**WA HEALTH RESEARCH PROTOCOL**

**TEMPLATE FOR NONCLINICAL TRIALS**

This protocol template is provided as a guide for investigators who do not already have a protocol for their research project. It is a requirement of WA Health that a protocol is submitted with the ethics application. This template is based on the Therapeutic Goods Administration (TGA) [“Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)” 2000](http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm) and the World Health Organisation [“Recommended format for a Research Protocol”](http://www.who.int/rpc/research_ethics/format_rp/en/index.html). To meet Good Clinical Practice Guidelines the Protocol should contain, but not be restricted to, the information contained within this template.

Projects not classified as Clinical Trials may include recruitment and procedures conducted on human participants, which may or may not involve an intervention, but will generally not involve assessments of the efficacy/safety of drugs or other therapeutic or investigational products (including medical devices).

Some Heath Service Providers provide access to statistical advice for investigators. Contact the relevant Research Governance Office for further advice; contact details are available on the Research Governance Service website.

This first page is for information only and should be replaced with the cover page of your document, the current title WA HEALTH RESEARCH PROTOCOL TEMPLATE FOR NONCLINICAL TRIALS should be replaced with the name of the project, with the version and date. These guidelines should be before the document is submitted for review.

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| Project Details |
| **Protocol/Research Project Title:** | Primary Care Adherence To Heart Failure guidelines IN Diagnosis, Evaluation & Routine management (PATHFINDER) Study |
| **Protocol Number (Version and Date):** | Version 3.1, 04/04/2022 |
| **Amendment** **(Number and Date):** |  |
| **Project Start Date:** | March 2020 | **Project Finish Date:** | July 1, 2024 |
| **Coordinating Principal Investigator Name:** | Associate Professor Andrew Maiorana |
| **Coordinating Principal Investigator Contact Details:** | Email: Andrew.Maiorana@health.wa.gov.auPhone: 0433567369Mailing Address: Advanced Heart Failure and Cardiac Transplant Service Ground floor, Clinic 9A, 11 Robin Warren Drive, MURDOCH WA 6150 Postal address: Locked Bag 100, PALMYRA DC WA 6961  |
| **Sponsor Name (if applicable):** | WA Health Translation Network through grant administered through FSH |
| **Laboratory Name (if applicable):** |  |

## Project Summary

There will be 3 phases to this project. We have described the project across the three phases to provide context of the overall project. Some aspects, including the detail in Phase 3 may change based on the outcomes of Phase 1 and 2 and if this occurs we will notify the Committee by way of an amendment during the course of the project.

**Phase 1: Audit of current practice**
This will involve an audit of discharge information from the hospital sites, and in collaboration with our research partner in the Western Australian Primary Health Alliance (WAPHA), an audit of the management of CHF patients in primary care. These audits will provide detailed information about current practice in relation to CHF management.

**Phase 2: Engage with key stakeholders including clinicians (medical and non-medical in tertiary and primary care), consumers, health service providers and policy makers**
We will conduct deliberative forums, focus groups and interviews to get input from key stakeholders to inform the development of the PATHFINDER intervention. The objective of the PATHFINDER intervention is to tailor information on medication titration, multidisciplinary care and self-management to individual CHF patients at the time of hospital discharge.

**Phase 3: Implement and evaluate PATHFINDER compared with usual care**
We will conduct a pilot study of the PATHFINDER intervention through follow up of patients admitted to FSH initially, and subsequently RPH, as the project is scaled-up.

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| Rationale / Background |

**Background**

Chronic heart failure (CHF) is the common end stage of cardiovascular disease and a leading cause of morbidity and mortality in Australia and worldwide.(1, 2) In Australia, the prevalence of CHF is estimated to be 2.1%, equating to approximately 480, 000 people with the condition.(1) Whilst there are currently no data relating to CHF incidence in Australia, it is anticipated that the prevalence of CHF will increase markedly in Australia over the next 20 years due largely to an ageing demographic.(3, 4)

High rates of hospitalisation remain a hallmark of CHF. Within 30 days of a ***de novo*** CHF admission, 1/3 of patients are readmitted to hospital and, on average, a patient will experience three additional hospital admissions over a year.(5) This results in approximately 158,000 admissions per year, totally 1.1 million days of hospitalisation and $2 billion in hospital care.(5) Even poorer clinical outcomes occur among the population who live in rural and remote areas, with a higher risk of 30-day death (Odds Ratio 1.16) and 1-year death in 30-day survivors (Hazard Ratio 1.11), even after controlling for socioeconomic status, Aboriginality, private insurance status and risk factors.(6) It is telling that patients with CHF experience overall survival worse than non-haematological malignancies.(6, 7) However, many of these admissions are preventable with improved adherence to guideline-advocated care, such as increased adherence to evidence-based pharmacological therapy, better non-pharmacological management (including self-management by patients), and improved medical surveillance.(4)

In Australia, many patients with CHF are managed in primary care, especially older patients, those from lower socio-economic backgrounds, individuals living in regional and remote locations and Aboriginal people. Many patients with CHF are managed primarily by their General Practitioner (GP), however adherence to CHF management guidelines is often suboptimal, a factor that is likely to contribute to the high rates of preventable hospitalisations.

In addition to the health impact, CHF results in a significant economic burden to society, encompassing $867 million in community care and $1.82 billion in hospital care.(1) It is predicted that the annual health care cost will reach $3.8 billion within ten to fifteen years,(1) highlighting the importance of new approaches to improve CHF management across the Australian healthcare landscape.

***What is contemporary guideline-advocated HF-management?***

The following guideline-directed strategies are crucial to decrease hospitalisations for CHF:

*Optimal pharmacological therapy*:

For patients with moderate to severe CHF, ACE inhibitors, beta blockers and low-dose mineralocorticoid receptor antagonists (MRA) have all been shown to improve survival and decrease hospitalisations. An angiotensin receptor blocker (ARB) is recommended in patients in whom ACE inhibitors are contraindicated or who are intolerant.(9-11)

A recent recommendation for selected patients with moderate to severe CHF, is replacing the ACE inhibitor or ARB to a low or moderate dose of an angiotensin receptor neprilysin inhibitor (ARNI) (sacubitril-valsartan).(4) This recommendation is based on the findings of the PARADIGM-HF study which found that ARNI, can improve survival and decrease hospitalisation compared with an ACE inhibitor (enalapril). (12)

Ivabradine should also be considered in patients with moderate to severe CHF and with a sinus rate of 70 bpm and above, despite receiving maximally tolerated or target doses of an ACE inhibitor (or ARB) and a beta blocker, with or without an MRA, to decrease the combined endpoint of cardiovascular mortality and hospitalisation for heart failure.(4) Other medications, such as hydralazine plus nitrates and digoxin may also be beneficial to reducing hospitalisations in subgroups of patients with CHF, but the evidence is less definitive.(4)

A diuretic should be considered in patients with CHF and clinical symptoms, or signs of congestion, to improve symptoms and manage congestion. However, diuretics may have an adverse effect on electrolyte balance and renal function so regular review to ensure adequate management of congestion and avoidance of over-diuresis is important. Diuretics should be started at low dose and treatment adjusted according to fluid volume status and biochemistry (renal function, sodium and potassium). Once a euvolaemic state has been achieved, physicians should aim to decrease the dose unless this has previously resulted in exacerbation of CHF. Patients may also be educated to adjust the dose of diuretic (e.g., increase frusemide dose by 40 mg daily if weight increases over 2 kg).

Medications are typically commenced at the time of hospitalisation and titrated to optimal dose in primary care. However, GPs are often reluctant to change CHF medication commenced in hospital and some find it challenging to achieve the balance between optimum dose and symptom management.(13) This can be improved with medication titration plans.(14) A study to improve medication titration found that patients were more likely to achieve target doses of ACEI/ARB and beta blockers within six months if they received a structured CHF medication titration plan.(14)

*Discharge planning*

Discharge planning plays a key role in optimising patient management after discharge to provide a seamless transition of care from the hospital into the community. Discharge planning should commence early during a patients period of hospitalisation and involves referrals to CHF programs after discharge (when they exist), community services as appropriate, CHF exercise programs, early outpatient clinic appointments, and GP follow-up.

*Referral to Exercise Training Program*

The benefits of regular physical activity for patients with stable CHF have been highlighted,(4) and include improved quality of life, increased cardiorespiratory fitness and reduced symptoms of fatigue and dyspnea. The HF-ACTION trial involving 2331 patients concluded that the aerobic exercise training group had a 15% reduction in all-cause mortality and a decreased number of hospitalisations due to CHF, when compared with the usual care group, after adjusting for predetermined prognostic factors.(15)

*Patient self-management*

Educating patients about self-management, including adherence to fluid and salt restrictions, daily weight monitoring, and undertaking regular physical activity reduces the risk of CHF complications.(14) There is strong evidence supporting the benefits of educating patients and their caregivers about the self-management of CHF on reducing hospitalisations. A meta-analysis of 20 RCTs involving over 5600 patients found that self-management interventions significantly prolonged the time patients spent out of hospital.(16)

*Comorbidities and risk factors management of heart failure*

Patients with CHF experience a high rate of cardiac and non-cardiac comorbidities. Cardiac comorbidities include hypertension, coronary artery disease and angina, atrial fibrillation and non-cardiac comorbidities include diabetes, chronic obstructive pulmonary disease and asthma, sleep-disordered breathing, gout, arthritis, depression, anemia and iron deficiency.(4) It is important to recognize and treat comorbidities among CHF patients to reduce readmission and mortality.

***Non-adherence-to-guideline advocated CHF-management in Australia***

The CHF Snapshot study revealed that evidence-based management strategies were underutilized in routine care resulting in suboptimal patient outcomes.(8) It was estimated that non-adherence to medication, dietary advice and fluid restrictions accounted for about one-fifth of hospitalisations due to CHF,(8) leading to a call for innovative management interventions to improve the uptake of evidence-based guidelines and decrease the high rates of non-adherence.(8)

CHF is a complex medical condition and management can be challenging. Best practice involves optimisation of medication, supporting the patient with self-management and linking them with appropriate multidisciplinary services. However for many patients this is not achieved.

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| Project Aims / Objectives / Hypotheses |

Detailed description of the specific primary and secondary objectives and the purpose of the project. Describe any hypotheses that will be tested.

The objective of the PATHFINDER project is to support patients and general practitioners in the adherence to evidence-based pharmacological and non-pharmacological therapy for the management of CHF in primary care, thereby reducing unnecessary, clinically detrimental and very costly hospital admissions. The study will be conducted in three phases. Firstly, the study will audit both discharge information provided following a hospital admission for CHF and subsequent adherence to CHF-management guidelines in primary care to get a clear indication of current practice. This is a unique approach as most guideline adherence studies have had an in-hospital focus alone, missing the opportunity to examine continuity of guideline adherence in general practice. In Phase 2, the study will conduct deliberative forums, interviews and focus groups with key stakeholders to acquire information which will be used to refine the PATHFINDER intervention. Finally, in Phase 3, we will apply the PATHFINDER intervention using a randomised controlled trial design. This will be piloted initially at Fiona Stanley Hospital (FSH), with Royal Perth Hospital (RPH) added as a secondary site during the course of the project. The aim will be to test an educational intervention (Heart Health Plan) delivered to participants and GPs aiming to improve CHF guideline adherence in primary care.

The specific aims of the project across the three phases are:

Phase 1 Aims:

1. To determine the comprehensiveness of discharge planning following a CHF admission to the research hospitals.
2. To determine the level of compliance with contemporary Australian guidelines by GPs in managing patients discharged from hospital following a CHF admission.

Phase 2 Aims:

1. To seek stakeholder input about the barriers and facilitators to managing patients with CHF in primary care, including potential solutions.

Phase 3 Aims:

1. To conduct a pilot randomised controlled trial to determine the efficacy of PATHFINDER on patient reported outcomes for CHF over a 6-month period.
2. Assess resource use, costs, and economic outcomes for PATHFINDER, versus usual care, to support further scale-up of this model of care.

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| Project Design |

***The scientific integrity of the project and the credibility of the project data depend substantially on the project design and methodology.***

## Project Design

Type (e.g. pilot, qualitative, quantitative) and design (e.g. observational, intervention) of the project to be conducted, including how the objectives (listed in 3.1) will be measured. If applicable, include a schematic diagram of the project design, procedures and stages.

**Phase 1**

***Aim 1:*** *To determine the comprehensiveness of discharge information following a CHF admission to the research hospitals.*

We will undertake an audit of discharge planning and processes from different wards (including Cardiology Wards and General Medical Wards) for patients admitted to the research hospitals with CHF. The audit will review discharge summaries to determine medication prescribed at discharge, whether a CHF Medication Titration Plan was provided, and details of patient educational resources, and follow-up appointments.

***Aim 2:*** *To determine the level of compliance with contemporary Australian guidelines by GPs in managing patients discharged from hospital following a heart failure admission*

We will undertake a GP CHF management audit by utilizing our GP research networks and partnerships with Primary Health Networks. The audit will provide detailed information about the adherence to guidelines in contemporary general practice. Currently we have no mechanism to determine whether the current Cardiac Society of Australia and New Zealand/National Heart Foundation CHF guidelines (4) are being adopted in the community setting and this audit will provide a “benchmark” from which improvement or deterioration in community-based HF management can be determined.

**Phase 2.**

***Aim 3.*** *To seek stakeholder input about the barriers and facilitators to managing patients with CHF in primary care, including potential solutions.*

This phase will help refine the PATHFINDER intervention to support both patients and GPs in guideline-advocated management of CHF. This will involve engagement with relevant stakeholders (clinicians, consumers, policy makers and health service providers).

**Phase 3:**

***Aim 4:*** *To conduct a pilot randomised controlled trial to determine the effectiveness of PATHFINDER over 6 months.*

***Study Design:***We will conduct a pilot randomised controlled trial of the implementation of PATHFINDER for patients admitted to FSH and RPH.

Two hundred patients with CHF will be randomised to receive the PATHFINDER Heart Health Plan or control (usual care). For the PATHFINDER group, the project’s Nurse Practitioner (NP) will help facilitate the transition from tertiary to primary care including a Heart Health Plan, and be a point of contact for GPs needing support for medication titration. Referrals for a cardiac rehabilitation program or exercise training program will be facilitated by the NP, with input from other Allied Health Professionals. Complex issues will be triaged for cardiologist support through the Advanced Heart Failure and Cardiac Transplant Service (FSH).

## Source and Selection of Participants

Source of participants, datasets or collections - research population, sample size, source, and sampling frame (if possible, split by site if multicentre project). For further information refer to NHMRC ["National Statement on Ethical Conduct in Human Research" 2007 (updated 2018)](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research)

**Phase 1**

***Aim :***

100 patients with a CHF diagnosis on discharge, at Fiona Stanley Hospital (FSH) and Royal Perth Hospital within the past 12 months (most recent admission for those with multiple readmissions) will be evaluated.

Aim 2:

GP HF Management audits will be conducted in metropolitan and regional practices in Western Australia. Utilising our collaboration with the WA Primary Health Networks 40 GPs will be recruited to the audit for a total of 200 patient cases (5 cases per GP).

**Phase 2:**

This phase will involve engagement with relevant stakeholders including cardiologists, nurses, and allied health professionals involved in providing services to patients with CHF, consumers with lived experience of CHF and their carers, health policy and service provider managers through deliberative forums, focus groups and interviews.

**Phase 3:**

*Patients:* Eligible participants will include patients discharged from FSH or RPH following a discharge diagnosis of CHF.

## Participant inclusion criteria.

**Phase 1**: Patients with a CHF discharge diagnosis at Fiona Stanley Hospital (FSH) or Royal Perth Hospital within the past 12 months (most recent admission for those with multiple –readmissions).

**Phase 2**: The broad inclusion criteria is clinicians providing services to patients with CHF, patients with CHF and their carers, and health policy and service provider managers

**Phase 3:** Patients: Inclusion criteria include men and women over the age of 18 years with a diagnosis of Heart Failure with reduced Ejection Fraction (HFrEF),with left ventricular ejection fraction less than 50%; life expectancy expected more than 6 months for conditions other than CHF; able to identify provide contact details of a primary care general practitioner, willing to provide written informed consent.

## Participant exclusion criteria.

Phase 1: NA

Phase 2: NA

Phase 3:

Patients: Exclusion criteria: Patients attending the Advanced Heart Failure Service (FSH), patients who need palliative care, nursing homes/assisted living residents; impaired cognitive function; patients with end-stage renal failure (eGFR <15 ml/min per 1.73 m2).

## Participant withdrawal criteria

Participant withdrawal criteria and procedures specifying (if applicable):

This question is not relevant to Phases 1 and 2. For Phase 3:

1. When and how to withdraw participants from the project;
* Participants will be able to withdraw of their own volition at any time without prejudice. This will be done by giving verbal or written notice.
1. The type and timing of the data to be collected for withdrawn participant(s);
* Phase 3 - We will apply an intention to treat analysis so will collect all available data for withdrawn participants.
1. Whether and how participants are to be replaced;
* Participants who withdraw will be replaced to maintain the desired sample size.
1. Follow-up for participants withdrawn from the project:
* Participants will be given the opportunity to attend follow-up assessments after they withdraw, but this will be entirely at their discretion.

## Bias

Measures taken to minimise/avoid bias, including randomisation and blinding.

Phase 3: Randomisation will be applied. Researchers undertaking analysis of data will be blinded to group allocation

## Blinding and Randomisation

Maintenance of any blinding records or randomisation codes and procedures for breaking codes.

Phase 3: Randomisation will be applied. Researchers undertaking analysis of data will be blinded to group allocation.

## Method

Methods to be used for the project, including justifications for interventions, procedures, measurements, observations, laboratory investigations.

**Phase 1:**

1. ***Discharge Planning Audit***

Discharge planning will be audited for patients with a CHF diagnoses and discharged form either Fiona Stanley Hospital (FSH) or Royal Perth Hospital within the past 12 months (most recent admission for those with multiple –readmissions).

**Methods:**

***Data Management and Sample Size and Analysis:*** Discharge planning will be audited for 100 consecutive patients discharged from cardiology wards and 100 consecutive patients for general medical wards, discharged between 1st January 2019 and 30th December 2019 using a Heart Failure Admission and Discharge Audit Form. The audit will involve a review of discharge summaries and medical records (BOSNET). De-identified data will be collected on a case record form as source data and transferred to a secure web-based data collection system. Analysis will be reported on a hospital level in terms of proportion of patients whose management aligns to current management guidelines on a categorical scale according to the proportion of guideline recommendations achieved per patient.

1. ***GP Management Audit***

***Methods:*** GP heart failure management audits will be conducted in metropolitan and regional practices in Western Australia. Utilising our GP networks established through our Primary Health Partner links, 40 general practitioners will be recruited to the audit. Once a GP has agreed to participate in the audit program, a researcher will visit the practice and identify through GP electronic medical records, all patients identified as having a HF hospitalisation within the past 12 months. Preliminary data from our general practice record searches suggests 5 patients from a practice with a CHF admission over the past 12 months is common.

Data will be collected from each participant record in the GP Heart Failure Case Management Form

***Data Management and Sample Size and Analysis:*** All data will be collected on a case record form as source data and transferred to a secure web-based data collection system. We plan to recruit 200 patients Analysis will be reported on a practice level in terms of proportion of patients whose management aligns to current management guidelines on a categorical scale according to the proportion of guideline recommendations achieved per patient.

**Phase 2:**

This phase will involve the engaging with stakeholders to refine the PATHFINDER intervention to support both patients and GPs in guideline-advocated management of CHF. The deliberative forums involving stakeholders will help inform the individualised “Heart Health Plan” to support guideline-advocated care.

**Phase 3:**

Two hundred patients with CHF and reduced ejection fraction will be randomised to the PATHFINDER intervention, or control. For the PATHFINDER group, the project’s Nurse Practitioner (NP) will help facilitate the transition from tertiary to primary care including the provision of the “Heart Health Plan”, and be a point of contact for GPs needing support for medication titration. Complex issues will be triaged for cardiologist support through the Advanced Heart Failure Service (FSH).

***Randomisation*:** 200 CHF patients will be randomised to PATHFINDER or control.

***Subjects*:**

*Patients:* Eligible participants will include patients discharged from FSH or RPH following a discharge diagnosis of HFrEF. Inclusion criteria include men and women over the age of 18 years, able to identify provide contact details of a primary care general practitioner, with LVEF < 50%; life expectancy expected more than 6 months for conditions other than CHF willing to provide written informed consent. Exclusion criteria: advanced heart failure, patients who needs heart failure palliative care, nursing homes/assisted living residents; impaired cognitive function; patients with end-stage renal failure (eGFR <15 ml/min per 1.73 m2.

***Intervention****:*

The PATHFINDER intervention will be centred around the “Heart Health Plan”;

Discharge planning:

* For participants this will include information and resources to support self-management.
* Participants will receive HF education from a heart failure nurse practitioner (HF NP)
* Participants will be referred to cardiac rehabilitation program (facilitated by HF NP)
* GP follow-up appointments will be suggested by NP at 1 week, 4 weeks, 3 months post-discharge. If participants do not receive optimal HF medications and are still symptomatic after 3 months post-discharge, more frequent GP follow-up will be suggested between M3 and M6.

Post-discharge: GP support

GPs will be provided with PATHFINDER study forms via the participant for post-discharge HF follow-up. These forms consist of a HF medication titration plan, guidance on lab tests and a HF medication titration problem solving guide. GPs will be asked to return the completed form to the study’s HF NP. If the GP requires further guidance in any aspect of care, they can contact the NP who will provide guidance that is within their scope of practice, or escalate the request to a cardiologist for more complex cases.

The Usual Care (Control) Group will receive standard inpatient and outpatient care, without additional heart failure management support being provided to either the patient or the GP. The Control group will be contacted by phone at 1 week, 4 weeks and 3 months to ascertain the dose and frequency of their HF medication at this time.

Assessments:

1. **Primary:** Proportion of patients adhering to guideline-recommended treatment at 6 months following index discharge.

-Participants receiving 5 out of 5 guideline-recommended treatments if indicated amongst eligible patients (4)

1. Either reaching 50% of the recommended dose for ACEI/ARB/ARNI or documentation that such a dose was not tolerated or otherwise inappropriate.
2. Either reaching 50% of the recommended dose for beta-blocker or documenting that such a dose was not tolerated or otherwise inappropriate.
3. Receiving MRA at 6 months following index discharge.
4. For patients with atrial fibrillation, receiving anticoagulation.
5. Referral to an exercise training program or cardiac rehabilitation program.
6. **Secondary:**
7. Six minute walk test distance (baseline and 6 months post-discharge)
8. Proportion of patients receiving each guideline-recommended treatment independently (6 months post-discharge)
9. Proportion of patients prescribed of ACEI/ARB/ARNI, beta-blocker, and MRA at the target dose or maximum tolerated dose (6 months post-discharge)
10. Proportion of patients receiving any dose of each HF medication (ACEI/ARB/ARNI, beta-blocker, MRA) independently (1 week, 4 weeks, 3 months and 6 months post-discharge )
11. Proportion of patients reaching 50% of the target dose of each HF medication (ACEI/ARB/ARNI, beta-blocker, MRA) independently (1week, 4 weeks, 3 months and 6 months post-discharge )

f. Exercise training program or cardiac rehabilitation program adherence (proportion of patient’s attending ≥16 sessions) (by 6 months post-discharge)

g. Kansas City Cardiomyopathy Questionnaire-short version (KCCQ12) (baseline and 6 month post-discharge)

h. PROMIS Physical Function Short Form 4a, Patient Health Questionnaire (PHQ-2) (6 months post-discharge)

i. Patient Health Questionnaire (PHQ-2) (baseline and 6 months post-discharge)

j. Self-care of Heart Failure Index (6 months post-discharge)

k. Medication Compliance Questionnaire (baseline and 6 months post-discharge)

All direct costs associated with PATHFINDER implementation and health care costs attributed to participants in the interventional and control groups will be collected. Administrative costs will be ascertained though the use of published costs of medicines, and costs listed as part of the hospital DRG codes. Cost effectiveness will be determined through the comparison of quality adjusted life years between treatment and usual care.

***Clinical outcomes***

* Numbers of re-admission to hospital and length of stay
* All-cause mortality

Deaths will be determined following the six-month follow-up and death certification will be sourced from GP records. Cause of death will be classified including death due to heart failure.

Hospital re-admissions will be sourced directly from participating hospital records (i.e. identifying participants who were hospitalised at the hospital from which they entered the study) and from broader state-based hospital admission systems.

***Implementation Outcome Measures***: - The RE-AIM (Reach Effectiveness Adoption Implementation Maintenance) evaluation framework will be utilised to measure acceptability, appropriateness, feasibility, sustainability and costs of implementation as part of project evaluation and to help inform scale-up for a subsequent definitive trial

## Project Duration/Schedule

Expected duration of the project, and a description of the sequence and duration of all techniques or assessments to be performed, including follow-up (if applicable).

Phase 1: 2 months (April - May 2020)

Phase 2: 1 month (June 2020)

Phase 3: 3 years (July 2020 to July 2023)

## Project Termination

Criteria for the termination of the project (if applicable).

NA

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| Treatment of Participants |

## Description and justification for treatments, interventions or methods to be utilised

The treatments, interventions or methods to be utilised and the follow-up period for participants for each treatment group/arm of the project.

Phase 1 and Phase 2: NA

Phase 3: The intervention will be based on guideline-advocated management for CHF. Participants will be followed up over a period of 6 months.

## Permitted medications/treatments

The medications/treatments permitted (including rescue medication) and not permitted before and/or during the project.

The project will be undertaken with patient participants taking usual medication (as recommended by guidelines)

## Monitoring of participant compliance

The procedures for monitoring participant compliance (if applicable).

NA

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| Assessment of Efficacy |

## Outcomes

Specification of the efficacy parameters (if applicable).

NA

## Efficacy assessment

The methods and timing for assessing, recording, and analysing efficacy parameters (if applicable).

Potential efficacy of the intervention on improvement in exercise capacity (measured by six minute walk distance), quality of life (measured by KCQ12 and PHQ2), self-management (measured by the Self-care in Heart Failure Index), medication compliance and decrease in readmissions.

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| Assessment of Safety |

## Risks and Benefits

Summary of known and potential risks and benefits (including emotional trauma), if any, to research participants.

Phase 1: NA

Phase 2: Some patients or their carers may have experienced some trauma related to the management of the patients CHF. The surveys/focus groups may raise these issues for consumers involved. In the event that patients/their carers request counselling to address this, this will be offered through clinical psychology services at FSH.

Phase 3: Some participants may feel self-conscious about answering some of the questions in the questionnaires. However, responses won’t be available to anyone outside the research team and we will use a participant ID code rather than the participants name so their identity won’t appear on their responses. This will be clearly explained to participants.

## Safety

The procedures for assessing and responding to potential participant safety events.

While it is not anticipated that there will be any safety issues, should such an issue arise the study’s cardiologist at the hospital site will be notified, as will the participants GP. The precipitating factor will be identified and ceased or modified as clinically appropriate.

## Adverse events reporting

The procedures for eliciting reports of and for recording and reporting adverse events. Include definitions of adverse events. For further information on adverse events refer to the TGA [*“The Australian Clinical Trial Handbook” 2006.*](http://www.tga.gov.au/industry/clinical-trials-handbook.htm) and the NHMRC ["Safety monitoring and reporting in clinical trials involving therapeutic goods" 2016](https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods). It is useful to note that even administering a research questionnaire can have adverse effects on participants.

At each visit and phone contact, the researchers will collect information pertaining to unusual manifestations or adverse events (AEs) and will record them on the AE page of the Case Report Forms (CRFs) as described below:

* Subject and date
* Description of event
* Reporting source
* Duration
* Frequency
* Intensity
* Seriousness
* Action taken upon AE
* Outcome and sequalae if any
* Relationship to study intervention

## Follow-up of Adverse Events

The type and duration of the follow-up of participants after adverse events.

All AEs will be followed up until the outcome is resolved or stable. In case of AEs persisting beyond the trial termination, a follow up visit will be scheduled. If further analyses are required for the evaluation of a potential cause-effect relationship between study procedures and AE, all examinations and laboratory analyses will be documented in the CRF or in an attached file.

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| Data Management, Statistical Analysis and Record Keeping |

## Statistics and Interim Analysis

Description of the statistical methods to be employed, including timing of any planned interim analysis.

Phase 1: Descriptive statistics will be used to report the audit across the selected hospital and primary care sites.

Phase 2: A maximum variation sampling technique will be used to ensure a wide diversity of opinions. Grounded theory will be used to analyse the findings.

Phase 3: Outcomes will be assessed on an intention to treat basis using linear regression for the primary research hypothesis to estimate group differences and 95% confidence intervals (CI). Similar linear regression models will be used to estimate the intervention effect and corresponding 95%CI for secondary outcomes (physical activity, quality of life, readmission, vital status).

## Sample Size

If applicable, the number of participants planned to be enrolled (if possible, including number at each site). Document the reason for choice of sample size, including reflections on (or calculations of) the power of the project and clinical justification.

Phase 1: Hospital Discharge Audit: 100 patients from each of Cardiology and General Medical Wards.

GP Audit: 40 general practices to obtain a representative sample of 200 patient cases

Phase 2: We will aim to involve at least 30 individuals from stakeholder groups in the focus groups/deliberative forums.

Phase 3: 200 patients will be randomised (100 to each group). This will constitute pilot data for a larger multicentre trial.

## Study Power and Significance

The level of significance to be used.

A level of significance of P < 0.05 will be used across all phases

## Statistical plan deviations

Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in the protocol and/or in the final report, as appropriate). For further information refer to NHMRC ["Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods" 2018](https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods).

Any deviations from the original statistical plan will be described in the final report.

## Selection of participants for analyses

If applicable, the selection of participants to be included in the analyses (e.g. all randomised participants, all eligible participants, or all evaluable participants).

Phase 1: Hospital Discharge Audit: Consecutive patients from the start of January 2019 until the required sample is reached.

GP Audit: GP practices accepting an invitation to participate in the audit.

Phase 2: Volunteers from relevant stakeholder groups who accept our invitation to participate in the focus groups/deliberative forums.

Phase 3: All randomised participants (according to intention to treat)

## Data Management

Information on how data will be managed, including coding for computer analysis and data handling (collection, storage, maintenance, security and archiving). Include details regarding these processes if the data is sent off-site (e.g. encryption). For further information refer to NHRMC ["Management of Data and Information in Research" 2019](https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018)

Data collected from the study will be held at Fiona Stanley Hospital (FSH) and Curtin University. All patient information pertaining to the selection of participants will remain on FSH and RPH servers (i.e. the treating hospital). Upon receipt of consent to take part in the study, participants will be allocated a research code-number. Digital data will be stored on the Curtin Research Drive (R:Drive), a dedicated research drive with password protected access, backup and recovery capabilities. Hardcopies will be stored in locked filling cabinets and computer records will be maintained on password protected secure servers. All data management and disposal will be compliant with the WA Health data management policy.

1. Only authorised researchers will have access to the data. The CPI will only grant access to the project’s research data and primary materials in accordance with contractual obligations, confidentiality requirements, legislation, privacy rules and other guidelines.

ii. The study data will be retained a minimum of seven years after completion of the project or publication. Hard copies of material collected during the project, such as signed consent forms, the research protocol for the project, and subsequent electronic files will all be retained during this period.

iii. Disposal of research data and primary materials will be in accordance with the Information Management Policy of Curtin University. This process is as follows:

For authorisation:

* enter the required information into the Curtin Records and Information System (CRIS).
* Print one copy of the box summary sheet (to be placed inside the box).
* Forward to Curtin Information Management and Archives who will then review the information in CRIS.

After authorisation:

* Once authorised for destruction, hard copies will then be labelled, collected and transferred to Curtin Information Management and Archives for secure destruction. Electronic copies will be permanently deleted.

## Procedure for accounting for missing, unused, and spurious (*false*) data.

Procedure for accounting for missing, unused, and spurious (false) data.

In the case of missing or false data, efforts will be made to correct the information. If this is not possible, the data will be excluded from the study, and this will be described in the final report.

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| Monitoring / Audit |

## Monitoring, Audit and Regulatory Inspections Statement

Statement that the project investigators/institutions will permit project-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents. This may include, but not limited to, review by external sponsors, Human Research Ethics Committees and institutional governance review bodies.

The investigators agree to monitoring, audit and regulatory inspections in accordance with standard procedures.

## Procedures for Monitoring and auditing

Description of the procedures for monitoring and auditing. *The sponsor may nominate the form of monitoring and auditing and will indicate the times of audit visits.*

NA

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| Quality Control And Quality Assurance |

## Compliance statement

Statement that the project will be conducted in compliance with the protocol, Good Clinical Practice and the application regulatory requirements.

Trial investigators/institutions will permit trial-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents. This may include, but not limited to, review by external sponsors, Human Research Ethics Committees and institutional governance review bodies.

## Quality control

Quality control & quality assurance measures to ensure quality of data.

Data collected during Phase 3 will be monitored at regular intervals throughout the trial to ensure quality and fidelity of data.

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| Ethics |

Description of ethical considerations related to the project with particular reference to participant consent (including Participant Information and Consent Forms or waiver of consent, where relevant). For further information see NHMRC ["National Statement on Ethical Conduct in Human Research" 2007 (updated 2018)](https://www.nhmrc.gov.au/research-policy/ethics/national-statement-ethical-conduct-human-research)

Participants involved in Phase 2 and 3 of the trial will be required to provide written informed consent. PICFs have been submitted with this application.

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| Budget, Financing, Indemnity And Insurance |

Budget, financing, indemnity and insurance, if not addressed in a separate agreement.

The study has received a grant from the Western Australian Health Translation Network. Please refer to the budget form for further details.

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| Publication  |

Publication and dissemination of project results (including any limitations), if not addressed in a separate agreement.

Outcomes of this study will be presented at national and international conferences and published in peer-reviewed journals.

Reports will be written for the funder (WA Health Translation Network). Components of the project will contribute to a PhD thesis.

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| Appendices  |

1. Heart Failure Admission and Discharge Audit form
2. GP Heart Failure Case Management Form
3. Medication Titration Plan Form
4. Kansas City Cardiomyopathy Questionnaire-short version (KCCQ12)
5. PROMIS Physical Function Short Form 4a, Patient Health Questionnaire (PHQ-2)
6. Patient Health Questionnaire (PHQ-2)
7. Self-care of Heart Failure Index
8. Medication Compliance Questionnaire
9. Phase 3 master PICF ver 3 dated 11 Feb 2021
10. PATHFINDER study follow-up form GP visit 1 week, 4 weeks, 3 months ver 2 dated 11 Feb 2021
11. INFO PATHFINDER ver 2 dated 12 Feb 2021
12. Visit 1 baseline form ver 1 dated 6 Jan 2021
13. Assessment 2 6 month follow up form ver 1 dated 6 Jan 2021
14. Screening eligibility ver 1 dated 6 Jan 2021
15. Event capture form ver 1 dated 6 Jan 2021
16. PATHFINDER Medication Follow up ver 1 dated 11 Feb 2021
17. PATHFINDER patient-reported medication list ver 1 dated 11 Feb 2021