there is a possibility that we might unintentionally come to know of new information about your/ your loved ones health condition from health screening, survey assessments etc. that is/are conducted as part of the study. These are called “incidental findings”.

“Incidental findings” are findings that have potential health or reproductive importance to research participants like you/your loved ones and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study. These findings may affect your/ loved ones current or future life and/or health insurance coverage.

You will be asked to indicate whether you wish to be re-identified and notified in the case of a clinically significant incidental finding that is related to you/your child.

If you agree to be re-identified and notified, your study doctor/a qualified healthcare professional will explain the incidental finding to you/your child and discuss and advise you on the next steps to follow. For this purpose, please inform the Principal Investigator or any of the study contact persons listed in this document whenever there are changes in your contact details. You may wish to do more tests and seek advice to confirm this incidental finding.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by the study team undergo all the procedures that are outlined above.

5. What Is Not Standard Care or is Experimental in This Study

The study is being conducted because TIER-HF-PC is not yet proven to be a standard method of increasing access to palliative care for patients with heart failure and their caregivers. We hope that your participation will help us to determine the effectiveness of the TIER-HF-PC method.

6. Possible Risks and Side Effects

From questionnaires/ surveys/ interviews:

Some of the questions might make you feel uncomfortable or upset. You may refuse to answer any of the questions and/or take a break at any time during the study. Study procedures can also be stopped upon your request. The Principal Investigator will then be informed, and you will be offered a referral to the appropriate support.

Potential risk on personal privacy and confidentiality:

This study uses information that may affect your privacy. To protect your confidentiality, only a unique code will be used to identify data that we collected from you.

As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

For transcribing of the interviews, audio recording will be required. While we will protect your confidentiality to the best of our abilities, absolute confidentiality cannot be guaranteed. However, all data will be de-identified prior to analysis. We will also protect your data through the following ways:

- Audio recordings and transcribes for the purpose of this research study will not be labelled with your name or identifiable information. Instead, a study ID will be used and assigned.

- Audio recordings and transcribes collected (which will eventually be deleted after the end of the study) will only be stored in devices with secured and restricted access. Access to data will also be limited.

- We will only report information in its aggregated form and will not identify the responses of any individuals.

7. Possible Benefits from Participating in the Study

There is no assurance you will benefit from this study. However, your participation may help to implement a better model of palliative and supportive care for heart failure patients and their caregivers. A better care model would also potentially lead to better outcomes for patients and caregivers through the heart failure journey.

8. Alternatives to Participation

There is no alternative to the study procedures. You can choose not to take part in this study. The study procedures will not be carried out.

9. Costs & Payments if Participating in the Study

There is no cost to you for participating in this research study.

Instead, you will be reimbursed for your time, inconvenience and transportation costs as follows:

- If you complete the intervention and all necessary procedures, you will be paid SGD40 in cash.

- Should you be selected and choose to participate in the interview after completing the intervention, you will be further reimbursed with SGD10 in cash upon completion of the interview.

- If you do not complete the study for any reason, you will not be reimbursed.

11. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, the data that have been collected until the time of your withdrawal will be kept and analyzed. The reason is to enable a complete and comprehensive evaluation of the study. Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legally acceptable representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative.

12. Compensation for Injury

If you follow the directions of the Principal Investigator of this research study and you are injured due to the research procedure given under the plan for the research study, our institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

13. Confidentiality of Study and Medical Records

Your participation in this study will involve the collection of “Personal Data”. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. This includes medical conditions, medications, investigations and treatment history.

Information and “Personal Data” collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available.

However, the Sponsoring company (NMRC), Regulatory Agencies and NHG Domain Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you (or your legally acceptable representative, if relevant) are authorising (i) the collection, access to, use and storage of your “Personal Data”, and (ii) the disclosure to authorised service providers and relevant third parties.

Data collected and entered into the Case Report Forms are the property of NHG. In the event of any publication regarding this study, your identity will remain confidential.

Research arising in the future, based on your “Personal Data”, will be subject to review by the relevant institutional review board.

By participating in this research study, you are confirming that you have read, understood and consent to the Personal Data Protection Notification available at www.research.nhg.com.sg.

14. Who To Contact if You Have Questions

If you have questions about this research study, you may contact the Principal Investigator:
Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000

In case of any injuries during the course of this study, you may contact the Principal Investigator:
Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000

The study has been reviewed by the SingHealth Centralized Institutional Review Board for ethics approval. This approval is mutually recognized by NHG Domain Specific Review Board (DSRB).

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain Specific Review Board Secretariat at 6471-3266. You can also find more information about participating in clinical research, the NHG Domain Specific Review Board and its review processes at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

CONSENT FORM

Protocol Title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Principal Investigator & Contact Details:

Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000
Khoo Teck Puat Hospital, 90 Yishun Central, Singapore 768828

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction. I have also been informed and understood the alternative treatments or procedures available and their possible benefits and risks.

By participating in this research study, I confirm that I have read, understood and consent to the NHG Personal Data Protection Notification.

Consent to be Re-Identified and Notified in the Case of an Incidental Finding

☐ Yes, I agree to be re-identified and notified in the case of an incidental finding from this research.

In the event that I cannot be reached, please contact my next of kin

Name of next of kin:
Contact:

☐ No, I do not agree to be re-identified and notified in the case of an incidental finding from this research.

Name of Participant	Signature	Date

Translator Information

The study has been explained to the participant / legally acceptable representative in

_____ _____ by _____ _____

(Language)_ (Name of Translator)

Witness Statement

I, the undersigned, certify that:

- ☐ I am 21 years of age or older.
- ☐ To the best of my knowledge, the participant/ the participant's legally acceptable representative signing this informed consent form has the study fully explained in a language understood by him/ her and clearly understands the nature, risks and benefits of his/ her participation in the study.
- ☐ I have taken reasonable steps to ascertain the identity of the participant/ the participant's legally acceptable representative giving the consent.
- ☐ I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date

1. In accordance with Section 6(d) of the Human Biomedical Research Act and Regulation 25 of the Human Biomedical Research Regulations 2017, appropriate consent must be obtained in the presence of a prescribed witness who is 21 years of age or older, and has mental capacity. The witness must be present during the entire informed consent discussion, and must not be the same person taking the appropriate consent. The witness may be a member of the team carrying out the research.
2. However, if the participant/ the participant's legally acceptable representative is unable to read, and/ or sign and date on the consent form, an impartial witness should be present instead. The impartial witness should not be a member of the study team.

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his/ her participation in the study.

Name of Investigator / Person administering consent	Signature	Date

The Parties (Investigator, Participant / Legally Authorised Representative & Witness) may execute this Informed Consent Form requiring a party's signature by using electronic signature process (e.g. by DocuSign, E-signature by Adobe Sign etc) and agree that signatures obtained or transmitted through electronic means, including the

abovementioned signature process, shall be binding and effective for all purposes as if the signatures were executed in-person.

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Doc Name : Informed Consent Form Template	
Doc Number : 207-001	
Doc Version : 13	**Date :** 31 Jan 2022

INFORMED CONSENT FORM

1. Study Information

Protocol Title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Principal Investigator & Contact Details:

Dr Laurence Tan Lean ChinD
epartment of Geriatric Medicine
Institution Mainline: 6555 8000

Study Sponsor:

National Medical Research Council (NMRC)

2. Purpose of the Research Study

You are invited to participate in a research study. It is important to us that you first take time to read through and understand the information provided in this sheet. Nevertheless, before you take part in this research study, the study will be explained to you, and you will be given the chance to ask questions. After you are properly satisfied that you understand this study, and that you wish to take part in the study, you must sign this informed consent form. You will be given a copy of this consent form to take home with you.

You are invited because you are a caregiver for a heart failure patient, are 21 years or older and able to communicate in English or Chinese.

This study is carried out to find out the effectiveness and implementation of a novel model of palliative care to improve access to supportive and palliative care for patients with heart failure and their caregivers.

This study will recruit 10 participants from National Cancer Centre Singapore, 400 participants from National Heart Centre Singapore, 35 participants from Sengkang General Hospital and, 35 participants from Khoo Teck Puat Hospital over a period of 3 years. About 480 participants will be involved in this study.

3. What procedures will be followed in this study

If you take part in this study, your loved one (who is also a participant) will be randomized to receive “usual care” or “TIER-HF-PC” intervention. Randomization means assigning them to one of the two groups by chance, like tossing a coin or rolling dice.

If you take part in this study, you will be asked to follow certain study procedure based on the group your loved one is randomized into.

Your participation in the study will last for 48 weeks. You will go through either the “usual care” or “TIER-HF-PC” intervention for about 24 weeks and be followed up with thereafter till the 48th week of your participation in the study with your loved ones.

If you agree to take part in this study, the following will happen to you:

Intervention (TIER-HF-PC):

"Usual care" arm

For participants who are randomised into the "usual care" arm, we will monitor your quality of life and other measures regularly. Your loved one will continue to receive their usual clinical care by their cardiologist.

"TIER-HF-PC" arm

For participants who are randomised into the "TIER-HF-PC" arm, your loved ones will be further screened with the Distress thermometer (DT) and the Integrated Palliative Care Outcome Scale (IPOS). Their scores on the DT and IPOS will determine which tier of the intervention you are allocated to.

- First tier

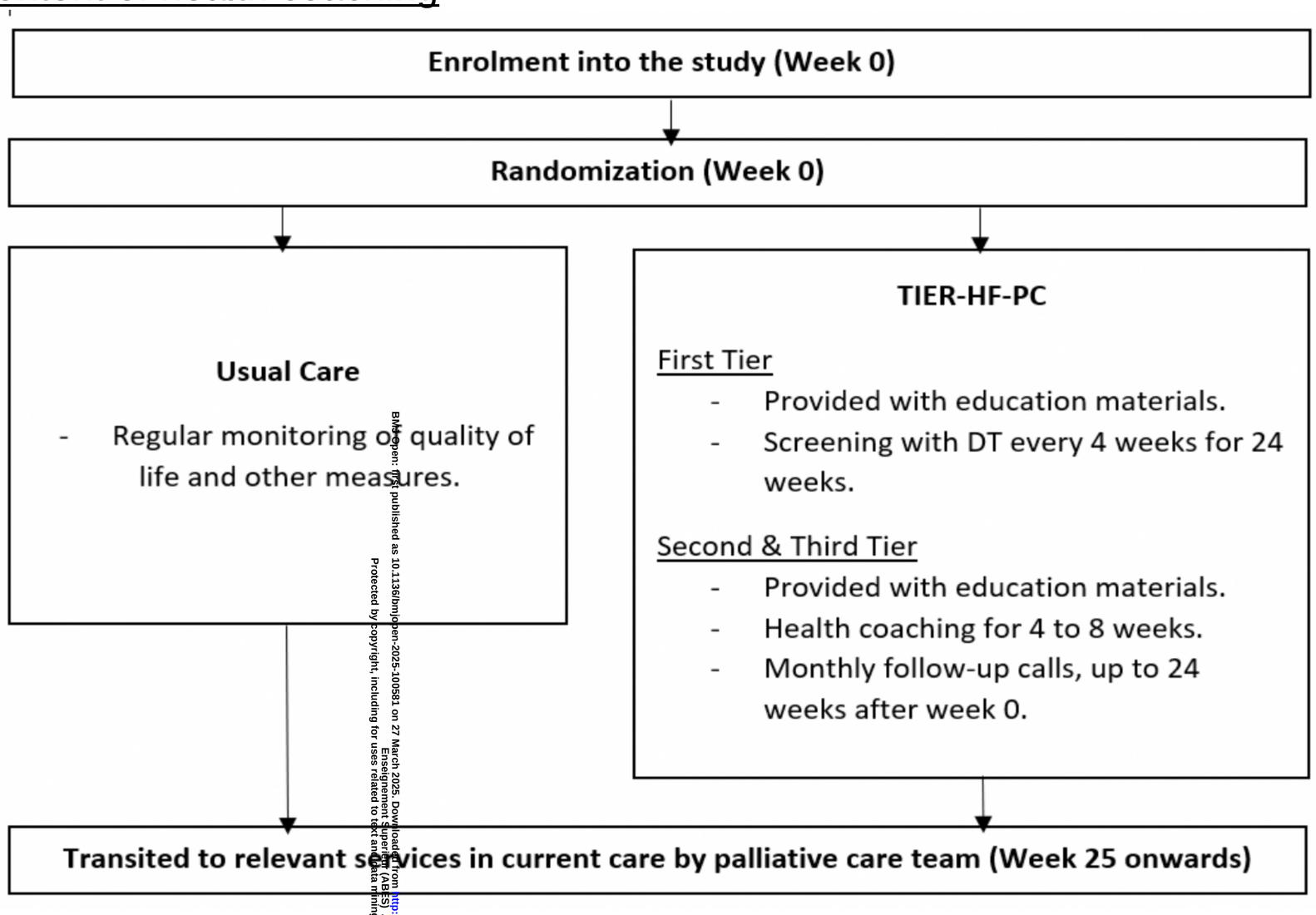
You will be given educational resources, either hard copy or soft copy, by the palliative care team. You will continue to be screened every 4 weeks, for a total period of 24 weeks from baseline, using the DT. You will be escalated up the tiers according to your love ones' DT scores.

- Second and Third tier

You will be given educational resources, either hard copy or soft copy, by the palliative care team. The palliative care team will start health coaching with you and your loved ones within 1 week of DT screening. Each health coaching session is expected to last about 1 hour over a period of 4 to 8 weeks. After completion of health coaching, you will receive monthly follow-up calls, up to 24 weeks after baseline, to check in on your concerns and reinforce skills taught during coaching. If you are in the second tier, you may be escalated up the tier according to the team's assessment of your loved one's concerns.

Participants in all 3 tiers will be transited by the palliative care team to relevant services in current care after week 48.

Content of health coaching



A structured manual for health coaching will be used. The culturally adapted topics of are "maintaining

positivity and problem solving", "self-care", "coping with stress and spirituality", "being a partner in managing symptoms" will be coached. The sequence of the topics will be individualized, based upon participant's requests.

Questionnaire/ interview:

We will ask you to complete questionnaires about your quality of life, psycho-emotional status, coping methods, spirituality, and satisfaction with care, through your preferred medium (either hardcopy or softcopy).

"Usual care" arm

At week 0, 8, 16, 24, 32 and every 8 weeks after till week 48 the study team member would follow-up with you to complete the questionnaire.

"TIER-HF-PC" arm

You will have to complete some survey at week 0, 8, 16, 24, 25, 32 and every 8 weeks after till week 48.

After week 25, you will be invited to participate in a semi-structured interview to share about your experience and feedback about the intervention. The semi-structured interview will be conducted through your preferred medium (either face-to-face, phone call or video conferencing) at a mutually agreed time and date. Audio-recording of the interviews will be mandatory for the purpose of analysing the interviews.

	Week 0, Week 8, Week 16, Week 24	**Week 25 onwards**
TIER-HF-PC	SCQOL, Brief COPE, Facit-SP-12	Week 25: CSQ, semi-structured interviews. Week 32 and every 8 weeks after till week 48: SCQOL
Usual Care	SCQOL, Brief COPE, Facit-SP-12	Week 32 and every 8 weeks after till week 48: SCQOL

SCQOL: Singapore Caregiver Quality Of Life Survey
Brief COPE: abbreviated Coping Orientation to Problems Experienced Scale
Facit-SP-12: Functional Assessment of Chronic Illness Therapy-Spiritual Well-being Scale (12 items)
CSQ-4: Client Satisfaction Questionnaire (4 items)

Incidental Findings

Any individually-identifiable data obtained during the course of this study will be stored and analysed for the purposes of this study and will not be used for future biomedical research.

During the course of the study, there is a possibility that we might unintentionally come to know of new information about your/ your loved ones health condition from health screening, survey assessments etc. that is/are conducted as part of the study. These are called "incidental findings".

"Incidental findings" are findings that have potential health or reproductive importance to research participants like you/your loved ones and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study. These findings may affect your/ loved ones current or future life and/or health insurance coverage.

You will be asked to indicate whether you wish to be re-identified and notified in the case of a clinically significant incidental finding that is related to you/your child.

If you agree to be re-identified and notified, your study doctor/a qualified healthcare professional will explain the incidental finding to you/your child and discuss and advise you on the next steps to follow. For this purpose, please inform the Principal Investigator or any of

the study contact persons listed in this document whenever there are changes in your contact details. You may wish to do more tests and seek advice to confirm this incidental finding. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

4. Your Responsibilities in This Study

If you agree to participate in this study, you should follow the advice given to you by the study team undergo all the procedures that are outlined above.

5. What Is Not Standard Care or is Experimental in This Study

The study is being conducted because TIER-HF-PC is not yet proven to be a standard method of increasing access to palliative care for patients with heart failure and their caregivers. We hope that your participation will help us to determine the effectiveness of the TIER-HF-PC method.

6. Possible Risks and Side Effects

From questionnaires/ surveys/ interviews:

Some of the questions might make you feel uncomfortable or upset. You may refuse to answer any of the questions and/or take a break at any time during the study. Study procedures can also be stopped upon your request. The Principal Investigator will then be informed, and you will be offered a referral to the appropriate support.

Potential risk on personal privacy and confidentiality:

This study uses information that may affect your privacy. To protect your confidentiality, only a unique code will be used to identify data that we collected from you.

As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

For transcribing of the interviews, audio recording will be required. While we will protect your confidentiality to the best of our abilities, absolute confidentiality cannot be guaranteed. However, all data will be de-identified prior to analysis. We will also protect your data through the following ways:

- Audio recordings and transcribes for the purpose of this research study will not be labelled with your name or identifiable information. Instead, a study ID will be used and assigned.
- Audio recordings and transcribes collected (which will eventually be deleted after the end of the study) will only be stored in devices with secured and restricted access. Access to data will also be limited.
- We will only report information in its aggregated form and will not identify the responses of any individuals.

7. Possible Benefits from Participating in the Study

There is no assurance you will benefit from this study. However, your participation may help to implement a better model of palliative and supportive care for heart failure patients and their caregivers. A better care model would also potentially lead to better outcomes for patients and caregivers through the heart failure journey.

8. Alternatives to Participation

There is no alternative to the study procedures. You can choose not to take part in this study. The study procedures will not be carried out.

9. Costs & Payments if Participating in the Study

There is no cost to you for participating in this research study.

Instead, you will be reimbursed for your time, inconvenience and transportation costs as follows:

- If you complete the intervention and all necessary procedures, you will be paid SGD40 in cash.
- Should you be selected and choose to participate in the interview after completing the intervention, you will be further reimbursed with SGD10 in cash upon completion of the interview.
- If you do not complete the study for any reason, you will not be reimbursed.

11. Voluntary Participation

Your participation in this study is voluntary. You may stop participating in this study at any time. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, the data that have been collected until the time of your withdrawal will be kept and analyzed. The reason is to enable a complete and comprehensive evaluation of the study. Your doctor, the Investigator and/or the Sponsor of this study may stop your participation in the study at any time if they decide that it is in your best interests. They may also do this if you do not follow instructions required to complete the study adequately. If you have other medical problems or side effects, the doctor and/or nurse will decide if you may continue in the research study.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legally acceptable representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative.

12. Compensation for Injury

If you follow the directions of the Principal Investigator of this research study and you are injured due to the research procedure given under the plan for the research study, our

institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

13. Confidentiality of Study and Medical Records

Your participation in this study will involve the collection of “Personal Data”. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. This includes medical conditions, medications, investigations and treatment history.

Information and “Personal Data” collected for this study will be kept confidential. Your records, to the extent of the applicable laws and regulations, will not be made publicly available.

However, the Sponsoring company (NMRC), Regulatory Agencies and NHG Domain Specific Review Board and Ministry of Health will be granted direct access to your original medical records to check study procedures and data, without making any of your information public. By signing the Informed Consent Form attached, you (or your legally acceptable representative, if relevant) are authorising (i) the collection, access to, use and storage of your “Personal Data”, and (ii) the disclosure to authorised service providers and relevant third parties.

Data collected and entered into the Case Report Forms are the property of NHG. In the event of any publication regarding this study, your identity will remain confidential.

Research arising in the future, based on your “Personal Data”, will be subject to review by the relevant institutional review board.

By participating in this research study, you are confirming that you have read, understood and consent to the Personal Data Protection Notification available at www.research.nhg.com.sg.

14. Who To Contact if You Have Questions

If you have questions about this research study, you may contact the Principal Investigator:
Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000

In case of any injuries during the course of this study, you may contact the Principal Investigator:
Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000

The study has been reviewed by the SingHealth Centralized Institutional Review Board for ethics approval. This approval is mutually recognized by NHG Domain Specific Review Board (DSRB).

If you want an independent opinion to discuss problems and questions, obtain information and offer inputs on your rights as a research subject, you may contact the NHG Domain

Specific Review Board Secretariat at 6471-3266. You can also find more information about participating in clinical research, the NHG Domain Specific Review Board and its review processes at www.research.nhg.com.sg.

If you have any complaints or feedback about this research study, you may contact the Principal Investigator or the NHG Domain Specific Review Board Secretariat.

CONSENT FORM

Protocol Title:

Timely Interventions to Enable and Reach patients with Heart Failure, and their caregivers with Palliative Care (TIER-HF-PC).

Principal Investigator & Contact Details:

Dr Laurence Tan Lean Chi
Department of Geriatric Medicine
Institution Mainline: 6555 8000
Khoo Teck Puat Hospital, 90 Yishun Central, Singapore 768828

I voluntarily consent to take part in this research study. I have fully discussed and understood the purpose and procedures of this study. This study has been explained to me in a language that I understand. I have been given enough time to ask any questions that I have about the study, and all my questions have been answered to my satisfaction. I have also been informed and understood the alternative treatments or procedures available and their possible benefits and risks.

By participating in this research study, I confirm that I have read, understood and consent to the NHG Personal Data Protection Notification.

Consent to be Re-Identified and Notified in the Case of an Incidental Finding

☐ Yes, I agree to be re-identified and notified in the case of an incidental finding from this research.

In the event that I cannot be reached, please contact my next of kin

Name of next of kin:
Contact:

☐ No, I do not agree to be re-identified and notified in the case of an incidental finding from this research.

Name of Participant	Signature	Date

Translator Information

The study has been explained to the participant / legally acceptable representative in

_____ _____ by _____ _____

(Language)_ (Name of Translator)

Witness Statement

I, the undersigned, certify that:

- ☐ I am 21 years of age or older.
- ☐ To the best of my knowledge, the participant/ the participant's legally acceptable representative signing this informed consent form has the study fully explained in a language understood by him/ her and clearly understands the nature, risks and benefits of his/ her participation in the study.
- ☐ I have taken reasonable steps to ascertain the identity of the participant/ the participant's legally acceptable representative giving the consent.
- ☐ I have taken steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Name of Witness	Signature	Date

1. In accordance with Section 6(d) of the Human Biomedical Research Act and Regulation 25 of the Human Biomedical Research Regulations 2017, appropriate consent must be obtained in the presence of a prescribed witness who is 21 years of age or older, and has mental capacity. The witness must be present during the entire informed consent discussion, and must not be the same person taking the appropriate consent. The witness may be a member of the team carrying out the research.
2. However, if the participant/ the participant's legally acceptable representative is unable to read, and/ or sign and date on the consent form, an impartial witness should be present instead. The impartial witness should not be a member of the study team.

Investigator Statement

I, the undersigned, certify that I explained the study to the participant and to the best of my knowledge the participant signing this informed consent form clearly understands the nature, risks and benefits of his/ her participation in the study.

Name of Investigator / Person administering consent	Signature	Date

The Parties (Investigator, Participant / Legally Authorised Representative & Witness) may execute this Informed Consent Form requiring a party's signature by using electronic signature process (e.g. by DocuSign, E-signature by Adobe Sign etc) and agree that signatures obtained or transmitted through electronic means, including the

abovementioned signature process, shall be binding and effective for all purposes as if the signatures were executed in-person.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1 of title page
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Cover letter to editor, page18 of manuscript
	2b	All items from the World Health Organization Trial Registration Data Set	Page 2 of title page
Protocol version	3	Date and version identifier	Page 18 of manuscript
Funding	4	Sources and types of financial, material, and other support	page 18 of manuscript
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	title page
	5b	Name and contact information for the trial sponsor	page 18 of manuscript
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	page 18 of manuscript

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Methods, page 15 of manuscript
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Introduction, page 3 of manuscript
	6b	Explanation for choice of comparators	Methods, page 7 of manuscript
Objectives	7	Specific objectives or hypotheses	Introduction, page 5 of manuscript
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Methods, page 5 of manuscript
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Methods, page 5 of manuscript
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Methods, page 6 of manuscript
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Methods, page 7-9 of manuscript
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Methods, page 16 of manuscript

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Methods, page 15 of manuscript
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Methods, page 7 of manuscript
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Methods, page 10-11 of manuscript
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Methods, page 11-12 of manuscript
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Methods, page 15 of manuscript
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Methods, page 6 of manuscript
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Methods, page 7 of manuscript
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Methods, page 7 of manuscript
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	_methods page 7 of manuscript

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Methods page 7 of manuscript
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Not applicable
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Methods page 9-11 of manuscript
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Methods page 15 of manuscript
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Methods page 15 of manuscript
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Methods page 12-13 of manuscript
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Methods page 12-13 of manuscript
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	methods page 12-13 of manuscript
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	methods page 15 of manuscript

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Methods page 12 of manuscript
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Methods page 16 of manuscript
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Methods page 15 of manuscript
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Methods page 16 of manuscript
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Manuscript page 18 of manuscript
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Manuscript page 18 of manuscript
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Methods page 11 of manuscript
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Manuscript page 18 of manuscript
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Methods page 16 of manuscript
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Methods page 9 of manuscript

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Other information, Manuscript page 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	Title page
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset and statistical code	Manuscript page 18
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Attached.
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Not applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.